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Contact: 051- 4908582

Editor's Email

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AIMS & SCOPE

HMDJ is the journal of HITEC Institute of Medical Sciences (HITEC-IMS), Taxila. It is an open access, peer-reviewed, bi-annual journal that aims to keep the medical & dental health professionals updated with the latest information relevant to their fields.

HMDJ welcomes scholarly work from medical, dental and allied subjects (basic & clinical), community health issues and medical education. It publishes original research, review articles, case reports, editorials, letters to editor, short communication, book reviews, recent advances, new techniques, debates, adverse drug reports, current practices, and conference reports. All publications of HMDJ are peer reviewed by subject specialists from Pakistan and abroad.

OBJECTIVES

1. To publish original, peer reviewed clinical and basic sciences articles.
2. To promote research culture in HITEC-IMS and beyond, by inculcating the habit of medical writing in doctors.
3. To assist physicians to stay informed about the developments in their own & related fields.
4. To support knowledge & experience sharing among the health professionals for the benefit of the patients.
5. To attain top-notch ethical medical journalism by delivering credible and reader-friendly publications.

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EDITORIAL

PLAGIARISM- AN UNDERSTANDING

Hamid Shafiq[1]

[1]Principal HITEC-IMS (Medical College)

Academic research involves months and years of careful planning and hard work. Translating this research from bench to bedside gives a sense of thrill and satisfaction. It is essential to be completely honest while carrying out and publishing research. Deviations, also called scientific misconducts do occur during this process, and most common of these is plagiarism[1]. Plagiarism is derived from the Latin word "plagiarius", meaning a kidnapper, and the person who commits it is called a plagiarist[2,3]. Plagiarism is defined as "The use of another author's language, thoughts, ideas or expressions or the representation of them as one's original work without crediting the source"[4]. In easy words, it is "The practice of taking someone else's work or ideas and passing them as their own"[5]. Act of plagiarism goes back a long time in history and the first article on it was written by Halstead in "Science" in 1896, under the title "Complement or Plagiarism" [6] . Since then scores of articles have been published on the topic.

CAPSULE SUMMARY

Plagiarism is the most common type of misconduct in scientific writing and is defined as taking someone else's work or ideas and passing them as their own thus retarding progress. It carries serious penalties if proved. Plagiarism-free scientific writing is a shared responsibility of medical institutes initiating the scientific writings and the Journal editors who publish it.

Research has become a growing industry, and there is fierce competition to publish work. Researchers find themselves obliged to publish their work to get promotions or funds, to prove their academic competency, and to maintain their careers[7,8]. These pressures, coupled with a lack of time, research skills and ease of obtaining information from the internet, lead to intentional shortcuts and plagiarism. Although most researchers understand the obvious forms of plagiarism, there is a lack of clarity on the grey areas which is also a cause of plagiarism[9].

Around 23% of articles submitted for publication are rejected due to plagiarism [10] and its prevalence rate is reported to be between 11%-19% in different communities [11].

Plagiarism can occur in different forms, as depicted in (Table1). Whatever the type, plagiarism is divided into major and minor forms, depending upon the magnitude of the offence. Major forms include intentionally using large portions of another person's work and presenting it as one's own. In minor forms, insignificant parts of the text are not properly cited, which reflects academic immaturity. Plagiarism that is committed deliberately is a greater offence than when it is done unintentionally [2].

If this misconduct is detected before publication, the article is sent back to the author for making required changes or re-writing of the complete article. The penalties are different for different forms of plagiarism when it is detected after publication (Table 2). There are many examples where plagiarism has cost the authors their entire careers.

In the past, it was the responsibility of editors and reviewers, depending on their personal experience, to detect plagiarism. Recently, many software-based services for the detection of plagiarism are available. One free service is eTBLAST which is available on the website: http://etest.vbi.vt.edu/etblast3/. Another software is iThenticate, which offers options to filter direct quotations, bibliographies, and methodologies to minimize the chances of wrong reporting. Another paid tool is Turnitin plagiarism detection software. This is the most widely used software and is also used by our journal. There is no universally agreed percentage for similarity index to match over which plagiarism may be declared. However, most journals take a 20%-30% similarity as cut-off line[12,13]. The use of these software programs is not enough to make a decision, and the case must be taken in context.

The Higher Education Commission (HEC), Pakistan gave an anti-plagiarism Policy in 2007 and revised it in 2023. It allows a 19% overall similarity index and up to 5% similarity each in internet sources (Information available publicly), publications (Academic databases), and student-papers (Database of documents uploaded in Turnitin by Instructors or Students). Similarity with the student repositories may be ignored if the author is the principal investigator. The similarity index in the sections of results, conclusion, and recommendations should not be more than 9%, and these sections may be separately evaluated from the rest of the manuscript. The policy details all

Correspondence to: Maj Gen (R) Prof. Dr. Hamid Shafiq, HI(M)
Chief Editor HITEC Medical and Dental Journal

Email: hamidshafiq.amc@gmail.com

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aspects of Plagiarism[14].

In this era of artificial intelligence (AI), scientific medical manuscripts have been written using it. Moreover, software programs can rephrase the write-up by AI. If suspected, certain software can detect whether the paper is written by humans or by machines[1].

Production of plagiarism-free scientific writing is a shared responsibility of any medical institute. The recommendations given in Table 3 can help achieve this goal[3,13].

Publishing medical research is essential for increasing the knowledge of the medical community. Plagiarism is the most common problem in research writing and shakes the virtues of trust and honesty which are an integral part of such writings, creating an environment which retards scientific progress. It should be dealt with strictly at all levels and authors should be appropriately punished, to set an example in the scientific community and to discourage such behaviors.

Table 1: Types of Plagiarism

PLAGIARISM TYPES	
Depending upon intention	
Accidental (Unintentional)	Caused by a lack of awareness of limits of taking data and pieces of writing from another source
Deliberate (Intentional)	Intentionally copying other's work in any form
Depending upon nature of plagiarised material	
Plagiarism of Ideas	Conducting research on someone else idea without acknowledging it
Plagiarism of Text	Copy pasting or word to word writing
Patch working	Changing a few words of the copied work and presenting as one's own work
Mosaic Plagiarism	Using text from different sources and intertwining into one flow
Paraphrase Plagiarism	Rephrasing a text without proper attribution
Software based text modifications	Using softwares like text spinner to evade plagiarism
Self Plagiarism	When part an original work is used in different publications by the researcher without making a reference
Collusion plagiarism	Asking someone else to write an article and presenting as your own
Contract plagiarism	Paying someone else to write an article and presenting it as their own

Table 2: Penalties for Plagiarism

Severity of plagiarism	Penalties
Minor	• Letter of explanation
Major	• Formal letter to heads of institute of the plagiarist institution • Refusal of future submission from author • Refusal of future submission from institution • Reporting to Medical Council • Expulsion of authors/co authors from institute • Retraction of the article • Students i. Redo assignment/paper ii. Fail the assignment/paper iii. Redo class or degree iv. Fail the degree

Table 3: Recommendations for avoiding Plagiarism

Source credit (mentioning reference) should be given when another person's ideas, opinion, theory, facts, statistics, graphs or drawings are used in own research.
If exact words from the source are to be copied, then it should be between quotation marks "" followed by reference.
For copying scientific facts which are universal and cannot be changed, the text should be rewritten in author's own words followed by source crediting.
Obtain permission from the source article is large part of a previously published article needs to be included in the manuscript.
Use plagiarism software before submitting the manuscript.
The students and faculty within the institute should have enough knowledge about plagiarism, its forms, consequences and how to avoid committing it, and all institutes should provide training on how to write a scientific article without plagiarism.
For junior researchers, the article may be broken into small pieces, setting a deadline for each piece discussing with seniors at each stage.
"Publish or perish" leads to undue pressure and inadvertently to, plagiarism. Publishing should not be an academic promotion drive venture.

REFERENCES

1. Jitani A, Mandal PK, Jajodia E. Publication of medical research without plagiarism-How to achieve it? J Hematol Allied Sci.2023;3(3):88-92.
2. Berk RN. Is plagiarism ever in significant. Am J Roentgenol. 1991;157:614.
3. Mohammad RAA, Shaaban OM, Mahran DG et al. Plagiarism in medical scientific research. J Taibah Univ Med Sci. 2015;10(1): 6-11.
4. Merriam-Webster collegiate dictionary. 11th ed. Springfield (MA): Marriam Webster;2014.
5. Oxford English dictionary. 11 ed. Oxford(Oxon): Oxford University Press;2008.
6. Halstead GB. Compliment or Plagiarism. Science. 1896;4(102): 877-878.
7. Rawat S, Meena S . Publish or perish. Where are we heading? J Res Med Sci. 2014 ;19(2):87-89.
8. Neill US.Publish or parish, but at what cost. J Clin Investig. 2008 ; 118(7) : 2368.
9. Yi N, Nemery B, Dierickx K. Perceptions of plagiarism by biomedical researchers : an online survey in Europe and China. BMC Med Ethics. 2020;21:44-59.
10. Sophia L. Journal review process increasingly includes check for plagiarism. Chron High Educ.[Internet].2010 July 9[cited 2024 April 24]. Available from http://chronicle.com/blogs/ wiredcampus/journal-review-process-increasingly-includes-checkfor-plagiarism/25420.
11. Bazdaric K,Bilic-Zulle L, Brumini G, et al. Prevalence of plagiarism in recent submissions to Croatian Medical Journal. Sci Eng Ethics.2012;18(2):223-239.
12. White C. Plagiarism detection services to be launched in June. BMJ 2008;336(7648):797.
13. White SR. Murdoch-Eaton DG. Learning about Plagiarism using Turnitin detection software. Med Edu. 2008;42(5):528.
14. Anti Plagiarism policy (Version 2) August 2023[Internet]. Islamabad (ISL) : Higher Education Commission;[Cited 2024 Jun 24]. Available from https://www.hec.gov.pk/english/policies/Documents/Plagiarism-Policy.pdf.

ORIGINAL ARTICLE

DIAGNOSTIC ACCURACY OF CHEST X-RAY IN COVID-19 PATIENTS TAKING HIGH-RESOLUTION COMPUTED TOMOGRAPHY AS GOLD STANDARD

Uzma Abdullah[1], Nafeesa Tariq[2], Ayesha Rizwan[3], Arooj Zahra[4], Humaira Ali[5], Nain Sukh[6], Manahil Tipu[7], Amna Shoaib[8]

[1]Department of Radiology, Margalla Hospital, Taxila, [2]Department of Gynaecology and Obstetrics, Margalla Hospital, Taxila, [3]Department of Dermatology, Margalla Hospital, Taxila, [4]Department of Medicine, Margalla Hospital, Taxila, [5]Department of Anatomy, Swat Medical College, Swat, [6]Department of Surgery, Margalla Hospital, Taxila, [7]4th Year MBBS Student, Rawalpindi Medical University, Rawalpindi, [8]3rd Year MBBS Student, Al-Nafees Medical College, Islamabad

ABSTRACT

Objective: To determine sensitivity & specificity of chest X-ray in COVID-19, taking High-Resolution Computed Tomography as gold standard.

Study Design: Cross-sectional study.

Place and Duration of Study: Radiology Deptt, Margalla Hospital, Taxila and Islamabad Diagnostic Centre, Wah. Two years (February 2020 to February 2022).

Patients and Methods: The sample comprised 100 COVID-19 patients (Positive Polymerase chain reaction (PCR) test). Their High-Resolution Computed Tomography (HRCT) was done which was considered a gold standard for diagnosing COVID-19. Their Chest X-rays (CXR) were performed, and findings of both modalities were compared. Patients having respiratory tract symptoms but PCR negative for COVID-19 were excluded.

Results: The research had 49 males & 51 females having a median (IQR) age of 46.50(35-55.75) years. The minimum & maximum ages were 6 years and 83 years respectively. Among 100 PCR-positive patients, 29 were found normal on HRCT and 30 on CXR. For moderate cases, the chest X-rays were 72% sensitive & 90.67% specific, with Positive Predictive Value (PPV), Negative Predictive Value (NPV) & diagnostic efficacy of 72%,90.67% & 86% respectively. Similarly, other severity levels were assessed.

Conclusion: CXR has acceptable diagnostic accuracy for COVID-19 patients, especially with good sensitivity for moderate cases and better specificity for severe cases. A portable chest radiograph might be regarded as an initial alternative imaging modality for patients with COVID-19 signs and symptoms in remote areas.

Key words: *COVID-19, CXR , HRCT*

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INTRODUCTION

Coronavirus disease-19 (COVID-19) first surfaced in Wuhan, China, in 2019, and led to a pandemic, affecting many areas of the world [1]. The maximum number of casualties were observed in the United States and other parts of the world. It urged the medical community to develop and implement different diagnostic and therapeutic options to lessen the burden of this disease [2].

Correspondence to: Dr. Uzma Abdullah, Radiology Deptt, Margalla Hospital, PMO, Taxila.

Email: druzmaabdullah1@gmail.com

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Throughout the COVID-19 pandemic, global guidelines[3,4] have consistently stressed using viral testing to make the diagnosis instead of using imaging techniques. Real Time Polymerase Chain Reaction (RT-PCR) (throat or nasal swab) is recommended for diagnosis. This test presents a crucial aspect of triaging and monitoring patients suspected of having the virus[5]. However, the reliability of RT-PCR is limited, with sensitivity ranging between 38% and 89% [6,7,8]. Moreover, during the peak of pandemic, the time it took to receive RT-PCR results often prevented appropriate identification and treatment of affected patients who were continuously presenting in hospital emergencies on a large scale [9,10,11]. As a result, imaging was incorporated into the protocol used to diagnose patients to minimize the limitations of RT-PCR including the high probability of false negative results and increased turnaround time[4,12,13].

The development of RT-PCR was made possible by genetic

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sequencing of SARS-CoV-2, which is a gold standard for diagnosis today[14]. The high prevalence of false-negative results and the time it takes, make this serologic test limited. Therefore, it is necessary to perform radiological assessments in clinical-epidemiological suspicion of COVID-19, particularly in emergency, to evaluate the thoracic involvement, while RT-PCR result is awaited. The latest radiological research on COVID-19 primarily focuses on the findings of Computed Tomography (CT), which is superior to chest X-ray (CXR) in sensitivity and specificity. In China, CT is the primary diagnostic method for COVID-19 [15,16]. However, CT scans during this pandemic, present challenges, including excessive exposure to radiation (especially for younger patients), and the standard protocols for disinfecting scanners. Most Italian hospitals use CXR as their major diagnostic tool. It produces faster results than RT-PCR, particularly when employing portable X-ray machines. They minimise patient movement and lower the risk of cross-infection[17,18,19,20]. Our research was undertaken to find CXR's diagnostic accuracy in COVID-19, keeping the High resonance Computed Tomography (HRCT) as gold standard.

CAPSULE SUMMARY

This study reveals that chest X-ray has an acceptable sensitivity & specificity for RT-PCR-confirmed COVID-19 patients and can be regarded as an initial or alternate imaging modality in the protocol for patients in remote areas with signs and symptoms of COVID-19.

PATIENTS AND METHODS

A Cross-sectional, observational study was done in the Radiology Deptt, Margalla Hospital, Taxila in collaboration with Islamabad Diagnostic Centre, Wah. The research work started after the official approval of the Ethical Review Committee of Margalla Hospital. An informed, written consent for the study was taken from the patients. A total of 100 PCR-positive COVID-19 patients of either sex were included. Patients having respiratory symptoms but not having PCR-positive COVID-19 were excluded from the study. HRCT of all PCR-positive COVID-19 patients was done in Islamabad diagnostic centre, Wah, on Toshiba 16 slices CT scan machine. The radiologist reported HRCT and the CT, severity index was calculated for each case. CT severity score was considered mild if <20, moderate if 20-40 and severe if >40. It was requested of the reporting radiologists to check for septal thickening, consolidation, ground glass opacities and nodules. Additionally evaluated were the reverse halo sign and the existence of pleural effusions. The cases to score gradient/ diffuse involvement were additionally evaluated as craniocaudal, anterior/posterior & central/peripheral gradient.

The CXR of the same patients were performed by a portable Toshiba X-ray machine and were reported by the Radiologists. Based on opacities (interstitial, interstitial & airspace, peripheral & diffuse airspace), atelectasis, and lobar consolidation, the main pattern in chest radiographs was assessed, using the CXR. If no such pattern applied, the result was considered "normal." Pleural effusions and a craniocaudal gradient were also evaluated. The CXR findings were given four severity scores: normal, mild, moderate and severe.

A comparison of HRCT and CXR was done, to determine how sensitive & specific CXR is and what Positive Predictive Value(PPV), Negative Predictive Value (NPV) & diagnostic efficacy it has, taking HRCT as the gold standard. The patients having normal CXR & HRCT were labelled normal. Patients having the same degree of lesion on the CXR and HRCT were labelled true cases. Table 1 shows the rubrics used to check the diagnostic accuracy of CXR.

Formulae Used:

"Sensitivity" = a÷(a+c) x 100
"Specificity" = d÷(b+d) x 100
PPV = a÷ (a+b) x 100
NPV = d÷ (c+d) x 100
"Diagnostic Efficacy" = (a+d) ÷ (a+b+c+d) x 100

RESULTS

Total 49 males and 51 females participated in the study with the median (IQR) age of 46.50 (35-55.75) years. Patients' ages ranged from 6 to 83 years. Out of total of 100 PCR-positive patients, 29 were found normal on HRCT and 30 on CXR.

In mild cases, the sensitivity is 69.2%, the specificity is 87.8%, the positive predictive value is 66.7%, the negative predictive value is 89.04%, and the diagnostic efficacy is 83% (table 2).

In moderate cases, the sensitivity is 72%, the specificity is 90.67%, the positive predictive value is 72%, the negative predictive value is 90.67%, and the diagnostic efficacy is 86% (table 3).

In severe cases, sensitivity is 55%, specificity is 96.2%, PPV is 78.6 %, NPV is 89.5 and diagnostic efficacy is 88%. (Table 4)

Table 1. Rubrics to determine diagnostic accuracy of chest X-rays (CXR), using HRCT as the gold standard.

One severity lesion		Detected in HRCT (Gold Standard)	
		Other Severity levels including normal patients	
Detected in CXR	One severity lesion	a. True+ve	b. False +ve
	Other Severity levels including normal patients	c. False -ve	d. True-ve

Table 2. Sensitivity and specificity of mild cases of CXR, using HRCT as the gold standard (n=100).

		Detected in HRCT (Gold Standard)	
		Mild	Other severity levels
Detected in CXR	Mild	18	09
	Other severity levels	08	65

Table 3. Sensitivity and specificity of moderate cases of CXR, using HRCT as the gold standard (n=100).

		Detected in HRCT (Gold Standard)	
		Moderate	Other Severity levels
Detected in CXR	Moderate	18	07
	Other severity levels	07	68

Table 4. Sensitivity and specificity of severe cases of CXR, using HRCT as the gold standard (n=100).

		Detected in HRCT (Gold Standard)	
		Severe	Other Severity levels
Detected in CXR	Severe	11	03
	Other severity levels	09	77

DISCUSSION

In our study, the sensitivity (72%) of CXR increased in moderate cases while a high specificity (96.2%) was observed in patients with severe findings of COVID-19 considering HRCT as a gold standard. In another study conducted in 2020, CXR was found to be a useful portable device with an acceptable sensitivity (61%) and specificity (76%) to diagnose COVID-19 patients compared to RT-PCR [21].

Stephanie S., Shum T., Cleveland H., et al. conducted a retrospective analysis in 02 sizable urban medical academic centres, encompassing 03 tertiary care and 01 community hospital in the United States. According to the study, CXR severity and sensitivity for COVID-19 detection grew with time, rising from 55% at 2 days (or less) to 79% at more than 11 days ($p<0.001$), however, CXR specificity dropped from 83% to 70%($p=0.02$). For COVID-19 detection, the first CXR had 73% sensitivity and 80%specificity, the second CXR had 83% sensitivity and 73% specificity, and the CT had 88% sensitivity and 77% specificity. Most false negative CXRs (normal 40% & combined normal or mild 87%) were caused by normal & mild severity. The false-negative rate was also higher in young people and African Americans. With time, CXR accuracy for COVID-19 detection increases, and in patients who test positive for the virus, repeated CXRs are as accurate as chest CT scans[22].

A study by Borakati A, et al. found that CXR diagnosed COVID-19, with a sensitivity & specificity of 0.56 (with 95% CI 0.51 to 0.60) and 0.60 (with 95% CI 0.54 to 0.65) correspondingly. Whereas, CT, for the same diagnosis, was 0.85 in sensitivity (95% CI 0.79 to 0.90) & 0.50 in specificity (95% CI 0.41 - 0.60). Comparing CT to CXR, there was a statistically significant mean increase of 29% in sensitivity (95% CI 19% to 38%, $p<0.0001$). The two modalities did not significantly differ in terms of specificity[23].

Wong et al. found CT to have a higher sensitivity than CXR. The initial CXR's sensitivity of 69%, according to Wong et al., was much below the 97–98% sensitivity of CT [24].

Another study by Guan et al. also revealed that in order to detect opacifications in COVID-19 patients, CT had a much greater sensitivity (86.2%) than CXR (59.1%)[25].

CONCLUSION

Chest X-ray has an acceptable sensitivity & specificity for RT-PCR-confirmed COVID-19 patients, especially in patients having moderate and severe conditions respectively considering HRCT as the gold standard. Although CT chest is a superior imaging modality to CXR, a portable chest radiograph can evaluate the severity of the disease course and prognosis. It can be regarded as an initial or alternate imaging modality in the treatment protocol for patients in remote areas with signs and symptoms of COVID-19.

AUTHORS' CONTRIBUTION

Uzma Abdullah, Nafeesa Tariq, Arooj Zahra, Humaira Ali, Nain Sukh, Manahil Tipu, Amna Shoaib	Drafting the Article
Uzma Abdullah, Nafeesa Tariq, Ayesha Rizwan, Arooj Zahra, Humaira Ali, Nain Sukh, Manahil Tipu, Amna Shoaib	Analysis and interpretation of data
Uzma Abdullah	Conception and design
Uzma Abdullah, Ayesha Rizwan, Arooj Zahra	Acquisition of data
Uzma Abdullah	Critical revision

REFERENCES

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet. 2020;395(10223):497-506.
2. Sanders JM, Monogue ML, Jodlowski TZ, et al. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): a review. JAMA. 2020;323(18):1824-36.
3. Rubin GD, Ryerson CJ, Haramati LB, et al. The role of chest imaging in patient management during the COVID-19 pandemic: a multinational consensus statement from the Fleischner Society. Radiology. 2020;296(1):172-80.
4. Akl EA, Blažić I, Yaacoub S, et al. Use of chest imaging in the diagnosis and management of COVID-19: a WHO rapid advice guide. Radiology. 2021;298(2):E63-9.
5. Dramé M, Teguo MT, Proye E, et al. Should RT-PCR be considered a gold standard in the diagnosis of Covid-19?. J Med Virol. 2021;93(1):137-138.
6. Liu R, Han H, Liu F, et al. Positive rate of RT-PCR detection of SARS-CoV-2 infection in 4880 cases from one hospital in Wuhan, China, from Jan to Feb 2020. Clinica chimica acta. 2020 ;505:172-175.
7. Long C, Xu H, Shen Q, et al. Diagnosis of the Coronavirus disease (COVID-19): rRT-PCR or CT?. Eur Jo Radiol. 2020;126:108961-108966.
8. Loeffelholz MJ, Tang YW. Laboratory diagnosis of emerging human coronavirus infections–the state of the art. Emerg Microbes Infect. 2020;9(1):747-56.
9. Corman VM, Landt O, Kaiser M,et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill. 2020;25(3):2000045-2000052.
10. Bwire GM, Majigo MV, Njiro BJ, et al. Detection profile of SARS-CoV-2 using RT-PCR in different types of clinical specimens: a systematic review and meta-analysis. J Med Virol. 2021;93(2):719-725.
11. Tahamtan A, Ardebili A. Real-time RT-PCR in COVID-19 detection: issues affecting the results. Expert Rev Mol Diagn. 2020;20(5):453-454.
12. Mossa-Basha M, Meltzer CC, Kim DC, et al. Radiology department preparedness for COVID-19: radiology scientific expert review panel. Radiology. 2020;296(2):E106-112.
13. Sverzellati N, Milanese G, Milone F, et al. Integrated radiologic algorithm for COVID-19 pandemic. J thorac Imaging. 2020;35(4):228-33.
14. Wang C, Horby PW, Hayden FG, et al. A novel coronavirus outbreak of global health concern. The lancet. 2020;395(10223):470-473.
15. Yang W, Sirajuddin A, Zhang X, et al. The role of imaging in 2019 novel coronavirus pneumonia (COVID-19). Eu Radiol. 2020;30:4874-4882.
16. Zhou S, Wang Y, Zhu T, Xia L. CT features of coronavirus disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. Am J Roentgenol. 2020;214(6):1287-94.
17. Giovagnoni A. Facing the COVID-19 emergency: we can and we do. La radiologia medica. 2020;125(4):337.
18. Neri E, Miele V, Coppola F, et al. Use of CT and artificial intelligence in suspected or COVID-19 positive patients: statement of the Italian Society of Medical and Interventional Radiology. La radiologia medica. 2020;125(5):505-8.
19. ACR recommendations for the use of chest radiography and computed tomography (CT) for suspected COVID-19 infection [Inter net]. Reston Varginia (VA):American College of Radiology; 2020 [updated 2020 March 22; cited 2023 June 12]. Available from https://www.acr.org/Advocacy-and-Economics/ACRPosition-Statements/Recommendations-for-Chest-Radiography-andCT-for-Suspected-COVID19-Infection.
20. Garg M, Prabhakar N, Bhalla AS, et al. Computed tomography chest in COVID-19: When & why?. Indian J Med Res. 2021;153(1-2):86-92.
21. Tsakok M, Shaw R, Murchison A, et al. Diagnostic accuracy of initial chest radiograph compared to SARS-CoV-2 PCR in patients with suspected COVID-19. BJR Open. 2020; 2(1): 20200034-20200038.
22. Stephanie S, Shum T, Cleveland H, et al. Determinants of chest radiography sensitivity for COVID-19: a multi-institutional study in the United States. Radiol Cardiothorac Imaging. 2020;2(5):e200337- 200344.
23. Borakati A, Perera A, Johnson J, et al. Diagnostic accuracy of X-ray versus CT in COVID-19: a propensity-matched database study. BMJ open. 2020;10(11):e042946-042959.
24. Wong HY, Lam HY, Fong AH, et al. Frequency and distribution of chest radiographic findings in patients positive for COVID-19. Radiology. 2020;296(2):E72-78.
25. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708-1720.

ORIGINAL ARTICLE

ONLINE LEARNING: DEPRESSION, ANXIETY AND STRESS SYMPTOMATOLOGY AMONG STUDENTS OF WAH MEDICAL COLLEGE DURING COVID-19 QUARANTINE

Anwar Bibi[1], Sidra Farooq[2], Robina Mushtaq[3], Aashi Ahmed[4], Raima Siddiqui[5], Mohsin Raza[6]

[1]Associate professor, community medicine HITEC-IMS Taxila, [2] Assisstant professor, community medicine HITEC-IMS Taxila, [3]Professor of community, Wah Medical College, Wah Cantt, [4]Professor of Community Medicne, HITEC-IMS Taxila, [5]Lecturer Community Medicine , HITEC-IMS Taxila, [6]Lecturer Community Medicine, HITEC-IMS Taxila

ABSTRACT

Introduction: The students faced new worries and issues with the discontinuation of on-campus teaching and the change to online education during the COVID-19 quarantine. This significant change had a detrimental effect on their mental health and cognitive functioning.

Objectives:

1. To assess depression, anxiety & stress among medical students during online learning.
2. To determine the association of depression, anxiety & stress with gender & residential status of the students.

Study Design: Cross-sectional study.

Place and Duration of Study: Wah Medical College, Wah Cantt. 06 months (December 2020-May 2021).

Material and Methods: Data collection was done by Google Forms, using Depression, Anxiety & Stress Scale (DASS) 21questionnaire (Cronbach alpha >0.70). The Google form link was shared with all 500 MBBS students through their class WhatsApp groups. Only 180 students submitted the response giving a response rate of 36%. Statistical Package for Social Sciences (SPSS) version 26 was used for data analysis. The descriptive variables were determined as Means & Standard Deviation (SD), frequencies & percentages. The Chi-square test executed the inferential analyses, with a predetermined alpha (α) < 0.05.

Results: Male students were 60(33.3 %) and female students were 120(66.6%) . The proportion of rural students was 32 (17.8%) and 148 (82.2%) were urban students. Stress was reported more than anxiety and depression among the students. Gender did not significantly correlate with depression, anxiety, or stress (p-value>0.5). Depression was significantly more reported among rural students than urban students (p-value <0.05).

Conclusion: In terms of mental health, both male and female students were equally affected by online learning during the quarantine period of COVID-19.

Keywords: *Anxiety, COVID-19, Depression, e-learning, Medical students, Online learning, Stress.*

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INTRODUCTION

COVID-19 was deemed a worldwide public health emergency in January 2020. The World Health Organisation (WHO) labelled it a pandemic on March 11, 2020. Many countries implemented strict precautions for their citizens to prevent the spread of infection[1]. A stressful situation was created for all societies due to lockdown instructions. Without social interaction or face-to-face communication, people were isolated and went through phases of loneliness, rage, anxiety, boredom, and melancholy[2]. The pandemic affected all the domains of life, including education. Health education was challenging during the pandemic. Face-to-face teaching sessions were terminated. To address the disruption in learning caused by the pandemic, numerous universities globally shifted onto emergency remote teaching (ERT) or e-learning by using online platforms for video lectures or live streams[1,3,4]. The initial shift to digital learning caused significant confusion, particularly with subjects that are more difficult to teach online, such as those in health sciences[5].

Students are usually vulnerable to developing stress disorders and depression. Disease outbreaks have badly affected the mental health & well-being of individuals[1]. Because of the

Correspondence to: Dr. Raima Siddiqui, HITEC Institute of Medical Sciences (HITEC-IMS), Taxila.

Email: raima.siddiqui@hitec-ims.edu.pk

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psychologically taxing circumstances they were in, throughout the COVID-19 quarantine, the likelihood of such consequences was significantly higher[2,5].

The switch from transitional teaching to emergency remote teaching has increased student anxiety[3].Difficulties & limitations experienced by the students through online learning increased the level of stress in the students. Women aged between 16 and 24 years were the most vulnerable group for developing psychological distress[1,2].Procrastination can be the result of social isolation and decreased physical activity during period of quarantine which may augment anxiety & depression among students[5]. Students were anxious and depressed, which had a severe bearing on their cognitive functioning & learning, as students of a medical school [4,6]. Particular to this study, prior research has shown how pandemics can impact students' psychological health, resulting in severe anxiety and depression[3]. Research has been done in several countries regarding medical students' anxiety and depression during the pandemic. The results demonstrated that, even in the preclinical setting, medical students experienced higher levels of anxiety and sadness during the COVID-19 pandemic[6]. Studies also showed that during the H1N1 pandemic, depression and feelings of emotional disturbance were reported. A population-based survey during the SARS outbreak reported post-crisis mental distress. During Middle East Respiratory Stress (MERS) in KSA, a comparatively high level of stress was reported among medical students[1].

CAPSULE SUMMARY

During learning transition to online format during COVID -19 lockdown, stress levels were notably higher compared to depression and anxiety in medical students, affecting male and female students equally, with rural students experiencing higher levels of depression as compared to urban students.

Medical teaching involves interaction with the patients and is different from other teaching. We were on e-learning during the pandemic for almost one and half years and we were facing so many hurdles and barriers in both teaching and learning. This study was done to evaluate the effect of online learning on the mental well-being of medical students. The primary aim was to find out the symptomatology of stress, anxiety, and depression in Wah Medical College students during the COVID-19 pandemic, with an emphasis on the shift to online instruction. **Rationale:** Unprecedented difficulties were introduced by the COVID-19 pandemic, affecting various aspects of life, including education. Medical students face unique stressors due to the nature of their studies. The pandemic and its associated restrictions such as lockdowns, social distancing measures, and transition to online learning have significantly impacted mental health, globally. Students, especially those pursuing medical education, are more vulnerable to mental health issues because of the rigorous nature of their coursework, exposure to distressing clinical scenarios, long study hours, and limited work-life balance. Currently, the literature reveals a dearth of data on the well-being and mental health issues of students of higher studies during this pandemic, particularly in Asian nations. More information is needed, particularly from developing nations, to investigate students' mental health status for prevention and intervention. Understanding the prevalence & severity of depression, anxiety, and stress in medical students during pandemic days has value for the identification of risk factors, specific to this population. Findings from this study can tell us about the development and implementation of targeted interventions to strengthen the mental health & well-being of medical students during and beyond this pandemic. This study can potentially adds useful insights to the existing literature and help guide relevant future research.

MATERIAL AND METHODS

A Cross-sectional study was done in Wah Medical College, Wah Cantt, from Dec 2020 to May 2021. A Sample of 374 was calculated by applying the WHO sample size formula taking the prevalence of severe depression at 42.09 % (1) and α of 0.05

$n=z^2 PQ/e^2$

$n= (1.96)^2 0.42x0.58/ (0.05)^2= 374$

Convenience sampling technique was adopted for data collection. All enrolled students of Wah Medical College who had been involved in online learning were included in the study except for diagnosed cases of any psychiatric illness. A structured questionnaire, Depression, Anxiety & Stress Scale (DASS) 21, was utilized for the assessment of mental health status of medical students, undertaking online learning during the COVID-19 quarantine. Few questions related to demographic variables were included in the questionnaire. DASS-21 is a psychometrically accurate, reliable and valid tool (Cronbach alpha >.70). It is a 03 self-report scales set, to determine the emotional states of depression, anxiety & stress. Seven elements are there in each scale, further categorized in subscales of related information. The response to each item is recorded in a 04-point Likert scale, from 0 ("did not apply to me at all") to 3 ("applied to me very much or most of the time"). The scores of different subscales were obtained by adding the scores of individual items. The cut-off points of each dimension were set, to assess depression, anxiety and stress levels, as of Lovibond[2]. Data was collected through Google Forms. Google form link was shared in the WhatsApp groups of all five years of MBBS. All enrolled students of Wah Medical College who were involved in online learning during the phase of home quarantine were included in the study. In the Google form, a brief description of the aim of the study was given. Students were informed about the confidentiality of the data. Consent was written on the questionnaire and taking part in the study was voluntary. Out of 500 students, 180 students returned the questionnaire giving a response rate of 36%. Statistical Package for Social Sciences (SPSS) version 26 was used for analysis. Descriptive and inferential analysis was done. The chi-square test determined the association of depression, anxiety & stress with gender and residential status. Predetermined alpha (α) was taken at <0.05.

Operational definition: The cut-off points for depression, anxiety & stress were as of DASS 21manual by Lovibond [2].
Depression: Students scoring 0-9 were labelled normal, 10-12 as having mild depression, 14-20 as having moderate depression, 20-27 as severe depression & 28+ as having extremely severe depression.
Anxiety: A score from 0 to 7 was considered normal for anxiety, 8 & 9 were categorized as mild anxiety, 10-14 as moderate,15-19 as severe and a 20+ score, as extremely severe.
Stress: A stress score from 0 to 14 was taken as normal, from 15 to 18 as mild, from 19 to 25 as moderate, from 26 to 33 as severe and 34+ as extremely severe.

RESULTS

Our sample consisted of 180 undergraduate medical students of Wah Medical College who were involved in online learning at the time of the lockdown. Out of 180 students, 120 (66.6%) were females and 60(33.3 %) were males. According to age, students were categorized into three main categories. Students belonging to the age category of 21-23 years were 134 (74.4%), 38 (21.1%) belonged to the age group of 18-20 years and 8(4.4%) were > 23 years of age. The residential distribution of the participants showed that 148 (82.2%) participants were from urban areas and 32(17.8%) were from rural areas. Students from all the five years of MBBS took part in the study. Participants from the first year were 42 (23.3%), from 2nd year were 23(12.8%), from 3rd year were 64(35.6%) from 4th year were 45(25%) and 6(3.3%) students were from the final year of MBBS.

Descriptive analysis was done to determine depression, anxiety & stress among medical students. Mean score of depression was 9.13± 5.68, mean score of anxiety was 7.67± 5.27 and mean score of stress was 9.49± 5.33. Detailed results are given in Table 1.

Table 1: Depression, Anxiety & Stress Scale (Mean ± SD)

	Minimum	Maximum	Mean	SD
Depression	0	21	9.13	5.68
Anxiety			7.67	5.27
Stress			9.49	5.33

The three dimensions of DASS-21 were assessed as of the mentioned cut-off points, some scores indicate varying levels of depression, stress & anxiety. The descriptive analysis for various levels of depression, anxiety & stress are depicted in Table 2.

The chi-square test determined the difference between male and female students associated with recorded levels of depression, anxiety and stress. Analysis showed insignificance (p- value 0.9, 0.57, 0.15 respectively).

A significant difference on the level of depression (p- value 0.05) among rural and urban residents was observed on analysis. The rural residents were more depressed as compared to the urban residents. However, analysis showed insignificant difference in the level of anxiety and stress (p- value 0.74 & 0.58 respectively) among rural and urban residents.

DISCUSSION

The academic life of medical students makes them prone to depression & anxiety. Situations, such as a pandemic, might amplify the negative feelings. Coping with online education methods could be challenging for the students. This encompasses students' technological proficiency, a reliable internet connection, and sufficient home resources facilitating online learning. This research indicated that a significant portion of the students fell within normal ranges of anxiety stress and depression. Stress was more reported among the students than anxiety and depression and a notable number came out to be experiencing significant mental health challenges highlighting the widespread impact of online learning on student well-being. These results are similar to the [2,4-10]. Due to the lack of contact throughout the social distancing stage, these psychological reactions are more likely to arise and worsen. Isolation can have detrimental effects on the mental health of many. In addition, academic, social & financial difficulties can also cause stress and lead to anxiety and depression.

The insignificant difference in depression, anxiety, and stress with gender was reported by the current study. This finding is similar to that of Kira D, et al and in contrast to some studies which claimed that women have higher rates of stress, anxiety, and depression[2,4-6,11-12]. Whereas Azmi FM, et al stated that males have higher depressive symptoms than females[13]. This

Table 2: Level of Severity, Frequency and Percentage of Depression, Anxiety & Stress among Medical Students

	Depression		Anxiety		Stress	
Severity	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Normal	103	57.2	91	50.6	143	79.4
Mild	36	20	22	12.2	28	14.4
Moderate	36	20	45	25	100	61
Severe	5	2.8	21	11.7	0	0
Extremely severe	0	0	1	0.6	0	0

contrast may be attributed to the unequal distribution of males and females in the sample of our study.

The current study's findings show a significant association between depression, anxiety & stress in students from rural and urban settings. Rural students were found to be more depressed. This finding is similar to that of Jiang N, et al and in contrast to that of Azmi FM, et al which found those living in urban areas to have increased levels of anxiety & depression [2,13]. The disparity in resources between urban and rural areas in terms of economic, cultural, social, and educational aspects could be the cause. The urban community has better educational resources and provides students with greater opportunities as compared to the rural community. In addition, internet facilities are also ahead in the urban sector, which helps students maintain communication with their friends and family, through social media, when they are unable to meet them in person due to the pandemic.

CONCLUSION

Our research evaluated depression, anxiety, & stress levels among medical students during COVID-19 lockdown, when learning transitioned to an online format. Stress levels were notably higher compared to depression and anxiety. The pandemic emotionally affected both male and female students, with rural students experiencing higher levels of depression during online learning.

To address these challenges, it is essential to develop interventions targeting the stress, anxiety, and depression associated with online learning. Integrating new courses in the curriculum to improve computer-using skills, which in turn will lead to improvement in the online learning experience. Additionally, improving internet accessibility in rural areas is imperative. Further research is necessary to devise more effective interventions to support students in managing their mental health during online education.

Limitations

- The sample size was small with a low response rate.
- Self-selection-based participation in the survey.
- Asymmetry of sample in terms of gender and study year.

AUTHORS' CONTRIBUTION

Raima Siddiqui	Drafting the Article
Sidra Farooq, Mohsin Raza	Analysis and interpretation of data
Anwar Bibi	Conception and design
Robina Mushtaq	Acquisition of data
Anwar Bibi, Aashi Ahmed	Critical revision

REFERENCES

1. AlAteeq D A, Aljhani S, AlEesa D. Perceived stress among students in virtual classrooms during the COVID-19 outbreak in KSA. J Taibah Univ Med Sci. 2020;15(5):398-403.
2. Jiang N, Siaw YL, Pamanee K, et al. Depression, Anxiety, and Stress During the COVID-19 Pandemic: Comparison Among Higher Education Students in Four Countries in the Asia-Pacific Region. J Popul Soc Stud. 2021; 29: 370-383.
3. Jabeen S, Muhammad A, Sadiq F. Students' satisfaction from E-learning system. Int J E-Adoption. 2014; 6(2):1-13.
4. Abdulghani H, Ahmed T, Sattar K, et al. Association of COVID-19 Pandemic with undergraduate Medical Students' Perceived Stress and Coping. Psychol Res Behav Manag. 2020; 13(1): 871-881.
5. Fawaz M, Samaha A. E-learning: Depression, anxiety, and stress symptomatology among Lebanese university students during COVID19 quarantine. Nurs Forum. 2021;56(1):52-57.
6. Manuaba IBAP , Darmayani IGAS , Sindhughosa DA. Levels of anxiety and depression of students and responses to online learning methods during the COVID-19 pandemic. Bali Med J 2023; 12(1): 550-555.
7. Son C, Hegde S, Smith A, et al. Effects of COVID-19 on College Students' Mental Health in the United States: Interview Survey Study. J Med Internet Res. 2020; 22(9): 1-14.
8. Kira D, Nebebe, f, Saadé RG. The persistence of anxiety experienced by new generation in online learning. In: Eli Cohen editor. Proceedings of the informing science and information technology education conference; 2018 June 23-28; Santa Rosa, CA. Informing science institute; 2018.p.79-78.
9. Faisal RA, Jobe MC, Ahmed O, et al. Mental Health Status, Anxiety, and Depression Levels of Bangladeshi University Students During the COVID-19 Pandemic. Int J Ment Health Addict. 2022;20(3):1500-1515.
10. Cao W, Fang Z, Hou G, et al. The psychological impact of the COVID-19 epidemic on college students in China. Psychiatry Res. 2020 ;287: 112934-112938.
11. Shah T D, Pol T. Prevalence of depression and anxiety in college students. J Mental Health Hum Behav. 2020;25(1):10-13.
12. Islam M A, Barna S D, Raihan H,et al. Depression and anxiety among university students during the COVID-19 pandemic in Bangladesh: A web-based cross-sectional survey. PLoS ONE. 2020;15(8):e0238162-238173.
13. Azmi FM, Khan HN, Azmi AM. The impact of virtual learning on students' educational behavior and pervasiveness of depression among university students due to the COVID-19 pandemic. Global Health. 2022 Jul 14;18(1):70-78.

ORIGINAL ARTICLE

ASSESSMENT OF NUTRITIONAL STATUS OF CHILDREN AGED 1-5 YEARS ATTENDING THE OUTDOOR PATIENTS DEPARTMENT OF SHEIKH ZAYED HOSPITAL, RAHIM YAR KHAN, PAKISTAN

Ghazala Yasmeen Iqbal[1], Hafiz Umer Farooq[2], Naila Jabeen[3], Rafay Ur Rehman Cheema[4], Shazia Sultan[5], Tariq Hussain[6]

[1,2]Assistant professor, Community Medicine, [3]Demonstrator, Biochemistry Department, [4]Assistant professor, Biochemistry Department, [5]Assistant professor, Physiology Department, [6] APMO Biochemistry Department, Sheikh Zayed Medical College, Rahim Yar Khan.

ABSTRACT

Background: Enforcement of corrective nutritional measures to combat malnutrition in children requires local data for planning strategies.

Objective: To assess the nutritional status of children, 1-5 years of age, presenting at the Children Outdoor Patient Department (OPD).

Study Design: Descriptive, Cross-sectional.

Place and Duration of Study: Sheikh Zayed Hospital, Rahim Yar Khan, Pakistan, June to July 2022(02 months).

Patients and Methods: All children, 1- 5 years of age, presenting to OPD were enrolled in the study, by convenience sampling method. Data was collected through a questionnaire that contained information regarding the assessment of nutritional status of children according to WHO growth standards. The data was compared with the growth charts and summarized into tables, graphs and bar diagrams by using SPSS software 23.

Results: A total of 56 (62.2%) children had normal weight, 32 (35.6%) were underweight and 2 (2.2%) were overweight. The gender-specific underweight percentage in boys was 41.7% while in girls it was 26.5%.

Conclusion: Considerable proportions of children presenting in the OPD were underweight. Those who were not properly breastfed, had poor vaccination status and low socio-economic status were mostly malnourished. Proper breastfeeding, immunization and monitoring of growth of children should be done to ensure good nutritional health of children.

Key words: *Age 1-5 years, Assessment, Children, Nutritional status*

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INTRODUCTION

Nutrients are the organic or inorganic contents of the food that are responsible for multiple functions and so protect the body from disorders. A balanced nutrition ensures optimal physiological growth and prevents disease. The science of nutrition principally identifies two classes: macro and micronutrients. Both macronutrients (Proteins, Fats and Carbohydrates) and micronutrients (Vitamins & Minerals) are crucial for growth. Lack of even one of them can have devastating consequences[1-3].

Stunting, wasting, and being underweight are the indicators of malnutrition in children. Stunting results from prolonged nutrient insufficiency and repeated infections while wasting is caused by acute food deficiency & illness. Being underweight combines reduced linear growth and weight for length/height[4] and is a composite indicator that encompasses both acute (wasting) & chronic (stunting) malnutrition[5]. Various types of malnutrition might concurrently be found.

A correct proportion of nutrients is necessary for growth, development and proper functioning of the body. The pediatric age at each period has its own specific requirements & characteristics, and any specific nutrient deficiency can delay growth and/or compromise specific organ functions [6].

Study of nutritional status of children measures nutritional

Correspondence to: Dr. Ghazala Yasmeen Iqbal, Assistant Professor, Community Medicine Department, Sheikh Zayed Medical College. Rahim Yar Khan.

Email: farrukhnme@gmail.com

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imbalance or malnourishment resulting in undernutrition. It aids in identifying high-risk populations and evaluating the influence of various epidemiological factors in nutritional insufficiency. Nutrient deficiency may have specific effects on physical growth and development like marasmus, kwashiorkor, night blindness, nutritional anemia etc. Some causes of malnutrition are: Failure of lactation, early weaning due to second pregnancy, poverty (meat, milk and eggs are not appropriately consumed), cultural pattern (best food is served to males), lack of immunization, and lack of family planning. Other causes include infections, congenital diseases, metabolic disorders etc. Malnutrition in Pakistani children is linked to both maternal and child-related causes, majority of them can be prevented[7].

CAPSULE SUMMARY

More than one-third of the children in this study were underweight. Improper breastfeeding, poor vaccination and low socio-economic status were the main contributing factors. Children from rural background were more effected than the urban population.

More than 50% of children under the age of five, die from acute malnutrition alone, which results in the deaths of 3.5 million children worldwide each year[8]. In Pakistan, population of malnourished children is 58%. These results were determined in a study conducted by National Nutritional survey in 2018[9]. Major factor is improper distribution of food in different areas e.g. in KPK the malnourished children population is up to 58.9% while in Baluchistan this percentage is up to 68% which shows the absence of primary health care and proper food in respective areas[10,11]. According to a survey, children who were underweight, stunted, or wasted had a prevalence of 46.2%, 62.6%, and 11.1%, respectively[12]. According to a study conducted in India, children between the ages of three and twenty-three months had an increasing percentage of underweight and stunted weight. The highest incidences of wasting and low BMI for age were observed at birth[13]. With 3.5% of stunted children under the age of five, the United States is on track to fulfil its target[14].

In order to combat malnutrition, some strategies should be adapted like Special Nutrition Program, Integrated Child Development Services, Immunization Program, Nutritional vitamin A Deficiency Program, and education through mass media. These strategies are dependent upon local logistics and dynamics. For this purpose, local data is required for the assessment of the brunt of the problem. The objective of our study was to evaluate the nutritional status of children aged, 1-5 years, presenting at the Children Out Patient Department (OPD)of Sheikh Zayed Hospital, Rahim Yar Khan, Pakistan.

PATIENTS AND METHODS

Ethical approval for the study was sought from the Institutional Review Board. All children from 1 to 5 years of age, presenting in the Children OPD from June to July 2022, were selected by non-probability convenience sampling technique. Children whose parents were unwilling to participate were excluded from the study.

After getting informed consent from respondents, data was collected through a preformed questionnaire. It contained basic and specific information about the nutritional status of children, 1-5 years of age, according to WHO growth standards. Weight was measured by weight scale and height by measuring tape or meter rod. The data was compared with the growth charts and summarized into tables, graphs and bar diagrams by using SPSS software 23. According to WHO criteria the data was analyzed by descriptive analysis by frequency distribution of variables with nutritional statuses.

RESULTS

Total 90 children were assessed according to WHO criteria. The mean age of participants was 33.3±15 months. Among all participants, 56 (62.2%) were males and 34 (37.8%) were females. Out of the total (n=90), 46(51.1%) children were from the age group 18-36 months. The 14 (15.3%) children fell in age groups 12-18 months, 12 (13.6%) in 36-48 months, and 18 (20%) in 48-60 months.

The mean weight of participants was 10.5±3.9 kg. Out of 90 children presented in the OPD, 62.2% were normal weight, 35.6% underweight and 2.2% overweight (Figure1).

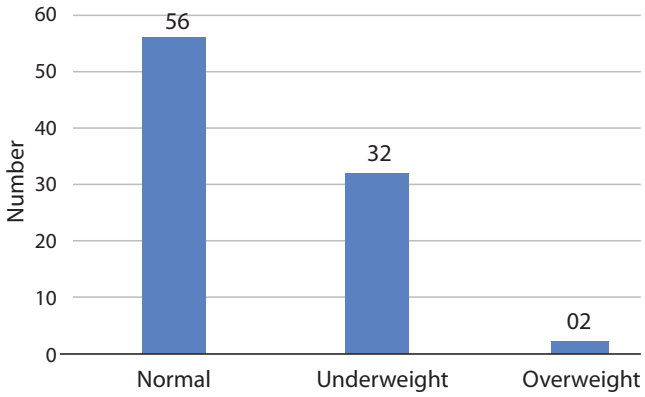

Figure 1: Nutritional Status of the Children

A total of 47 (52.2%) children had complete immunization, 29 (32.2%) had partial and 14 (15.6%) had none. Out of 90 children, 59 (65.5%) belonged to families of low, 21 (24.4%) middle and 9 (10%) high socio-economic status. As compared to middle and high socioeconomic status, a significantly large number of children (47.5%) of low socioeconomic status were underweight. Regarding gender, a large number of male children (41%) were in the undernutrition group. Out of the children, 50 (55.6%) came from rural areas and 40 (45.4%) from urban areas. Rural children (44%) were more malnourished as compared to urban children (32.5%). A total of 61 (67.8%) children were breastfed and 29 (32.2%) were fed formula milk. A total of 12 (41.4%) children who were not breastfed were

Table 1: Association of nutritional status of children with other variables (n=90)

Variable	Nutritional Status			p-value
	Normal n(%)	Undernutrition n(%)	Overnutrition n(%)	
Socioeconomic status				
Low	31(52.5)	28 (47.5)	0 (0)	0.01
Middle	17(80.9)	4 (1)	1 (4.5)	
High	8 (88.9)	0 (0)	1 (11.1)	
Sex				
Male	32(57.1)	23 (41)	1 (1.7)	0.36
Female	24(70.6)	9 (26.5)	1 (2.9)	
Residence				
Rural	27 (54)	22 (44)	1 (2)	0.53
Urban	26 (65)	13 (32.5)	1 (2.5)	
Breastfeeding				
Yes	40 (65)	20 (32.8)	1 (1.6)	0.59
No	16(55.2)	12 (41.4)	1 (3.4)	

underweight, while in breastfed children, 20 (32.8%) were underweight (Table 1).

DISCUSSION

Out of total children, 32 (35.6%) were underweight and 2 (2.2%) were overweight. In a similar study conducted in Quetta, Baluchistan 48.1% children were underweight[11]. A study conducted in Aboottabad showed 21% underweight children and implicated macro-nutrient deficiencies with infections as the major cause[15]. Another study from the same city showed that underweight students were maximum in public school setups as compared to private schools[16]. Another study conducted in Pakistan also supported our results showing underweight percentage higher in rural areas i.e., 67%, as compared to urban area 45.3%. It was due to many reasons like poverty and non-availability of health care services etc[17]. According to our study malnutrition is more in rural areas and in child with low socioeconomic class.

In a study conducted in Abakaliki metropolis, Ebonyi State, Nigeria, the prevalence of under & overnutrition was 15.7% and 2.1% respectively. Prevalence of underweight was 8%, that of thinness 7.2%, stunting 9.9%, overweight 1.4% & obesity 0.7%[18]. Another study, conducted in Nghean, Vietnam, is also in agreement with our study. According to which, 44.3% children were found underweight and stunted. The highest proportion of underweight children were between 3-4 years of age and highest proportion of stunting was observed in children of 12-23 months. Moreover, the mean z-score differences between males and females were also statistically significant[19]. It also collaborates with our results. In short, multiple factors affect the nutritional growth of the child. Mother's milk and balanced diet are the most essential need for the proper growth of the children.

A similar study, conducted in Multan, also favoring our study concludes prevalence of malnutrition due to lower socioeconomic status among major populations in the community specifically in rural areas[20]. A research in Nankana Sahab Punjab found socioeconomic status and food insecurity as significant positive predictors for stunting among children[21].

According to the 2022 Global Nutrition Report, Pakistan has 37.6 % stunting in children under 5 years which is the highest in the South Asia region (the average in the region is 21.9%). The results of the Global Nutrition Report are in accordance with our study. The report also states that Pakistan is 'on course' to reach the global nutrition targets for young child nutrition for which there was sufficient data to assess progress[22]. IPC Acute Malnutrition Analysis March 2023 – January 2024 stated that over two million children in the flood-hit areas of Pakistan had acute malnutrition in the aftermath of the 2022 flooding[23].

We conducted this study on a small scale in district Rahim Yar Khan due to which the results could not be generalized. Nonetheless, the results are an indication of the situation prevailing in this district concerning the nutritional status of children.

CONCLUSION

The nutritional status of children depends on their socioeconomic status, proper breastfeeding, and immunization. Children who were residents of rural areas and had poor financial status were malnourished, so proper breastfeeding and monitoring of the growth of children should be done to ensure good nutritional. Complete immunization of children should be done according to EPI schedule. Children should be breastfed, at least up to 6 months, according to WHO, with

ongoing breastfeeding along with complementary food up to two years of age, and awareness about weaning should be created.

In view of the above demonstrated results, it is suggested that similar area-based studies, with bigger sample sizes should be carried out in Pakistan to figure out the actual brunt and dynamics of the problem. This will help the policymakers to develop initiatives to address the actual malnutrition status among the children< 5 years of age.

AUTHORS' CONTRIBUTION

Naila Jabeen, Rafay Ur Rehman Cheema, Shazia Sultan	Drafting the Article
Ghazala Yasmeen Iqbal, Naila Jabeen, Shazia Sultan, Tariq Hussain	Analysis and interpretation of data
Ghazala Yasmeen Iqbal, Hafiz Umer Farooq, Rafay Ur Rehman Cheema	Conception and design
Hafiz Umer Farooq, Naila Jabeen, Rafay Ur Rehman Cheema	Acquisition of data
Ghazala Yasmeen Iqbal, Hafiz Umer Farooq, Naila Jabeen, Rafay Ur Rehman Cheema, Shazia Sultan, Tariq Hussain	Critical revision

REFERENCES

1. EFSA (European Food Safety Authority), 2017. Dietary Reference Values for nutrients Summary report. EFSA supporting publication. 2017: 14(12):e15121.98pp.
2. Carreiro AL, Dhillon J, Gordon S. et al. The Macronutrients, Appetite, and Energy Intake. Annu Rev Nutr. 2016;36:73–103.
3. Shergill-Bonner R. Micronutrients. Paediatr Child Health. 2017;27(8);357–62.
4. Sinha RK, Richa Dua R, Bijalwan V, et al. Determinants of Stunting, Wasting, and Underweight in Five High-Burden Pockets of Four Indian States. Indian J Community Med. 2018; 43(4):279-283.
5. De Onis M, Blössner M. The World Health Organization Global Database on Child Growth and Malnutrition: methodology and applications. Int J Epidemiol. 2003;32(4):518-526.
6. Savarino G, Corsello A, Corsello G. Macronutrient balance and micronutrient amounts through growth and development. Ital J Pediatr. 2021; 47 (1): 109-122.
7. Khan S, Zaheer S, Safdar NF. Determinants of stunting, underweight and wasting among children < 5 years of age evidence from 2012-2013 Pakistan demographic and health survey. BMC Public Health. 2019 ;19(1):358-372.
8. Park SE, Kim S, Ouma C, et al. Community management of acute malnutrition in the developing world. Pediatr Gastroenterol Hepatol Nutr. 2012 ;15(4):210-219.
9. Arshad K. National nutrition survey of 2018 key finding report, J Ayub Med Coll Abbottabad. 2010;20(3):111-112.
10. Mehmood Y, Ahad B, Riaz Gul R, et al. Nutritional Status of Children Under 5 years of Age in Three Tertiary Care Hospitals of Peshawar. J Islamabad Med Dent Coll.2016;5(2):50-53.
11. Achakzai P, Khan R. Nutritional status and associated factors among children less than five years of age in tehsil zarghoon town, district Quetta, Baluchistan. J Ayub Med Coll Abbottabad. 2016 ;28(1):146-151.
12. Al-Sobaihi S, Nakamura K, Kizuki M. Undernutrition among children/ under 5 years of age in Yemen: Role of adequate childcare provided by adults under conditions of food insecurity. J Rural Med. 2016;11(2):47-57.
13. Ramachandran P, Gopalan HS. Assessment of nutritional status of children in Indian pre school children using WHO 2006 growth standards. Indian J Med Res. 2011;134(1):47-53.
14. United States of America. The burden of malnutrition at a glance 2022 [Internet]. Creative Commons Attribution BY-NC-ND;[cited 2022 August]. Available from https:// globalnutritionreport.org/resources/ nutrition-profiles/north-america /northern-america/united-states-america/.
15. Lodhi HS, Rehman M, Lodhi FS, et al. Assessment of nutritional status of 1-5 year old children in an urban union council of Abbottabad. J Ayub Med Coll Abbottabad. 2010;22(3):124-127.
16. Siddique S, Ayub M, Shore N, et al. Nutritional status of primary school children at Abbotabad. J Ayub Med Coll Abbottabad, 2013;21(5): 123-126.
17. Anwer I, Awan JA. Nutritional status comparison of rural with urban school children in Faisal Abad District, Pakistan. Rural Remote Health.2003;3(1):130- 136.
18. Umeokonkwo AA, Ibekwe MU, Umeokonkwo CD, et al. Nutritional status of school age children in Abakaliki metropolis, Ebonyi State, Nigeria. BMC Pediatric. 2020 ;20(1):114-122.
19. Hien NN, Kam S. Nutritional status and the characteristics related to malnutrition in children under five years of age in Nghean, Vietnam. J Prev Med Public Health. 2008 ;41(4):232-240.
20. Ahmad D, Afzal M, Imtiaz, A. Effect of socioeconomic factors on malnutrition among children in Pakistan. Futur Bus J. 2020 ;6(1) : 30-40.
21. Razzaq R, Majeed MF, Ali H. Effects of Socioeconomic Status and Food Insecurity on Stunting among Children aged 06-59 Month. Pakistan Soc Sci Rev. 2024; 06(02):986-995.
22. Pakistan. The burden of malnutrition at a glance2022. [Internet]. Creative Commons Attribution BY-NC-ND;[cited 2022 October25]. Available from https://globalnutritionreport.org/resources/nutrition-profiles/asia/southern-asia/pakistan/.
23. Pakistan: IPC Acute Malnutrition Analysis - March 2023 - January 2024[Internet]. OCHA; [cited Jan 2024]. Available from https:// reliefweb.int/report/pakistan/pakistan-ipc-acute-malnutrition-analysis-march-2023-january-2024.

ORIGINAL ARTICLE

UNVEILING ALPHA-NAPHTHOFLAVONE MEDIATED CYP1A2 SUPPRESSION AND ANALYSIS OF CONSEQUENT STRUCTURAL DYNAMICS

Zahra Zahid Piracha[1], Umar Saeed[2], Naila Azam[3]

[1]International Center of Medical Sciences Research (ICMSR), United States of America (USA). [2] AssociateProfessor Biocamistry, Clinical and Biomedical Research Centre (CBRC) and Multidisciplinary Lab (MDL), Foundation University School of Health Sciences (FUSH), Foundation University, Islamabad, Pakistan. [3]Professor, Community Medicine, Foundation University School of Health Sciences (FUSH), Foundation University, Islamabad, Pakistan

ABSTRACT

Background: Cytochrome P450 enzymes play vital roles in metabolizing drugs, endogenous compounds, and environmental pollutants. Among them, Cytochrome P450 1A2 (CYP1A2), CYP1A1 and CYP1B are particularly important for activating carcinogens. Computational modeling of CYP1A2 is essential for understanding its interactions with various molecules, substrates, and inhibitors.

Objective: To characterize the structure of CYP1A2 and explore the binding of alpha-naphthoflavone to its active site.

Study Design: In Silico study (Computational modeling).

Place of Study: International Center of Medical Sciences Research (ICMSR), Islamabad, Pakistan.

Material and Methods: Using the Swiss PDB Viewer, the structural features of CYP1A2 were assessed, focusing on key residues, motifs, helices, and conserved regions.

Results: Our findings identified specific binding sites for Alpha-Naphthoflavone (ANF), highlighting its potential as a potent inhibitor of CYP1A2. This research contributes to our knowledge of the clinical and toxicological implications associated with CYP1A2.

Conclusion: Structural differences were found between CYP1A2 and related enzymes, with less than 40% sequence identity compared to several other P450s. The study predominantly compares CYP1A2 with CYP 2A6 and CYP3A4 due to these differences. The developed structural models offer a fast and precise method for studying CYP1A2, aiding in understanding its role in drug metabolism and toxicology.

Key words: *Alpha-naphthoflavone Cytochrome P450, Computational modeling, CYP1A2, Structural characterization*

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INTRODUCTION

Cytochrome P450 (CYP) enzymes, a diverse superfamily of hemeproteins is found in both prokaryotes and eukaryotes, playing critical roles in the metabolism of various compounds, including lipophilic xenobiotics, procarcinogens, drugs, and environmental toxins[1]. They are pivotal in drug metabolism, where they catalyze oxidation, reduction, and hydrolysis reactions that significantly influence the bioavailability and efficacy of drugs[2]. Genetic variations in CYP enzyme activity due to polymorphism can lead to differences in drug response and metabolism among individuals. Beyond drug metabolism, cytochrome P450 enzymes are central to detoxification and elimination of xenobiotics, including environmental pollutants and carcinogens. By converting the lipophilic substances into more hydrophilic forms, CYP enzymes facilitate their excretion from the body, providing a crucial defense mechanism against toxic insults [3]. In addition to xenobiotics, CYP enzymes are also important in metabolizing some compounds formed in the body, like bile acids, steroids and fatty acids. This metabolic activity is essential for maintaining physiological homeostasis and regulating biological processes like hormone synthesis and cholesterol metabolism.

Certain cytochrome P450 enzymes, including CYP1A1, CYP1A2, and CYP1B1, are implicated in the activation of procarcinogens to reactive intermediates that can initiate DNA damage and promote carcinogenesis[4]. Conversely, other CYP enzymes contribute to detoxification of carcinogens, helping to mitigate their harmful effects. Cytochrome P450 enzymes are also critical in mediating drug-drug interactions due to their involvement in the metabolism of multiple medications.

Correspondence to: Zahra Zahid Piracha, International Center of Medical Sciences Research (ICMSR), United States of America (USA).

Email: piracha.zahra@gmail.com

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Inhibition or induction of specific CYP enzymes by one drug can alter the metabolism of co-administered drugs, potentially leading to adverse effects or therapeutic failure. Genetic polymorphisms in cytochrome P450 genes contribute to significant inter-individual variability in enzyme activity[5]. This variability can impact drug response, predisposition to drug-induced toxicity, and susceptibility to certain diseases. For example, polymorphisms in CYP2D6 and CYP2C19 are linked with altered metabolism of psychotropic drugs and cardiovascular medications. The study of cytochrome P450 genetics and their impact on drug metabolism forms the basis of pharmacogenomics, a field focused on tailoring drug treatments based on individual genetic profiles. Understanding CYP enzyme polymorphisms enables the prediction of drug responses and facilitates personalized therapeutic approaches [6].

CAPSULE SUMMARY

There are significant structural differences between cytochrome P450 1A2 and other cytochrome P450 enzymes (2A6 and 3A4). The developed structural models in the study show that cytochrome 1A2 has a compact and closed active site cavity, well-suited for oxidizing large planar substrates providing a better understanding its role in drug metabolism and toxicology.

CYP1A2, known as Phenacetin-O-deethylase, constitutes approximately 15% of total liver P450 enzymes and is constitutively expressed in the liver, metabolizing 8-10% of clinically significant drugs[4,7,8]. The CYP1A2 *gene*, located on chromosome 15, comprises six introns and seven exons, including a 55bp non-coding exon[5]. It shares a 5'-flanking region with *CYP1A1*, indicating evolutionary linkage. Genetic as well as environmental factors influence *CYP1A2* expression & activity, with over 15 variant alleles and numerous SNPs identified [6, 7-10]. Substrates of CYP1A2 are typically aromatic, flat, lipophilic, and neutral, with planar structures that fit well into its active site [10,11]. Together with CYP1A1 and CYP1B, CYP1A2 plays a critical role in activating carcinogens[12-14]. Inhibitors of CYP1A2, such as alpha-naphthoflavone, often contain chloro, fluoro, or methyl groups and can impact drug metabolism [15-17]. Understanding the structure and function of CYP1A2 through computational modeling and in silico studies is crucial for identifying potential inhibitors and understanding their clinical implications in drug metabolism and toxicity [18-20].

MATERIAL AND METHODS

An in-silico study was conducted to investigate the structural features of CYP1A2. The analysis aimed to characterize the molecule's architecture, focusing on important residues, motifs, helices, and functional regions. Using the Swiss PDB Viewer, CYP1A2 was observed to consist of twelve Alpha helices and four Beta sheets.

The secondary structural elements were designated from A - L for helices and from 1 - 4 for beta sheets, sequenced from the N-terminus. The prosthetic group (heme) and the substrate binding cavity were prominently identified. The structural analysis highlighted CYP1A2's specialization in oxidizing large planar, molecules such as Poly Aromatic Hydrocarbons (PAHs), laying the groundwork for an efficient xenobiotic biotransformation. Supplementary helices were also identified, beyond the twelve Alpha-helices and four Beta-sheets. Substrates got bound within the cavity, above the heme prosthetic group's distal surface.

This study underscores the structural adaptability of CYP1A2 for its biological function, elucidating key features essential for its role in metabolizing a variety of substrates, particularly PAHs, crucial for understanding its impact on xenobiotic metabolism.

RESULTS

In the structural analysis of CYP1A2, certain regions emerge as highly conserved and functionally critical within the protein's architecture. Among the most conserved regions were the heme binding site, nestled deep within the protein core, and the binding sites for redox partners. Notably, the proximal surface of the CYP1A2 redox partner has the binding site situated on it. NADPH-cytochrome P450 oxidoreductase & cytochrome b5(Redox partners) play pivotal roles in CYP1A2's enzymatic activities. Cytochrome b5, for instance, enhances specific cytochrome P450 monooxygenase reactions, augmenting the catalytic efficiency of CYP1A2. Meanwhile, NADPH-cytochrome P450 oxidoreductase (CYPOR) serves as the primary electron donor, facilitating electron transfer to all microsomal cytochromes P450, including CYP1A2. Furthermore, important motifs within CYP1A2 were identified through motif scanning techniques, unveiling their strategic positions within the protein structure. The accompanying diagram illustrates the precise locations of these motifs, providing valuable insights into their functional roles and contributions to CYP1A2's enzymatic capabilities.

Structural Variations in CYP1A2 and Alpha-Naphthoflavone (ANF) binding to Active Site Mediated Suppression

Within the structure of Cytochrome P450 1A2 (CYP1A2), certain regions exhibit notable divergence, particularly influencing substrate binding and catalytic activity. The most divergent regions turned out to be the C-terminal loop and the distal binding sites of the substrate binding cavity, imparting significant flexibility to this enzyme's ability to oxidize a broad range of structurally distinct substrates. A unique feature of CYP1A2 is observed in the F-G region, characterized by a reverse amphipathic nature resulting from substantial insertions between helices F and G. This structural alteration leads to a hydrophobic surface near the protein's tip, just about the transmembrane domain. This hydrophobic surface typically interfaces with a membrane, juxtaposed to the catalytic site. Despite existing as a helical fragment rather than a typical alpha-helix, this region maintains crucial reverse amphipathicity, critical for CYP1A2 function. In the B-C region of CYP1A2, three polar residues—Thr118, Ser122, and

Thr124—are strategically positioned, pointing towards the active site cavity. Notably, both Thr118 and Thr124 play unique roles in substrate interactions.

Thr118 promotes stable hydration within the distal active site, particularly with smaller substrates, while Thr124 aids in orienting substrates for specific enzymatic activities, including N-hydroxylation of heterocyclic aryl amines and dealkylation of resorufins. Additionally, both Thr118 and Thr124 contribute to the formation of hydrogen bonds with caffeine's carbonyl oxygen atoms. The active site is enriched with amino acid residues residing on helices F and I, that constitute dual substrate-binding platforms, flanking the cavity. Helix- F undergoes disruption across the distal surface by losing the pattern of hydrogen bonding at Val220 and Lys221, resulting in the unwinding of the helix.

Water-bridged contacts involving Thr223 play a pivotal role in this disruption, forming key interactions with solvent molecules and ultimately causing a bend in helix- F that closes down the cavity of the active site. An estimated volume of the active site, approximately 375 angstroms, underscores the critical involvement of these structural alterations in modulating substrate-binding and efficiency of catalysis. The analysis highlights the dynamic and functionally crucial regions within CYP1A2, shedding light on the structural adaptations that enable its broad substrate specificity. Understanding these structural variations is essential for elucidating the enzyme's diverse enzymatic capabilities and its role in xenobiotic metabolism.

The visual representation of key hydrogen bonds between amino acids and the heme moiety within close proximity, crucial for stabilizing the substrate binding cavity and optimizing enzymatic activity. Alpha-naphthoflavone (ANF) acts as a competitive inhibitor of CYP1A2 catalytic reactions by closely matching size & shape of the substrate -binding cavity, resulting in Van der Waals forces primarily from the non-polar side chains. According to the scientists' belief, ANF is metabolized rapidly by CYP1A1 to form ANF-5,6-diol & ANF-5,6-oxide. However, there happens a limited oxidation of ANF by CYP1A2.

ANF inhibits P450 1A2 in part because of the higher-affinity binding shown by the reduced oxidation rate. This property makes ANF useful for distinguishing the P450 family 1 enzymes. Alpha-naphthoflavone binds within CYP1A2's active site, positioned right above heme's distal surface. The electron density map's curvature can be used to determine this inhibitor's orientation. ANF forces the phenyl ring to be near the heme iron by binding in a single favoured configuration. This binding process is supported by the electron density map narrowing at the interface between the phenyl ring and the benzo-h-chromen-4-one moiety, as shown in Fig. 1 with red-colored heme and yellow ANF.

The substrate-binding site within the CYP1A2 complex features a uniformly narrow structure throughout its extent. Residues from helices F and I play a critical role in defining this planar substrate binding site. Particularly, Phe226 on helix F contributes to creating a parallel substrate-binding surface; any distortion in this structure results in a narrower substrate-binding cavity. Having no solvent channels in the CYP1A2 complex linked with ANF is indicative of this stable and narrow arrangement, which lowers the probability for water to occupy the cavity. Only one molecule of water is observed within the active site cavity, and there doesn't appear to be any solvent routes joining the protein surface to the cavity. This water molecule makes hydrogen bonding with the carbonyl groups of ANF & Gly316 on helix- I. The peptide backbone causes substrate-binding cavity to adopt a rather flat conformation, resulting in near-perfect coplanarity of Ala317 side chain, Gly316-Ala317 peptide link & Asp320-Thr321 peptide bond.

Strong hydrogen bonding between Thr223 on helix- F and Asp320 on helix- I, which connect the two helices at the cavity's roof, help to stabilise the active site's structure. Hydrogen-bonded water molecules, as well as the side chains of Tyr189, Val220, Thr498, and Lys500, influence active site's stability. A comprehensive understanding of the interactions involving these helices is illustrated in Figure 1.

DISCUSSION

The term "In Silico" refers to work conducted via computer simulation or computational methods. By integrating scientific experiments with theoretical and mathematical modeling, researchers can gain valuable insights. This interdisciplinary

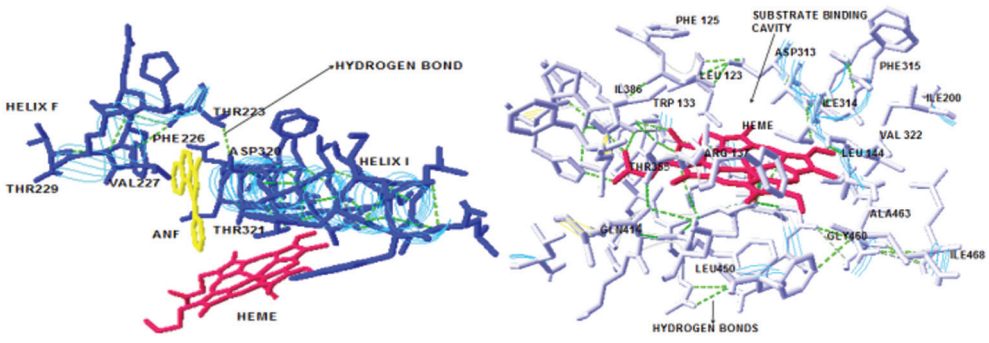

Figure 1: Structural Motifs of CYP1A2 and hydrogen bond interactions between amino acids and heme.

approach combines vivid computational imagery with biochemical experiments, offering critical information on the interactions between various intracellular components[18]. Collaborative investigations, combining physical techniques with chemical modification, immuno-localization studies, and site-directed mutagenesis experiments have increasingly verified the hypotheses based on P450 enzyme homology modelling.

Studies have found some common features of CYP1A2 ligands. These typically consist of one to two hydrophobic areas, one aromatic ring & one hydrogen bond acceptor [14]. Mutagenesis investigations have identified many amino acids within the substrate recognition sequence (SRS) sections of CYP1A2 that play critical roles in substrate-enzyme interactions, which is supported by homology modelling. Notable residues include Arg108, Thr124, Thr223, Glu225, Phe226, Lys250, Arg251, K253, Asn312, Asp313, Glu318, Thr319, Asp320, Thr321, Val322, Leu382, Thr385, and Ile386 [19]. Furthermore, research on non-SRS areas has shown that residues critical for ligand-CYP1A2 interactions include Lys99, Arg137, Gln141, Phe186, Phe205, Val227, Lys453, Arg455, and Thr501 [20].

Mammalian CYPs share a conserved core structure encompassing a heme-binding site & a proximal surface believed to interact with cytochrome b5 and other cytochrome P450 proteins. The structure of CYP1A2 differs from other family members due to variations in loop lengths connecting conserved secondary structures. Interestingly, CYP1A2 exhibits the F-helix disruption but CYP2A6 does not, suggesting a potentially less compact active site. On the other hand, a coil that joins F and F' in CYP3A4 extends above its active site. For CYP1A2, the active site cavity volume is about 375 Å, while the reported volumes for CYP2A6, CYP2C8, and CYP3A4 are 260 Å, 1438 Å, and 1385 Å, respectively [8]. This work supports ANF to be a potent inhibitor of CYP1A2, while Coumarin and Ketoconazole are identified as potent inhibitors for CYP2A6 and CYP3A4 respectively[10,11]. It is noteworthy that CYP1A2 cannot oxidize ANF, a capability possessed by CYP1A1[13]. The active site of P450 2A6 resembles the active site of P450 1A2, being approximately 50% bigger in volume though[14]. Typically, P450 1A2 exhibits a high-spin iron configuration in its native state, with no apparent solvent channels observed in crystal form. Mutants such as D320A, F226Y, and F226I display reduced catalytic efficiency, possibly due to alterations in the iron-oxygen intermediate [15]. Notably, mutations like CYP1A1 V328L and CYP1A2 L382V have been observed to alter substrate specificity. Cytochrome P450 enzymes are predominantly found in the hepatocytes but are also distributed throughout various cells in the body. They are localized inside the endoplasmic reticulum (ER) and mitochondria. Enzymes in the ER typically metabolize the foreign substances, especially drugs & environmental pollutants, while those in mitochondria are involved in synthesizing and metabolizing internal substances. These enzymes play a crucial role in drug metabolism, accounting for 70 to 80 percent of the enzymes involved.

Among the various P450 families, including 1, 2, and 3, enzymes within families 1, 2, and 3 are particularly significant in transforming xenobiotics into more polar metabolites that can be excreted. Recent studies indicate a strong link between exposure to dietary carcinogens like polycyclic aromatic hydrocarbons and colorectal cancer risk. Family -1 enzymes oxidize the polycyclic aromatic hydrocarbons efficiently. This study reports on the structural characterization of cytochrome P450 1A2, exploring its connection with substrates & inhibitors and emphasising structural distinctions. The developed models provide fast and precise tools for understanding CYP1A2's structure and comparing it with other cytochrome P450 family members. Notably, CYP1A2 shows a<40% amino acid sequence identity as compared to enzymes like 2A6, 2B4, 2C5, 2C8, 2C9, 2D6, and 3A4, making comparisons primarily with CYP2A6 & CYP3A4 more relevant. Analysis of cytochrome P450 1A2 structure serves as a foundational platform for further exploring its clinical and toxicological significance. Understanding the unique structural features of CYP1A2 enhances insights into its function and impact on drug metabolism and toxicology.

CONCLUSION

The structural analysis of cytochrome P450 1A2 provides valuable insights into its substrate interactions and inhibitor binding, shedding light on its unique features compared to other cytochrome P450 family members. The study highlights the adaptation of CYP1A2 with a compact and closed active site cavity, well-suited for oxidizing large planar substrates. Key findings include the significant structural differences between CYP1A2 and related enzymes, with less than 40% sequence identity compared to several other P450s. The study predominantly compares CYP1A2 with CYP2A6 and CYP3A4 due to these differences. The developed structural models offer a fast and precise method for studying CYP1A2, aiding in understanding its role in drug metabolism and toxicology. These findings provide a foundation to further explore the clinical & toxicological implications associated with cytochrome P450 1A2, for future research and potential therapeutic interventions.

AUTHORS' CONTRIBUTION

Zahra Zahid Piracha, Umar Saeed, Naila Azam	Drafting the Article
Zahra Zahid Piracha, Umar Saeed, Naila Azam	Analysis and interpretation of data
Zahra Zahid Piracha, Umar Saeed	Conception and design
Zahra Zahid Piracha, Umar Saeed, Naila Azam	Acquisition of data
Zahra Zahid Piracha, Umar Saeed, Naila Azam	Critical revision

REFERENCES

1. Granfors MT, Backman JT, Neuvonen M, et al. Ciprofloxacin greatly increases concentrations and hypotensive effect of tizanidine by inhibiting its cytochrome P450 1A2-mediated presystemic metabolism. Clin Pharmacol Ther. 2004;76(6):598–606.
2. Vasanthanathan P, Taboureau O, Oostenbrink C, et al. Classification of cytochrome P450 1A2 inhibitors and noninhibitors by machine learning techniques. Drug Metabolism and Disposition. 2009; 37 (3) 658-664.
3. P05177 · CP1A2_HUMAN [Internet].Cambridgeshire(CB): Elixir, Welcome Genome Campus Hixton.[cited 2024 Feb 26]. Available from http://www.uniprot.org/uniprot/P05177.
4. Nebert DW,Russell DW. Clinical importance of the cytochromes P450. Lancet. 2002; 360(9340):1155-1162.
5. Bauer E, Guo Z, Ueng YF Bell, et al, P. Oxidation of benzo[a]pyrene by recombinant human cytochrome P450 enzymes. . Chem Res Toxicol. 1995;8(1):136-42.
6. Shimada T, Yamazaki H, Foroozesh M, et al. Selectivity of polycyclic inhibitors for human cytochrome P450s 1A1, 1A2, and 1B1. Chem Res Toxicol. 1998;11(9):1048–1056.
7. Gunes A, Dahl ML. Variation in CYP1A2 activity and its clinical implications: influence of environmental factors and genetic polymorphisms. Pharmacogenomics. 2008;9(5):625–37.
8. Zhou SF, Wang, B, Yang, LP, et al. Structure, function, regulation and polymorphism and the clinical significance of human cytochrome P450 1A2. Drug Metab Rev. 2010; 42(2): 268–354.
9. Ikeya K, Jaiswal AK, Owens RA, et al. Human CYP1A2: sequence, gene structure, comparison with the mouse and rat orthologous gene, and differences in liver 1A2 mRNA expression. Mol Endocrinol. 1989;3(9):1399–1408.
10. Lewis DF, Lake BG, Dickins M, et al. Homology modelling of human CYP1A2 based on the CYP2C5 crystallographic template structure. Xenobiotica. 2003;33(3):239–254.
11. Rendic S. Summary of information on human CYP enzymes: human P450 metabolism data. Drug Metab Rev. 2002;34(1-2):83–448.
12. Parker AC, Preston T, Heaf D, et al. Inhibition of caffeine metabolism by ciprofloxacin in children with cystic fibrosis as measured by the caffeine breath test. Br J Clin Pharmacol. 1994;38(6):573–576.
13. Caldwell J. The current status of attempts to predict species differences in drug metabolism. Drug Metab Rev.1981;12(2): 221–237.
14. Shimizu T, Tateishi T, Hatano M,et al. Probing the role of lysines and arginines in the catalytic function of cytochrome P450d by site-directed mutagenesis. Interaction with NADPH-cytochrome P450 reductase. J Biol Chem. 1991;266(6):3372–3375.
15. Smith DA, Ackland MJ, Jones BC, et al. Properties of cytochrome P450 isoenzymes and their substrates part 2: properties of cytochrome P450 substrates. Drug Discov Today. 1997;2(11):479 – 486.
16. Saeed U, Waheed Y, Anwar A, et al . In-Silico Binding of ATP to Protein Kinase C Delta: Insights into the Structure and Active Site. Eur J Sci Res.2011; 52 (2) :177-187.
17. Liu J, Ericksen SS, Sivaneri M, et al. The effect of reciprocal active site mutations in human cytochromes P450 1A1 and 1A2 on alkoxyresorufin metabolism. Arch Biochem Biophys. 2004;424(1):33–43.
18. Zhou SF, Yang LP, Zhou ZW, et al. Insights into the substrate specificity, inhibitors, regulation, and polymorphisms and the clinical impact of human cytochrome P450 1A2. APPS J. 2009;11(3):481-494.
19. Sansen S, Yano JK, Reynald RL, et al. Adaptations for the oxidation of polycyclic aromatic hydrocarbons exhibited by the structure of human P450 1A2. J Biol Chem. 2007;282(19):14348-14355.
20. Cho US, Park EY, Dong MS, et al. Tight-binding inhibition by α-naphthoflavone of human cytochrome P450 1A2. Biochim Biophys Acta. 2003;1648(1-2):195–202.

ORIGINAL ARTICLE

PATTERN OF DENTAL DISEASES AMONG PATIENTS PRESENTING AT A TERTIARY CARE HOSPITAL

Ghulam Mustafa[1], Fahad Amjad Sheikh[2], Sana Shaukat Siddiqui[3]

[1]Assistant Professor Community Medicine, [2]Dental Surgeon/Administration Registrar, [3]Associate Professor Community Medicine, Sheikh Zayed Medical College, Rahim Yar Khan

ABSTRACT

Objective: To determine the pattern of the dental diseases among patients attending dental department of the Sheikh Zayed Hospital Rahim Yar Khan.

Study Design: Cross-sectional study.

Place and Duration of Study: Sheikh Zayed Hospital, Rahim Yar Khan. 06 months(July-December 2023).

Material and Methods: The study was carried out at the Dental Outpatient Department (OPD) of Sheikh Zayed Medical College and Hospital. Consecutive sampling was used to enroll a total of 300 patients. Patients of any age with dental conditions, regardless of gender, who were undergoing treatment at the Dental OPD were eligible to participate as long as they fulfilled the inclusion requirements. A predesigned and pretested questionnaire covering relevant study variables including demographic and different dental diseases was used for data collection. For analysis, data were imported into SPSS version 20.

Results: A total of 300 patients were included in the study, the mean age was 31±15 years, 181 (60.3%) were females. Most of the patients 160 (53.3%) presented with dental caries, 41(13.7%) with broken down root, 14 (4.7%) with calculus, 14 (4.7%) with gingivitis, 12 (4%) with periodontal disease, 6 (2%) with malaligned teeth, 4 (1.3%) with trauma, 1 (0.3%) with staining, 48(16%) with other diseases. About one third 93 (31%) of the patients had duration of disease as more than a year.

Conclusion: This study provides valuable insights into the distribution and management of dental diseases in a tertiary care setting. It emphasizes the need for targeted interventions to address dental health disparities and improve access to care in resource-constrained regions. Future research should focus on the socio-economic, environmental, and behavioral determinants of dental diseases to develop effective prevention and treatment strategies.

Keywords: *Calculus, Caries, Dental diseases, Frequency, Gingivitis*.

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INTRODUCTION

Dental disorders are among the most common health problems in the world, affecting people of all ages and socioeconomic status [1]. Although the prevalence of some dental problems has decreased as a result of preventive efforts like fluoridation and education on oral cleanliness, there are still gaps in access to oral healthcare services, especially in underprivileged communities [2]. For efficient resource allocation, management, and prevention within healthcare systems, it is imperative to comprehend the patterns and trends of dental illnesses.

In the management of complicated and advanced dental illnesses, tertiary care facilities are essential. They frequently act as referral hubs for patients in need of specialized oral healthcare procedures [3,4]. Even with their importance, there is still a dearth of study on the prevalence and epidemiology of dental disorders in tertiary care settings, especially when considering a variety of patient populations and geographical areas [5]. By providing a thorough examination of the pattern of dental illnesses at a tertiary care hospital, this research piece seeks to close this gap. We aim to offer important insights into the burden of oral health disorders and the difficulties faced by patients and healthcare providers by looking at the prevalence, demographics, clinical presentations, and associated factors of various dental conditions encountered in this setting [6,7].

Additionally, a comprehensive grasp of the range of dental conditions found in tertiary care facilities is necessary to improve clinical judgment, maximize therapeutic approaches, and guide public health campaigns meant to lower the prevalence of oral disorders in general [8,9]. Furthermore, recognizing recurring patterns and new trends can help direct the creation of focused interventions and preventative measures catered to the unique requirements of the patient population, these specialized healthcare facilities serve [10,11]. This study seeks

Correspondence to: Dr. Ghulam Mustafa, Associate Professor Community Medicine, Sheikh Zayed Medical College, Rahim Yar Khan.

Email: mustafa.hsa@gmail.com

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to contribute to dental epidemiology by thoroughly analyzing patient records, clinical data, and diagnostic information. It also provides practical implications for improving the delivery of oral healthcare within tertiary care settings. Ultimately, our goal is to enable the development of more efficient methods for promoting oral health and enhancing patient outcomes by illuminating the complex patterns of dental illnesses seen in this environment.

CAPSULE SUMMARY

This study provides useful information about the prevalence of dental illnesses in the area demanding focused initiatives to enhance oral health outcomes and accessibility to dental care services. Based on this study, future research should explore the underlying determinants of dental diseases.

MATERIAL AND METHODS

The study was carried out at the Sheikh Zayed Medical College and Hospital's Outpatient Department (OPD) of the Dental Department in association with Community Medicine Department at Rahim Yar Khan. It used a cross-sectional design. The period of the study was June through December 2023. Assuming that 23% of the subjects in the population have the factor of interest i.e. dental problem,[11] the study required a sample size of 273 for estimating the expected proportion with 5% absolute precision and 95% confidence. The sample size was enhanced to 300 for improved representation and validity. Consecutive sampling technique was used to enroll a total of 300 patients. Patients of any age with dental conditions, regardless of gender, who were undergoing treatment at the Dental OPD of Sheikh Zayed Medical College and Hospital were eligible to participate as long as they fulfilled the inclusion requirements. Those patients who refused to take part in the trial were not included in the study. A predesigned and pretested questionnaire covering relevant study variables was used for data collection. Prior to the start of data collection, all patients who met the inclusion criteria such as patients of any age with dental conditions, regardless of gender, and exclusion criteria including those did not give consent for data collection, were informed of the objective of the study and were ensured of the confidentiality. The Institutional Review Board provided its ethical clearance. For analysis, data were imported into SPSS version 20. For numerical variables mean and standard deviation, such as age, monthly household income (in Pakistani Rupees), and illness duration were summarized. The percentages of several categorical characteristics, such as comorbidities, frequency of dental conditions, gender, residence, and education level, were displayed.

RESULTS

Of the 300 patients included in the study, the mean age was 31±15 years. Table 1 shows the demographic characteristics of the study participants. Similarly, Table 2 underscores the clinical characteristics of the patients included in the study. The mean duration of the disease was 580±80 days.

It is evident from figure 1 that a substantial number of patients 160 (53.3%) presented with dental caries, 4 (1.3%) with trauma, 41(13.7%) with broken down root, 14 (4.7%) with calculus, 12 (4%) with periodontal disease, 14 (4.7%) with gingivitis, 6 (2%) with malaligned teeth, 1 (0.3%) with staining, 48(16%) with other diseases. Table 2 outlines patient characteristics, including disease duration, with 93 patients (31%) having been ill for over a year. Dental caries affect the majority, with 160 patients (53.3%) diagnosed, and 250 patients (83%) have already received treatment for dental disease.

DISCUSSION

The study sought to assess the distribution of dental diseases among patients in the dental outpatient

Table 1: Demographic characteristics of the study participants

DEMOGRAPHIC PROFILE		n	%
Gender			
	Male	119	39.7
	Female	181	60.3
Residence			
	Rural	126	42
	Urban	174	58
Education			
	Illiterate	87	29
	Primary	97	32.3
	Matric	79	26.3
	Graduate	33	11
	Postgraduate	4	1.3
Monthly Family Income (Rs.)			
	≤ 18000	185	61.7
	18001-40000	99	33
	≥ 40000	16	5.3

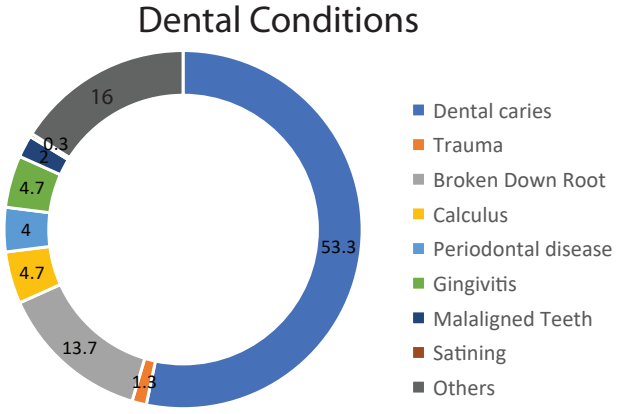

Figure 1: Dental diseases distribution among study population.

Table 2: Clinical characteristics of the study participants

CLINICAL PROFILE			
Disease Duration Groups		n	%
	Less than a month	69	23
	2-6 months	71	23.7
	7-12 months	67	22.3
	More than 1 year	93	31
Primary Diagnosis			
	Dental Caries	160	53.3
	Others	140	46.7
Comorbidities			
	None	228	76
	Diabetes Mellitus	23	7.7
	Hypertension	24	8
	Hepatitis	12	4
	Others	13	4.3
Affected Teeth Quadrant			
	Upper Right	49	16.3
	Upper Left	48	16
	Lower Right	98	32.7
	Lower Left	62	20.7
	Generalized	43	14.3
Recommended Treatment			
	RCT (Root Canal Treatment)	69	23
	Filling	28	9.3
	Extraction	116	38.7
	Others	87	29
Treatment Availed			
	Yes	250	83.3
	No	50	16.7
Treatment Provider (among those who received treatment)			
	Doctor	223	89.2
	Quack	27	10.8

- *Rs. refers to Pakistani Rupees.*
- *RCT (Root Canal Treatment) is a dental procedure to treat a severely infected tooth.*
- *Quack refers to a person who pretends to have medical skills that they do not possess.*

department of a tertiary care hospital and investigate the burden of dental diseases frequency and other variables in order to comprehend the behavioral approach of patients to disease management.

The demographic and clinical features of the patient group have been revealed by key findings. The mean age was 31±15 years, with almost one third 93 (31%) have duration of dental disease of more than 1 year. A family's monthly income of less than RS. 18000/- was noted in 185 (61.7%). The mean duration of disease was 580 days.

Analyses in comparison with other study provide insight into the dental care-seeking practices. For example dental diseases were found more among low income population, illiterate or low education level, and more in urban residence, which was consistent with the trends we saw in our study [10].

Dental caries was shown to be the most common dental ailment, affecting 53.3% of patients. This is in contrast to other researches where gum disease was more prevalent and tooth loss was more due to periodontal disease[11,12]. The study also revealed low awareness of and attitudes toward routine dental care, with a sizable percentage of patients delaying treatment until an issue developed. Different treatments were suggested, and a sizable percentage of patients chose extraction. Remarkably, a sizeable portion of patients sought care from non-professional sources, highlighting inadequacies in official dental care provision.

Interesting trends emerged from the analysis of disease duration by gender, residency, and income. For instance, compared to men, a larger percentage of females experienced longer disease durations. In a similar study, patients' illness durations tended to be higher for those with lower incomes and those living in rural areas[13].

Overall, the study offers insightful information about the prevalence and treatment of dental illnesses in the area, highlighting the necessity of focused initiatives to enhance oral health outcomes and accessibility to dental care services. Despite its contributions, this study has several limitations that warrant consideration. Firstly, it was a small sample size study and carried out at a single center. Additionally, the reliance on self-reported data and the use of a consecutive sampling method may introduce bias and affect the generalizability of the findings.

Building on the findings of this study, future research should explore the underlying determinants of dental diseases including socio-economic, environmental, and behavioral factors. Longitudinal studies tracking oral health outcomes longitudinally can provide insights into the natural history of dental diseases and help identify modifiable risk factors for targeted intervention.

CONCLUSION

In conclusion, this study sheds light on the patterns of dental diseases in our study subjects and underscores the need for targeted interventions to address the significant burden of dental health issues in the area. By identifying prevalent conditions and demographic disparities, the findings of this study contribute to the evidence base for designing effective dental health promotion strategies and improving access to dental care services.

AUTHORS' CONTRIBUTION

Ghulam Mustafa, Sana Shaukat Siddiqui	Drafting the Article
Fahad Amjad Sheikh, Sana Shaukat Siddiqui	Analysis and interpretation of data
Ghulam Mustafa, Fahad Amjad Sheikh	Conception and design
Ghulam Mustafa, Fahad Amjad Sheikh, Sana Shaukat Siddiqui	Acquisition of data
Ghulam Mustafa, Fahad Amjad Sheikh, Sana Shaukat Siddiqui	Critical revision

REFERENCES

1. Selvaraj S, Naing NN, Wan-Arfah N, et al. Epidemiological factors of periodontal disease among South Indian adults. J Multidiscip Health. 2022 :15:1547-1557.
2. AlTuraiki AM, Jaemal HM, Alamer AA, et al. Oral Health and Patterns of Dental Visits Among Diabetic Patients in the Eastern Province of Saudi Arabia. Clin Cosmet Investig Dent. 2021 ;13: 513-520.
3. Kumar A, Saini RS, Sharma V, et al. Assessment of Pattern of Oral Prosthetic Treatment and Prevalence of Oral Diseases in Edentulous Patients in North Indian Population: A Cross-sectional Study. J Pharm Bioallied Sci. 2021;13(Suppl 1):S187-S189.
4. Nagarajappa R, Ramesh G, Uthappa R, et al. Risk factors and patterns of traumatic dental injuries among Indian adolescents. J Dent Sci. 2020;15(1):96-103.
5. Batra P, Saini P, Yadav V. Oral health concerns in India. J Oral Biol Craniofac Res. 2020;10(2):171-174.
6. Ramanarayanan V, Karuveettil V, Sanjeevan V, et al. Measuring dental diseases: A critical review of indices in dental practice and research. Amrita J Med. 2020 ; 16(4):152-158.
7. Hopcraft M, Farmer G. Impact of COVID-19 on the provision of paediatric dental care: Analysis of the Australian Child Dental Benefits Schedule. Community Dent Oral Epidemiol. 2021;49(4):369-376.
8. Moharrami M, Bohlouli B, Amin M. Frequency and pattern of outpatient dental visits during the COVID-19 pandemic at hospital and community clinics. J Am Dent Assoc. 2022; 153(4): 354-364.
9. Watson S, Woodside JV, Winning L, et al. Associations between self-reported periodontal disease and nutrient intakes and nutrient-based dietary patterns in the UK Biobank. J Clin Periodontol. 2022;49(5):428-438.
10. Gao X, Ding M, Xu M, et al. Utilization of dental services and associated factors among preschool children in China. BMC Oral Health. 2020 ;20(1):9-18.
11. Almotairy N, Althunayyan A, Alkhuzayyim D, et al. Dental pattern diversity in a Saudi Arabian population: An orthopantomogram-based study. Saudi J Health Sci. 2022 ;11(3):190-196.
12. Alonaizan FA, Almas K, Nazir MA,et al. Medical conditions, oral health practices, and barriers to treatment among patients visiting a teaching dental hospital in Eastern Saudi Arabia. Sci World J. 2022;2022(2).1-7.
13. Alassiry A. Prevalence and distribution of selected dental anomalies in Najran City of Saudi Arabia. Egypt Dent J. 2020;66(3):1471-1482.

CASE REPORT

PULMONARY EMBOLISM IN A HIGH- RISK PREGNANCY: A CASE STUDY

Mahwash Jamil[1], Nida Khan[2], Shaista Zainab[3], Fehmida Shaheen[4]

[1]Associate professor HITEC-IMS, [2]Senior Registrar HITEC-IMS , [3]Post graduate trainee HITEC-IMS, [4]Professor HITEC-IMS

ABSTRACT

Management of high-risk pregnancy is challenging for the caregivers, and a healthy feto-maternal outcome is the utmost aim for antenatal care. A good pre-pregnancy screening, vigilant monitoring for obstetrical complications in pre and postnatal periods, multidisciplinary approach and timely decisions are key factors for successful management.

Keywords: *High risk pregnancy, Pregnancy, Pulmonary embolism*

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INTRODUCTION

A high-risk pregnancy is defined as a pregnancy where a woman and fetus have higher chances of adverse outcomes, as a result of pregnancy itself or because of pre-existing diseases such as diabetes, hypertension, autoimmune disorders, obesity etc[1]. Risk factors such as previous miscarriages and the existence of genetic disorders not only affect the outcome of the affected pregnancy but their chances of recurrence are very high in future pregnancies, thus affecting the physical and mental health of the woman[2].

This case study highlights the importance of individual antenatal care in high- risk pregnancy with regular and vigilant monitoring to have a healthy outcome for both mother and baby.

Case:

A female of 30 years of age, married for 9 years G5P3+1(with one alive issue) was booked at 8 weeks of pregnancy. Her Body mass index (BMI) calculated at the time of booking was 40, which fell into grade 3 obesity.

Her previous four pregnancies had complications with only one successful outcome of a baby girl in the second pregnancy. The first conception was eight years back which was complicated by polyhydramnios and intrauterine death which she delivered through caesarean section, due to failed induction. The second pregnancy was uneventful five years back, delivered through caesarean section and the outcome was a baby girl, alive and healthy. The third pregnancy two and half years back was complicated by gestational diabetes and delivered by caesarean section at 30 weeks due to preterm labor. The outcome was a baby boy, dying in the early neonatal period, on the third day. Her fourth pregnancy ended up as a first-trimester miscarriage which had a complication of excessive bleeding for which evacuation exploratory laparotomy was done with the application of Blynch suture.

CAPSULE SUMMARY

Management of high risk pregnancy requires a good pre-pregnancy screening program, vigilant monitoring for obstetrical complications in prenatal and postnatal periods, multidisciplinary approach and timely decisions to avoid any serious out come.

In this pregnancy, the patient was vigilantly monitored for any complication, especially considering her past obstetrical history for recurrence of risk factors such as diabetes, polyhydramnios and preterm delivery. At 23 weeks, on the anomalies scan, cervical length was found to be shortened for which progesterone support was given and cervical cerclage applied. Followed in the outpatient department till 35 weeks regularly and was screened for risk factors on every visit, she was admitted again for evaluation of raised blood glucose levels. During her hospital stay, Dexamethasone was given, and her blood sugar level was controlled through the American Diabetes Association-recommended diet plan and insulin on a sliding scale. A few days later during her admission, she developed lower abdominal pain, and considering her past obstetrics and present history of cerclage, her emergency cesarean section was done at 36 weeks. Intraoperative findings included a thinned-out scar, about to rupture with grade 1 meconium. The outcome of the cesarian section was a baby girl, with a good Apgar score, who was shifted to the Neonatal Intensive Care

Correspondence to: Dr. Mahwash Jamil. Associate professor HITEC-IMS

Email: mahwashdr26@gmail.com

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Unit (NICU) for observation. No other operative complications were encountered and the patient was moved to the surgical intensive care unit for monitoring. On the day of surgery, she developed shortness of breath, which was evaluated by a multidisciplinary team including a gynecologist, anesthetist and a medical specialist. A diagnosis of pulmonary embolism was suspected due to an intermediate risk score of 5(Table 1&2). Arterial blood gas analysis suggested respiratory alkalosis (pH 7.49, PO_2 132 mm Hg, PCO_2 24.6 mm Hg, Bicarbonates 20.4 mmol/l). D- Dimers were 0.7 (Normal < 0.5). Lower molecular weight heparin and oxygen inhalation were started on clinical findings. ECG, X-ray chest and Computerized tomography of pulmonary arteries (CTPA) were done, which were normal. The patient's symptoms improved and she remained stable and was discharged in healthy condition.

Table 1: Risk factors for Venous Thrombosis

Risk factors for VTE		
Pre-existing risk factors	Tick	Score
Previous VTE (except a single event related to major surgery)		4
Previous VTE provoked by major surgery		3
Known high-risk thrombophilia		3
Medical comorbidities e.g. cancer, heart failure; active systemic lupus erythematosus, inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease; current intravenous drug user		3
Family history of unprovoked or estrogen-related VTE in first-degree relative		1
Known low-risk thrombophilia (no VTE)		1a
Age (> 35 years)		1
Obesity		1 or 2b
Parity ≥ 3		1
Smoker		1
Gross varicose veins		1
Obstetric risk factors		
Pre-eclampsia in current pregnancy		1
ART/IVF (antenatal only)		1
Multiple pregnancy		1
Caesarean section in labour		2
Elective caesarean section		1
Mid-cavity or rotational operative delivery		1
Prolonged labour (> 24 hours)		1
PPH (> 1 litre or transfusion)		1
Preterm birth < 37+0 weeks in current pregnancy		1
Stillbirth in current pregnancy		1
Transient risk factors		
Any surgical procedure in pregnancy or puerperium except immediate repair of the perineum, e.g. appendicectomy, postpartum sterilisation		3
Hyperemesis		3
OHSS		4
Current systemic infection (requiring intravenous antibiotics or admission to hospital)		1
Dehydration		1
TOTAL		

ART Assisted Reproductive Technology; IVF In Vitro Fertilisation; OHSS Ovarian Hyperstimulation Syndrome; VTE Venous Thromboembolism.

a. If the known low-risk thrombophilia is in a woman with a family history of VTE in a first-degree relative postpartum thromboprophylaxisshould be continued for 6 weeks.

b. BMI ≥ 30 = 1; BMI ≥ 40 = 2

Table 2: Risk assessment for venous thromboembolism (VTE)

(Adopted from Green-Top Guideline. 2015 (37a))[11]

If total score ≥ 4 risk factors antenatally, consider thromboprophylaxis from the first trimester. • If total score 3 risk factors antenatally, consider thromboprophylaxis from 28 weeks. • If total score ≥ 2 risk factors postnatally, consider thromboprophylaxis for at least 10 days. • If admitted to hospital antenatally consider thromboprophylaxis. • If readmitted to hospital within the puerperium consider thromboprophylaxis.

The patient was followed up in the obstetrical and medical outpatient department. Contraception was planned with injectable contraceptives after a discussion with the patient. Weight reduction was advised and referred to a dietician for weight reduction.

DISCUSSION

This was a high-risk pregnancy with poor outcomes in the previous four pregnancies which were complicated with polyhydramnios, diabetes, and preterm deliveries and with the added risk of three caesarean sections, had high chances of recurrence in the current pregnancy. In her current pregnancy at booking, she was classified as category 3 obesity, thus increasing the recurrence risk of the above complications.

Obesity is becoming an increasingly prevalent factor in obstetric practice, with 21.3% of the antenatal population being obese[3]. According to the MBRRACE-UK (Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK) review, 30% of women who died, were obese and 22% were overweight[4]. Other studies also reported that high pre- pregnancy BMI is associated with a small but statistically significant increase in severe maternal morbidity or mortality with the highest risk in class 3 obesity having an adjusted risk of 61.1 (95% CI 44.8–78.9)[3,5.] It is highly recommended that women in pre-pregnancy should be advised for effective contraception and weight reduction to optimize the weight of the patient[3]. Obesity in pregnancy is associated with increased risk of miscarriage, diabetes, hypertensive disorders especially preeclampsia, venous thromboembolism (VTE), induced labour, dysfunctional or prolonged labour, caesarean section, anesthetic complications, postpartum hemorrhage (PPH), wound infections and mortality [6].

Pregnancy with diabetes is also associated with high morbidity and mortality especially in obese patient, with increase risk of congenital anomalies, miscarriage, polyhydramnios, hypertensive disorders, operative deliveries and postpartum bleeding[7]. Optimization of blood sugar levels have crucial role in prevention of still birth in this condition. So it's recommended to monitor blood glucose levels seven times a day. The post-prandial levels have direct relation with fetal weight gain[8].

Repeated cesarean section increases the risk of placenta previa / accreta, resulting in high rate of maternal morbidity and mortality. It is recommended to rule out this condition before proceeding for cesarean delivery[9]. Increase need of blood transfusion, adhesions between uterus and abdominal walls, wound infections and breakdown, increase chances of VTE are few the complications that are encountered with increasing number of scars on uterus[10]. Localization of placenta can be done by experienced radiologist with transvaginal ultrasound and decreases the need of expensive investigations, like MRI, to rule out accrete[9].

The incidence of VTE is 1–2 per 1000. The puerperium is the time of highest risk so it's important to repeatedly do risk scoring of every individual especially at increased risk such as, having prolonged hospital stay and obesity-related medical disorders[11]. Timely diagnosis and treatment of the patient is only way for the patient to survive this potentially fatal condition. Venous Dopplers for both legs, ECG, CXR, ventilation/perfusion (V/Q) lung scan and CTPA, are the investigations of choice [12]. Any woman with a clinical suspicion of VTE should be started on treatment with low-molecular-weight heparin (LMWH) until the diagnosis is excluded by objective testing[11]. Although X-ray chest and CTPA were negative, our patient was at high risk, with clinical and laboratory parameters suggestive of Pulmonary embolism (with an intermediate risk score of 5).

Our case study highlights the importance of timely recognition of risk factors involved with pregnancy to have a favorable outcome. It also emphasizes the need for pre-pregnancy counseling to reduce risks in future pregnancies and population awareness should be done to emphasize its importance. Risk scoring for VTE should be done in every high-risk pregnancy with initiation of prophylaxis, as soon as possible. Last but not the least, timely involvement of different specialties (multidisciplinary approach) always results in a better outcome.

REFERENCES

1. Khadivzadeh T, Shojaeian Z, Sahebi A. High Risk-pregnant Women's Experiences of Risk Management: A Qualitative Study. Int J Community Based Nurs Midwifery. 2023;11(1):57-66.
2. Shojaeian Z, Khadivzadeh T, Sahebi A, et al. Perceived Risk in Women with High Risk Pregnancy: A Qualitative Study. Iran J Nurs Midwifery Res. 2021;26(2):168-174.
3. Denison FC, Aedla NR, Keag O, et al . Care of Women with Obesity in Pregnancy. Green-top Guideline No. 72. BJOG 2019 ;126(3):e62-e106.
4. Knight M, (ed.), Kenyon S, (ed.), Brocklehurst P, (ed.), et al. Saving lives, improving mothers' care: lessons learned to inform future maternity care from the UK and Ireland confidential enquiries into maternal deaths and morbidity 2009–12. Oxford: National Perinatal Epidemiology Unit: University of Oxford, 2014. 120 p.

5. National Institute for Health and Care Excellence. Obesity: Identification, Assessment and Management (CG 189) [Internet]. Manchester(UK):NICE; 2014 [updated 2023 July 26; Cited 2024 Apr 4]. Available from https://www.nice.org.uk/guidance/cg189.
6. Knight-Agarwal CR, Williams LT, Davis D, et al. Association of BMI and inter pregnancy BMI change with birth outcomes in an Australian obstetric population: a retrospective cohort study. BMJ Open. 2016;6(5): e010667-e010675.
7. Luesley DM, Kilby M editors. Obstetrics &Gynaecology: An evidence-based text for MRCOG [Internet]. Boca Roton (BC): CRC Press; [cited 2024 Mar 30]. https://www.taylorfrancis.com/books/edit/10.1201/b19647/obstetrics-gynaecology-mark-kilby-david-luesley.
8. National Institute of Health and Care Excellence. Diabetes in pregnancy: management from preconception to the postnatal period.[Internet]. Manchester(UK): NICE; 2015[updated 2020 Dec 16;cited 2024 March 30]. Available from https://www.nice.org.uk/guidance/ng3/resources/diabetes-in-pregnancy-management-from-preconception-to-the-postnatal-period-pdf-51038446021.
9. Jauniaux ER, Alfirevic Z, Bhide AG, et al. Placenta praevia and placenta accreta: diagnosis and management: green-top guideline no. 27a. BJOG. 2018;126 (1):e1-48.
10. Royal College of Obstetricians and Gynecologists. Birth after previous caesarean birth. Green-top guidelines (45).[Internet]. Manchester(UK):NICE; 2015 [updated 2015 Oct 1; Cited 2024 Apr 4]. Available from https://www.rcog.org.uk/guidance/browse-all-guidance/green-top-guidelines/birth-after-previous-caesarean-birth-green-top-guideline-no-45/.
11. Royal College of Obstetricians and Gynecologists. Reducing the risk of venous thromboembolism during pregnancy and the puerperium.. Green-top guidelines (37a).[Internet]. Manchester(UK):NICE; 2015 [updated 2015 April 13 ; Cited 2024 Apr 4]. Available from https://www.rcog.org.uk/guidance/browse-all-guidance/green-top-guidelines/reducing-the-risk-of-thrombosis-and-embolism-during-pregnancy-and-the-puerperium-green-top-guideline-no-37a/.
12. Royal College of Obstetricians and Gynecologists. The Acute Management of Thrombosis and Embolism during Pregnancy and the Puerperium. Green-top guidelines (37b [Internet]. Manchester(UK):NICE; 2015 [updated 2015 April 13 ; Cited 2024 Apr 4]. Available from https://www.rcog.org.uk/guidance/browse-all-guidance/green-top-guidelines/thrombosis-and-embolism-during-pregnancy-and-the-puerperium-acute-management-green-top-guideline-no-37b/.

DIAGNOSTIC CHALLENGE

Check the correct answer on page 34

Case 1

Courtesy Dr. Moizza Tahir, Dr Jauhar Mumtaz
Pak Emirrate Military Hospital (PEMH), Rawalpindi

Figure 1

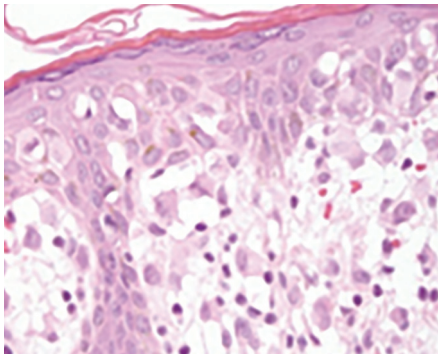

Figure 2a

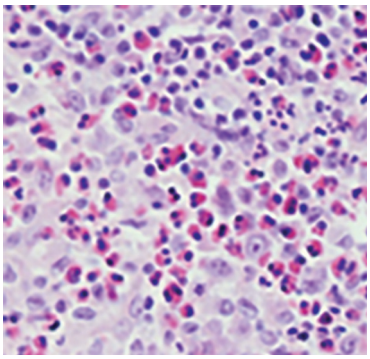

Figure 2b

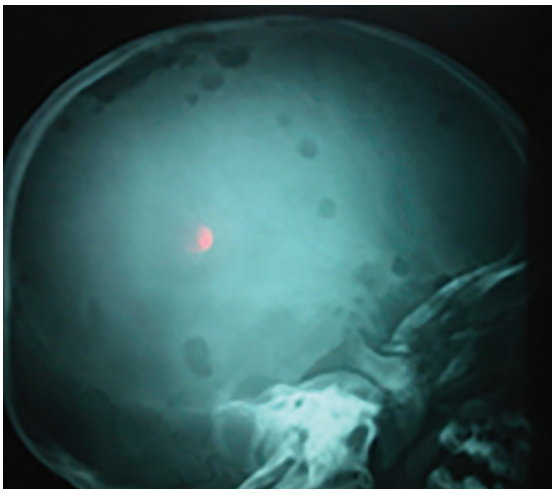

Figure 3

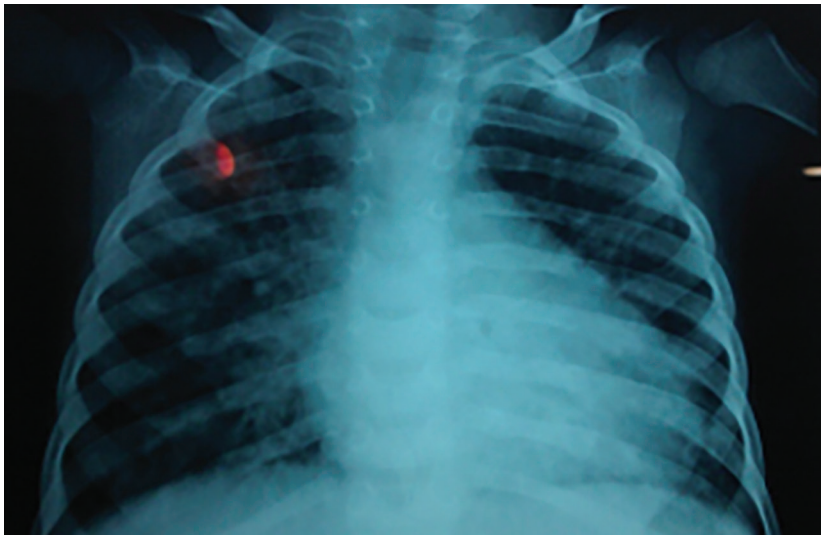

Figure 4

A three and a half years-old-child presented with a history of low-grade fever, off and on for nine months. There was a two-month history of progressive pallor, cough, skin rash, polydipsia, polyuria and a five-day history of epistaxis. Examination revealed pallor, proptosis, right posterior cervical lymphadenopathy, bilateral coarse lung crepitation and hepatosplenomegaly. There was erythematous macular rash over the scalp, covered with greasy crusts and showed multiple petechial spots over its surface (Figure1). Blood complete picture revealed TLC of 4.6 x10^9 /l, Hb 2.6 G/dl and Platelets 50/mm^3. Urine examination showed osmolality of <300mOsmol/L. Bone marrow biopsy showed a granulomatous infiltrate. Skin biopsy findings are shown in Figure 2a & b. X ray skull (Figure 3) and chest X ray (Figure 4) was also done.

1. What is your diagnosis?
2. What further investigation will you perform on skin biopsy specimen in order to confirm your diagnosis.

DIAGNOSTIC CHALLENGE

Check the correct answer on page 36

Case 2

Courtesy Dr. Memoona Aslam
Combined Military Hospital, Rawalpindi

Figure 1

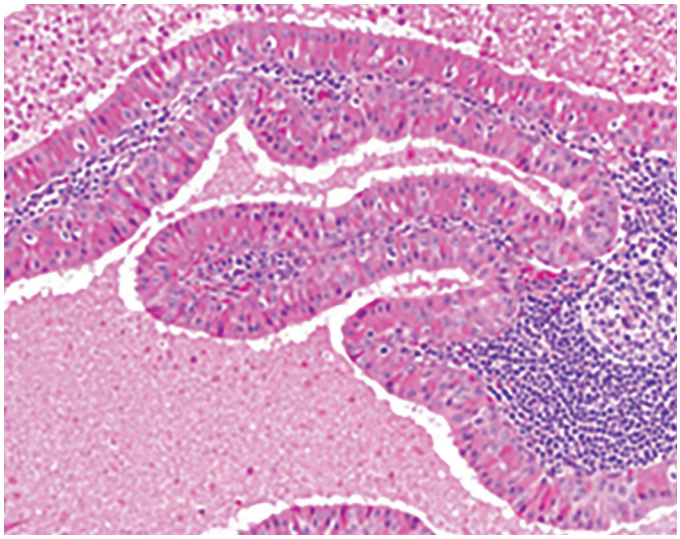

Figure 2

A 59-year-old male patient, a smoker for the past 30 years, presented with a complaint of a painless swelling near his left ear which he first noticed three months ago. The lump had been gradually increasing in size without causing pain or discomfort. On examination, a 3cm, firm, non-tender, mobile mass was found at the angle of the right mandible (Figure 1). Histopathological examination was performed to confirm the diagnosis (Figure 2).

1. What is the differential diagnosis of the case based on clinical findings?
2. Looking at histology, what is your definite diagnosis?

INSTRUCTIONS TO AUTHORS

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       b. Acquisition of data
       c. Analysis and interpretation of data
       d. Drafting the article or revising it critically for important intellectual content.
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   - **a.** Original Articles: Original articles should report original research of relevance to clinical medicine. These include randomized controlled trials, intervention studies, and studies of screening /diagnostic tests, outcome studies and cost- effectiveness analysis .The article should not exceed 4000 words in length (excluding title page, abstract, tables, figures, and references). The article words count for quantitative study should be in range 2000 - 2500 words (excluding references and abstract) with at least 18-25 references and 3–5 figures or tables. For qualitative study article word count should be in range of 3000-4000 words (excluding references and abstract) with at least 20-30 references and 3–5 figures or tables. Studies more than three years old at the time of submission are not entertained as per journal's policy. Any study ending

three years before the date of submission is judged by the Editorial Board for its suitability as many changes take place over the time period, subject to the area of the study. The original article should contain the following sections.

i. Title page: It should include the following information:
   1. Complete title as well as a short title of the article
   2. Name of author(s)
   3. Department(s)
   4. Institution(s) at which work was performed
   5. Author Affiliation
   6. Subject Specialty
   7. Corresponding authors phone/fax no, cell no, personal e-mail address and postal address
   8. Short running title for header

ii. Abstract: It should contain a structured abstract of about 250 words and should include following sections
   1. Background (optional)
   2. Objective
   3. Study Design
   4. Place and duration of study
   5. Material / Patients and Methods
   6. Results
   7. Conclusion
   8. Keywords 3–10 (Medical Subject Headings – MeSH) in alphabetical order. If suitable MeSH terms are not yet available for recently introduced terms, present terms may be used.

iii. Text
   1. Introduction: This should summarize the purpose and the rationale for the study. It should neither review the subject extensively nor should it have data or conclusions of the study. . At the end of the introduction, mention the rationale or scientific significance of the study.
   2. Material / Patients and Methods: This should include exact method or observation or experiment. If an apparatus is used, its manufacturer's name and address should be given in parenthesis. If the method is established, give reference but if the method is new, give enough information so that another author is able to perform it. If a drug is used, its generic name, dose and route of administration must be given. Methodology section should contain (without headings) study design, place and duration of study, sample size, sampling technique, inclusion and exclusion criteria, data collection and analysis procedure. Statistical method must be mentioned and specify any general computer programme used. The information system used should be clearly mentioned.
   3. Results: Must be presented in the form of text, tables and illustrations. The contents of the tables should not be repeated in the text. Instead, a reference to the table number may be given. Long articles may need sub-headings within some sections (especially the results and discussion parts) to clarify their contents. Extra or supplementary materials and technical details can be placed in an appendix where it is accessible. It may be omitted from the printed version but may be published in the electronic version of the journal.
   4. Discussion: This should emphasize present findings & the variations or similarities with other work done in the field by other workers. Detailed data should not be repeated in the discussion again. Emphasize the new and important aspects of the study and the conclusions that follow from them. It must be mentioned whether the hypothesis mentioned in the article is true, false or no conclusions can be derived.
   5. Conclusion: Should be in line with the objectives and results and should be same as given in abstract.
   6. Limitations of the study (if any)
   7. Recommendations of the study (if any)
   8. Acknowledgements (if any)
   9. References: References must be numbered as superscript consecutively according to their appearance in the text. References appearing in a table or figure should be numbered sequentially with those in text. References should be cited in the correct "Vancouver style". List all authors if the total number of authors is three or less and for more than three authors use et al. after six. Journal names should be abbreviated according to the Index Medicus/MEDLINE. The date of access should be provided for online citations. Twenty Percent References should be last five years and all references listed consecutively as superscript.
      a. Standard journal article:
         You CH, Lee KY, Chey WY, et al. Electrogastrographic study of patients with unexplained nausea, bloating and vomiting. Gastroenterol. 1980; 79(2): 311-314.
      b. Chapter in a book:
         Weinstein L, Swartz MN. Pathogenic properties of invading micro organisms. In: Sodeman WA Jr, Sodeman WA, eds. Pathologic physiology: mechanisms of disease. WB Saunders, Philadelphia 1974; 457-72.
   10. Tables: All tables should be numbered with numeric numerals. Headings should be placed above tables, left justified.
   11. Figures: All figures should be numbered with numeric numerals. Headings should be placed below figures, left justified.

b. Clinical Case Reports: Must be of academic & educational value and provide relevance of the disease being reported as unusual. It should have a non-structured abstract of about 100-150 words (case specific) with around 5-6 references and 3 keywords.

c. Letters to The Editor (LTE): It is usually a type of short communication that can be written on any topic that attracts the attention of the reader. There are different types of letters to the editor. If the purpose of the LTE

is to comment on a published article, the first sentence of the LTE should include the name of the published article's first author along with the title of the published article and then the comments. If the LTE is a reply to a previously submitted LTE, the first sentence should include the name of the letter's author and cite the letter as a reference. The previously published article should then be referenced as well either in the body of the text or at the end of the response to the LTE.

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e. Systematic Review Article: It should consist of a well-defined research question and should provide detailed review of a specific topic based on the existing literature. It should include the collection and analysis of data from all the relevant research in support of the research question being asked. The text should be 2500-3000 words. It should have a non- structured abstract with a minimum of three keywords.

f. Meta-Analysis: It should comprise a statistical analysis of combined results of numerous scientific studies addressing the same research questions. Meta-analysis is a quantitative and epidemiological study design that should critically analyze the results of previous scientific researches, mostly randomized controlled trials.

g. Short communication: Short communication or brief report of research works, containing new findings. The short communication consists of: Title, Abstract (structured - no more than 150 words), Keywords (max. 5), Introduction, Material / Patients and Methods, Results, Discussion, Conclusion, Ethical Consideration, Acknowledgment and References. Short communications should not exceeding 2500 words from introduction through references. Short communications should contain no more than 3000 words totally. The number of tables/figures should be in maximum 3.

h. Photo Essays: The journal accepts manuscripts for consideration as photo essays. These essays include the visual presentation of material where the prima, emphasis is on the images. These images can include colored images, angiograms, optical coherence tomography, histologic sections, x-rays, ultrasounds, and other studies. The images can be an outstanding presentation of classic findings, atypical findings or new findings. These are not case reports, but rather a visual presentation of material as a teaching tool. The images need to be of the highest quality. The accompanying manuscript should be limited to a total of 300 words. A maximum of 5 separate images and 5 references can be included. Please refer to the rest of the author's instructions for other requirements for manuscripts submitted to HMDJ.

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a. All manuscript should be typed in double spacing on A-4 paper (8.25" x 11.70" = 21.0 cm x 29.70 cm) with one inch (2.5 cm) margin on both sides.

b. All pages must be numbered starting with the title page being page one.

c. Each figure and table must be submitted separately.

d. All manuscripts must be submitted by email to the address: editor.hmdj@hitec-ims.edu.pk or OJS (https://hmdj.org/)

DIAGNOSTIC CHALLENGE Answers

Case 1

Diagnosis

Langerhan cell histiocytosis

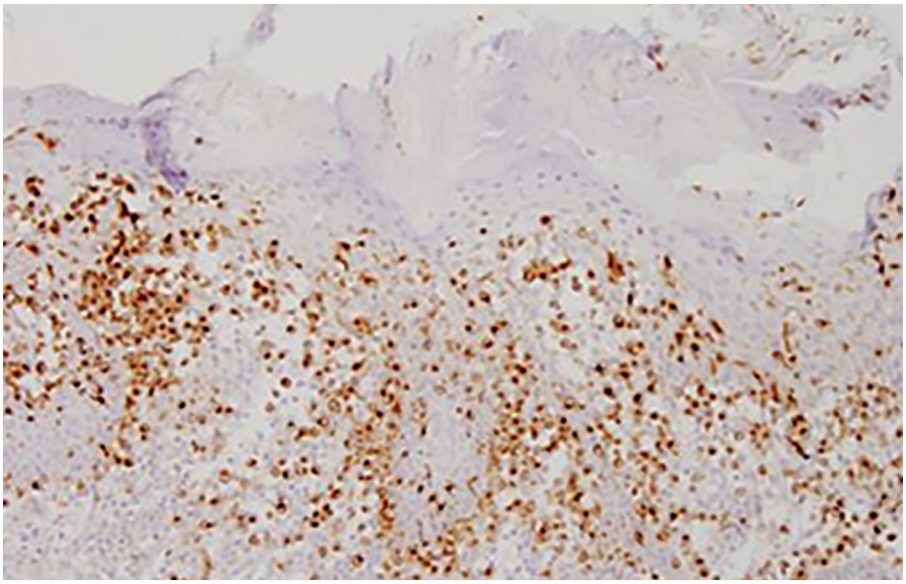

Figure 5

Diagnosis can be confirmed by positive immune histochemical staining of skin biopsy specimen by CD(1a) and langerine (CD 207) as shown in Figure 5.

Discussion

Langerhans cells are immune cells, normally found within the epidermis, where they act as antigen-presenting cells in an early warning system that fights foreign material. Langerhans cell histiocytosis (LCH) or histiocytosis X refers to a reactive increase in the number of Langerhans cells in the skin and other organs. LCH usually affects neonates, infants and young children, being rare in adults.

LCH can be localized, multifocal or multi-systemic. Systemic disease can involve organs such as bone marrow, liver, central nervous system, gastrointestinal tract, lungs and spleen. Systemic forms include Letterer-Siwe disease (with skin, lymph node and visceral involvement) and Hand-Schuller-Christian syndrome whereas a localized disease include eosinophilia granuloma. Self-healing reticulocytosis of infants is another self-limiting benign variant. All of these subtypes overlap and the skin disease is similar in all of them.

The clinical presentation depends upon the extent of organ involvement and symptoms depend upon the function compromised by the pressure effect of the mass of proliferating histiocytes in that organ. Cutaneous involvement presents in the form of an erythematous rash covered with greasy scales and petechiae over scalp and intertriginous areas but can also be widespread. There may be solitary or multiple papules or nodules with ulceration or necrosis. There may be hepato-spleeno-megaly, lung infiltration leading to cough and respiratory difficulty, involvement of the bones leading to lytic lesions on x ray and bone fractures. Involvement of the bone marrow causes pancytopenia leading to pallor, increased risk of infection and bleeding. There may be involvement of the pituitary stalk, causing Diabetes Insipidus.

Answers

LCH is usually diagnosed by characteristic rash and symptomatology of the involvement of a particular organ. The skin biopsy shows a predominant diffuse papillary dermal infiltrate composed of large cells with lobulated, eccentric grooved nuclei with a "coffee-bean shape" appearance and inconspicuous nucleoli. A variable polymorphic infiltrate of eosinophils, lymphocytes, plasma cells and neutrophils is usually admixed with neoplastic cells. Lagerhan cells can be confirmed by immunohistochemical staining with CD1a and CD 207 (Figure 2a & b). When histiocytosis is diagnosed in one organ (e.g., the skin or bone) other organs such as the bone marrow, lungs, liver, and kidneys are investigated accordingly to determine whether they are also affected by histiocytosis.

Treatment depends on the severity of the disease and the number of organs involved. Evidence of damage to the organs is more important than the involvement of the organ as such. Disease limited to the skin only may be treated with topical steroids, PUVA and topical nitrogen mustard. The disease affecting limited areas of the bone may be treated with steroid injections, curettage or radiotherapy. More extensive involvement is treated with systemic steroids and chemotherapy along with supportive treatment according to the dysfunction of the organ involved. LCH may respond to the BRAF-V600 inhibitors, vemurafenib and dabrafenib.

Persons with mild disease confined to one organ, with few or no symptoms, have a good prognosis but the condition may still last for many years and can become worse over time. Not all people with multiple organ involvement will respond to treatment. Children less than two years of age, with LCH affecting many organs, have a mortality rate of 40–50%.

Our Patient

Our patient had Langerhans cell histiocytosis with classical skin involvement, showing diagnostic histological and immune-histochemical features (Figure 1 & 2a/b). There was bone involvement, shown by lytic lesions on the x-ray skull (Figure 3), lung involvement depicted by coarse shadows in lung fields (Figure 4) and hepato-splenomegaly. Bone marrow was involved with pancytopenia and confirmed on bone marrow biopsy. Interestingly the patient also had diabetes insipidus with very low osmolarity of the urine. The patient was referred to a pediatric oncologist for chemotherapy.

Answers

Case 2

Differential Diagnosis

1. Pleomorphic adenoma
2. Warthin's tumor
3. Mucoepidermoid carcinoma
4. Adenoid cystic carcinoma
5. Oncocytoma
6. Metastatic lymph node
7. Sialadenitis

Differential Conditions	Important features
Pleomorphic adenoma	Painless, slow growing, firm mass
Warthin's tumor	Painless, slow growing mass, sometimes bilateral, typically in older adults, often males
Mucoepidermoid carcinoma	Painless or painful mass, possible facial nerve involvement
Adenoid cystic carcinoma	Slow growing, painful, often numbness in face, weakness of facial muscles and difficulty swallowing.
Oncocytoma	Painless, firm, slow growing mass
Metastatic lymph nodes	Often firm, possibly fixed
Sialadenitis	Painful, swollen, tender gland with systemic symptoms.

Diagnosis

Warthin's tumor of Parotid gland

Background

Warthin's tumor also known as papillary cystadenoma lymphomatosum is a benign salivary gland tumor that primarily affects the parotid gland. Etiology is not fully understood but several factors have been associated with it, with smoking being a significant risk factor. Warthin's tumor typically presents as a painless, slow-growing mass near the angle of the jaw. It is most commonly seen in older males.

Diagnosis involves a combination of clinical examination, and imaging studies. MRI and CT typically reveal a well-defined cystic lesion in the parotid gland. Confirmation is achieved through FNA and histopathological examination. The distinctive feature of Warthin's tumor on histopathological analysis is the presence of a double-layered oncocytic epithelium which forms papillary projections into cystic spaces, overlying a dense lymphoid stroma.

Superficial Parotidectomy is typically performed to remove the tumor, while preserving the facial nerve. Total Parotidectomy is considered if tumor involves deeper parts of the parotid gland.

Our Patient

Our patient had the typical features of Warthin's tumor. Superficial Parotidectomy of the patient was performed with regular follow-up visits every 6-12 months.

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