World Family Medicine Journal
incorporating the Middle East Journal of Family Medicine

ISSN 1839-0188

April 2023 - Volume 21, Issue 3

Jeddah street scene, Saudi Arabia

# Prevalence of Behavioral and Psychological Symptoms in Bedridden Dementia Patients. A Study from Jeddah, Saudi Arabia page 6

## Editorial



## Original Contribution



## Regional Covid

## Education and Training



## Review



## Case Report

# Editorial

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This is the third issue this year that include a number of papers on Covid that still generates a lot of research and papers in addition to good review papers on topics of interest to family medicine and the medical field.

In two papers the issue of medical education and career choice was raised. Bin Abdulrahman, et al., did a cross-sectional study surveyed 1,014 undergraduate medical students from several medical colleges in Riyadh. The study aimed to measure the prevalence of CVS and the frequency of exercising ergonomic practices among undergraduate medical students attending several medical colleges in Riyadh, Saudi Arabia. Out of the total surveyed medical students, 85.5% reported using electronic devices for educational purposes. Neck pains (42.5%), headaches (39.4%), and eye dryness (38.6%) were the most frequent symptoms. 60.8% of students were found CVS-positive. Male students were significantly less predicted to have CVS than female students (P<0.001). The authors concluded that CVS and its associated symptoms were relatively common among medical students. Future studies are necessary to measure CVS across larger samples. Further awareness and routine ophthalmic assessments are imperative to mitigate this issue and promote ocular health. Murad et al., did a cross-sectional survey that involved 4th, 5th, and 6th-year medical students and interns from different universities in Saudi Arabia. They aimed to identify the factors that affect and influence medical students and interns to choose a specialty as career. A total of 1178 participants with a mean age 23.1 were included. The most important factor related to the residency training that affected the decision among both genders was lifestyle during residency. The most commonly chosen specialty was internal medicine, followed by general surgery for both genders. Different factors affected the decision among both genders.

Basheikh et al., did a cross sectional study to determine the prevalence of Behavioral and Psychological Symptoms among bedridden dementia patients. The caregivers of bedridden patients diagnosed with dementia were targeted to fill the questionnaire. A total of (64) responses were analyzed. The mean age for patients was 77.3±8.8. Of the patients, 59.7% were males whereas 77.6% of the caregivers were females. The authors concluded that BPSD's prevalence in patients with dementia at community is found to be 50.7%.

Waheed, et al., attempt to evaluate the results of autologous dura replacement versus collagen-based grafts in individuals with dura deformities. The Institute of Neurosurgery at Liaquat National Hospital Karachi undertook this randomized evaluation to identify the most effective therapy for dura mater defects. Employing non-probability random selection, 82 cases among both sexes were selected. The operation duration for semi-synthetic collagen was significantly reduced. There was a 40 minute variation in total time spent by the two groups. Autologous grafts showed ideal tightness and better flexibility and fair workability on the other hand semi-synthetic collagen showed better tightness and workability and ideal flexibility. Postoperative hospital stays were seen to be 26 + 2.5 hours in Group 1A whereas they were 23 + 2.5 hours for Group B. According to the aforementioned findings, an accessible, secure, and efficient substitution for an autologous graft for dura restoration in dura abnormalities is the use of a semi-synthetic collagen substitute.

Alrajhi, et al., did a cross-sectional descriptive study was carried out among 458 Saudi parents/caregivers, whose children aged from 5 to 18 years. The aims was to determine the prevalence and to reveal the characters of Nocturnal Enuresis (NE) in affected children aged 5-18 years in Saudi Arabia. 75% of children suffering from NE were males and 51.9% had an age ≥ 10 years with a mean age of 8.78± 3 years. In this study 34% of the children with NE experienced 2-4 bouts of bedwetting, per week. The authors concluded that NE is occurrence among youngsters in various Saudi Arabian regions. Male gender, aged 5 to 10 and suffering from weakness of bladder muscles, chronic constipation, worry and depression was associated with NE and UTI. Families and caregiver utilized effective therapies such as alarm and behavioral stimulation, however, they do not look for a medical assistance.

Alotaibi, et al., did a cross-sectional online questionnaire-based study with the aim to assess the level knowledge and practices of health practitioner toward pulmonary tuberculosis in Saudi Arabia. In addition to assess the perception of health practitioner toward of role of CXR. A total of 95 participants had responded to our survey. Almost two third of the sample were general practitioner. The authors concluded that good understanding of TB and clinical knowledge among medical students and physicians are particularly important for both early detection, management and protective measures. Our results showed moderate knowledge regarding TB investigations and excellent knowledge in terms of dealing with positive or suspected cases.

In three papers issues related to Covid were raised. Alsawalem. et al., stressed that little is known about the concerns regarding the safety of COVID-19 vaccination of parents of children with ASD, because most of the studies focused on the hypothesised relationship between vaccines and ASD with parents with children without disabilities. Authorities should give the parents the time to understand the whole process so they can decide positively and solve any problems or

confusion that the parents had before and after receiving the vaccines for their students. Having influential people publicly advertise the importance of vaccines to encourage hesitant parents and imposing strict penalties on those who refuse to be vaccinated, not giving the parents, who refused the authorities in this matter and using the media channels to convince the community of the importance of the vaccine and the necessity of addressing it are suggested solutions to increase the rates of COVID-19 vaccinations in SA. Hussein, et al., did a cross-sectional observational study was done to assess the post vaccination symptoms among the health care workers who were vaccinated with COVID vaccine in Egypt. One hundred ninety-two health care workers (HCWs) respond to this questionnaire, the most common symptoms reported after 1st dose of vaccination were pain at injection site (81.7%), followed by tiredness (70.7%) then myalgia & bony pain (62.8%). The authors concluded that post vaccination symptoms among health care workers were mild short symptoms, there was no serious adverse effects after the first dose as well as the second dose. the majority of participants did not report COVID-19 infection after vaccination which confirm the efficacy and safety of the vaccine. Hassan-Hussein et al ., followed a cross-sectional study on the local population (n=262) of Makkah Al-Mukarramah. This study aimed to determine the prevalence of vaccine hesitancy and to assess the acceptance of COVID-19 vaccine during the ongoing MERS-CoV-2 pandemic in Makkah, Saudi Arabia. Of 262 participants, 76% were adults (18 to 60-year-old), and 24% were parents. Around 62% participants were keen to take the flu vaccine. The authors concluded that vaccine hesitancy in Makkah is high (38%) compared to previous findings. It is recommended that improved measures should be taken to create more awareness through increased communal educational campaigns. Moreover, continuing education about the importance of vaccinations should be conducted by health care providers. Additional studies are needed in Makkah to assess the vaccine hesitancy movement.

Alreshidi, et al., did a systematic review to search for evidence from the past fifteen years of literature, demonstrating the capability of PBL to improve critical thinking and problem-solving skills for medical students. The search process was conducted through electronic databases on publications related to the impact of PBL, particularly, on two fundamental skills; critical thinking and problem-solving for medical students. Searching the four aforementioned databases produced 657 publications, including 249 duplicates. Two of these seven studies assessed only the knowledge, comprehension, and application domains, as their evaluation of problem-solving and critical thinking abilities was based on student perspectives. The authors concluded that there is very little published evidence over the last fifteen years supporting the claim that PBL improves critical thinking and problem-solving skills in medical students. Therefore, recent practice is not based on evidence. As such, investigations are required to legitimise the claims that PBL improves critical thinking and problem-solving skills for medical students.

Mutluer et al., looked at the impact of vitamin D deficiency on gestational COVID-19 infection. They to described the most recent studies on the impact of vitamin D levels on pregnant women with COVID-19 infection. They used a narrative literature review in which using PubMed, Medline, ScienceDirect, Cochrane and Google Scholar databases were conducted to select the most relevant research published in English before December 2022 and available to the authors. The authors concluded that although lower serum vitamin D levels are associated with a higher chance of contracting a serious disease caused by several respiratory viruses like SARS-CoV-2, they are not associated with a higher possibility of COVID-19 occurring in expecting women.

Dr Haque discussed subclinical hypothyroidism in conception and pregnancy. It is a not an uncommon scenario in primary Care for a patient to attend their family practitioner after having tried and failed to conceive. Initial investigations may reveal a picture consistent with Subclinical Hypothyroidism (SCH); the patient may request thyroxine – should we treat? Furthermore, a pregnant patient may have first trimester blood results which show SCH – should this be treated? What is the evidence of benefit, if any? What are the risks associated with treatment? Increasingly more so, clinicians are opting to treat empirically. Anecdotally, multiple colleagues have noted successful conception shortly after starting treatment with low dose Levothyroxine (LT4). This narrative review will focus on the issue of SCH, its significance for females trying to conceive, its effects on pregnancy and consider the question of whether or not it should be treated with LT4 in both of these scenarios.

Bakkar et al., discussed the role of ultrasound in thyroid assessment. They stressed that the recent prevalence of ultrasonography (US) has facilitated the early detection and qualitative evaluation of thyroid nodules. Furthermore, novel technical developments are extending the application range of US for other thyroid diseases. They concluded that ultrasonography is useful for diagnosing various thyroid diseases, including thyroid carcinoma. The remaining issue to be resolved is the diagnosis of follicular carcinoma. Trials using novel techniques to differentiate these lesions are expected.

Imran and Chaudhry, discusses the atypical presentation of amelanotic melanoma in a 37-year-old Caucasian female patient and the challenges it poses for diagnosis and thence the delay in treatment. 5-year survival rate is 93% for all melanomas but amelanotic melanoma survival is 88% and this is predominantly due to delayed diagnosis. Better patient and doctor education and readily available histopathological diagnosis confirmation can lead to earlier diagnosis and better outcome.

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# Prevalence of Behavioral and Psychological Symptoms in Bedridden Dementia Patients. A Study from Jeddah, Saudi Arabia

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Received: February 2023. Accepted: March 2023; Published: April 1, 2023.
Citation: Mazen A. Basheikh et al. Prevalence of Behavioral and Psychological Symptoms in Bedridden Dementia Patients. A Study from Jeddah, Saudi Arabia. World Family Medicine. March 2023; 21(3): 6-12
DOI: 10.5742/MEWFM.2023.95256066

## Abstract

Background: Bedridden patients who are suffering from dementia require close care which is usually done by a relative or a professional caregiver. The caregiver may face inappropriate behaviors from the patient that should be handled with patience.

Objective: To determine the prevalence of Behavioral and Psychological Symptoms among bedridden dementia patients.

Methods: This is a cross-sectional study that utilized a structured questionnaire for data collection. The caregivers of bedridden patients diagnosed with dementia were targeted to fill out the questionnaire. No specific exclusion criteria were applied. The demography of the patients and caregivers was obtained along with BPSD and the responses of the caregivers.

Results: A total of (64) responses were analyzed. The mean age for patients was 77.3±8.8. Of the patients, 59.7% were males whereas 77.6% of the caregivers were females. The median (IQR) for caregivers was 40 (35-45). Repeating sentences/questions and complaining were the most common reported behaviors with 37.3% each, followed by constant demand for unnecessary assistance by 29.9% of the patients.

Conclusion: BPSD's prevalence in patients with dementia in the community was found to be 50.7%.

Key words: Alzheimer, Caregiver, Dependent, Elderly, Inappropriate behavior

## Introduction

Behavioral and psychological symptoms of dementia (BPSD), also known as neuropsychiatric symptoms, represent a heterogeneous group of non-cognitive symptoms and behaviors occurring in subjects with dementia [1]. Symptoms like delusions, anger, impatience, abnormal motor activity, impulsiveness, melancholy, anxiousness, and apathy are among the symptoms of BPSD [2]. Interactions among dementia severity, external conditions, and other (somatic) disorders are hypothesized to cause the manifestations [2][3].

BPSD were proven to cause stress on both formal and informal caregivers in contexts such as skilled nursing facilities and private residences and become harder to manage than cognitive deficiencies associated with dementia [4].

Dementia patients are at a greater risk of being admitted to hospitals and BPSD can make the treatment more difficult resulting in prolonged stays and higher expenses [5]. In professional acute clinical contexts such as psychogeriatric units, BPSD were already studied [6]. However, no comprehensive studies have been carried out about BPSD in community home settings.

This study aims to determine the prevalence of inappropriate behavioral and psychological acts among bedridden dementia patients toward their caregiver, toe improve the care setting which will affect the overall outcome.

## Methodology

### Study design

This is a cross-sectional study that targeted the caregivers of bedridden patients diagnosed with dementia.

### Study population

The population of the current study included bedridden patients with a documented confirmed diagnosis of dementia. There were no exclusion criteria. The targeted population included the caregivers of any relationship with bedridden dementia patients. The caregivers had to spend a minimum of 40 hours per week with the patient in the same household in order to be included in the study. One caregiver per patient was included.

### Data collection

The data collection was done through a structured questionnaire given to the caregivers at homes. The caregivers were the source of data in this study. The questionnaire inquired about sociodemographic characteristics for both the patient and the caregiver, representing the first two sections of the questionnaire. The third section included items identifying the inappropriate behaviors faced by the care givers while the last section included the responses and attitude of the caregiver towards inappropriate and aggressive behaviors. The data collection took place between January and March 2019

### Statistical analysis

A computer program (the Statistical Package for the Social Sciences, SPSS, version 27.0) was used for data analysis. Continuous variables were summarized using mean/ standard deviation (SD) or median/interquartile range (IQR) as appropriate. Inappropriate behaviors among the patients were measured using eight variables of scaled answers (never, once or twice an hour, many times an hour, once or twice a day, many times a day, once or twice a week, many times a week, less than once a week). The responses were re-coded to compose a binary variable describing the occurrence of the behavior regardless of its frequency. The outcome behaviour represented the outcome variables and were represented using proportions and tables. The Chi-square and Fisher exact tests were used to find associations between categorical variables. Findings were considered significant if the P-value was less than 0.05.

### Ethical considerations

The study was ethically approved by the research committee at King Abdulaziz University, Jeddah Saudi Arabia, approval number (HA-02-J-008). Prior to data collection, an introductory message was written to explain the study and to gain consent. The data were anonymous with no personal identifier and were used for research purposes only.

## Results

A total of (64) responses by caregivers were analyzed. The mean age of patients was 77.3±8.8 and 59.7% were males. All the patients had multiple comorbidities. Diabetes mellitus, hypertension and cardiovascular diseases were the most common comorbidities. The sociodemographic and comorbidities of the patients are shown in Table 1. The median age for caregivers was 40 (35-45) and 77.6% were females. The relationship with the patient, nationality, education level and other characteristics of caregivers are shown in Table 2.

The behaviours were inquired about using eight questions. 34 of the patients showed psychomotor symptoms. Complaining and repeating questions and sentences were the commonest behaviours reported (73.5%) each. Other behaviours are presented in Figure 2. The caregivers were also asked about their reactions to the BPSD. The questionnaire inquired about 16 suggested reactions to be scaled by the caregiver according to its frequency. The responses are shown in Table 3.

40% of the caregivers will try to find out the reason for the patient behaviour and act toward it to prevent its recurrence. Another 40% will adjust their daily schedule according to the patient's needs while 27% will conduct some activities to ensure memory condition stability.

The patients' characteristics, comorbidities and caregiver characteristics were tested for significant associations with the inappropriate behaviors. Screaming was significantly higher in female patients (P-value=0.043), 70% of the patients who experienced screaming were females.

**Table 1: Sociodemographic characteristics of the patients**

| | | N | % |
|---|---|---|---|
| Age of the patient | 75 or less | 30 | 44.8% |
| | >75 | 37 | 55.2% |
| Gender | Male | 40 | 59.7% |
| | Female | 27 | 40.3% |
| Diabetes | No | 28 | 41.8% |
| | Yes | 39 | 58.2% |
| Hypertension | No | 23 | 34.3% |
| | Yes | 44 | 65.7% |
| Cardiac diseases | No | 54 | 80.6% |
| | Yes | 13 | 19.4% |
| Marital status | Married | 44 | 65.7% |
| | Widow | 22 | 32.8% |
| | Single | 1 | 1.5% |

**Table 2: Sociodemographic characteristics of the caregivers**

| | | N | % |
|---|---|---|---|
| Age of the caregiver | <35 | 16 | 23.9% |
| | 35-45 | 36 | 53.7% |
| | >45 | 15 | 22.4% |
| Gender | Male | 15 | 22.4% |
| | Female | 52 | 77.6% |
| Have you been trained to deal with aggressive behavior | No | 67 | 100.0% |
| | Yes | 0 | 0.0% |
| Nationality | Saudi | 22 | 32.8% |
| | Non-Saudi | 45 | 67.2% |
| Have you been subjected to aggressive behavior in the past 12 months | No | 60 | 92.3% |
| | Yes | 5 | 7.7% |
| Relation to the patient | First degree relative | 34 | 50.7% |
| | Housemaid | 14 | 20.9% |
| | Driver | 5 | 7.5% |
| | Other | 13 | 19.4% |
| | Second degree relative | 1 | 1.5% |
| The percentage of time per day you spend accompanying the patient | >60% | 63 | 94.0% |
| | 30%-60% | 4 | 6.0% |
| | <30% | 0 | 0.0% |
| Education | Uneducated | 11 | 16.4% |
| | Bachelor's degree | 11 | 16.4% |
| | High/secondary school | 24 | 35.8% |
| | Middle school | 7 | 10.4% |
| | Primary school | 14 | 20.9% |

**Figure1: Prevalence OF BPSD**

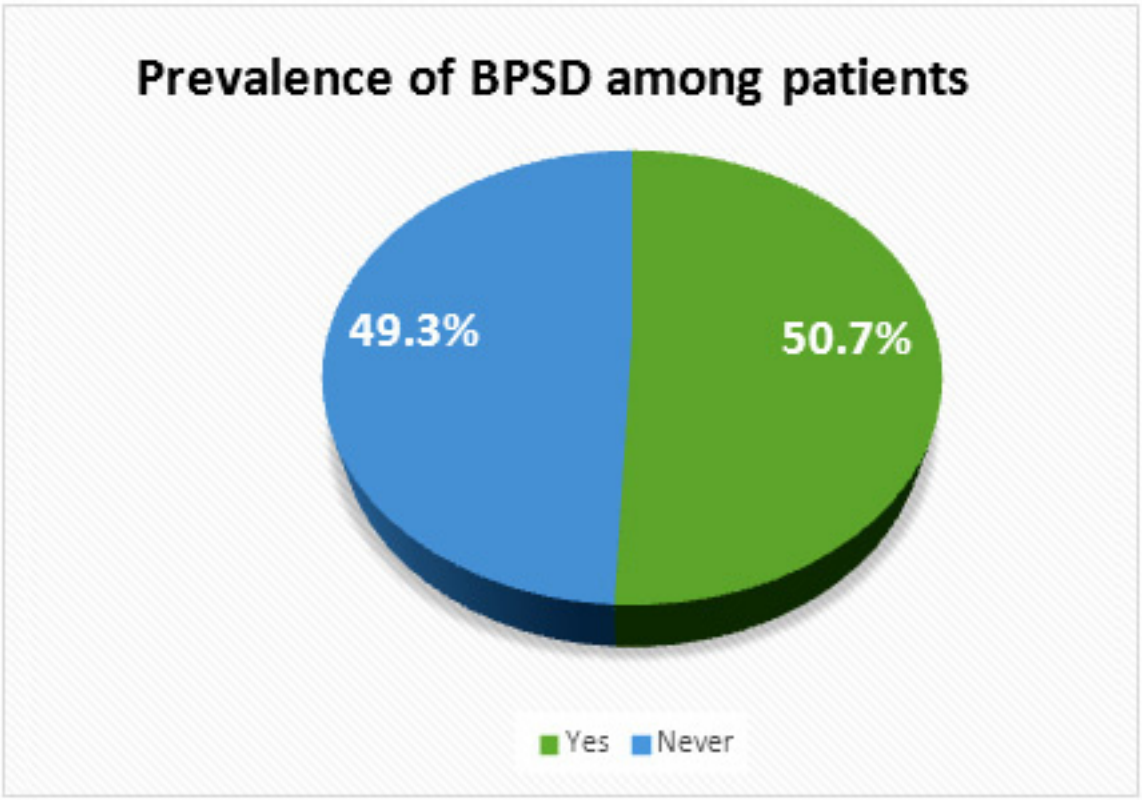
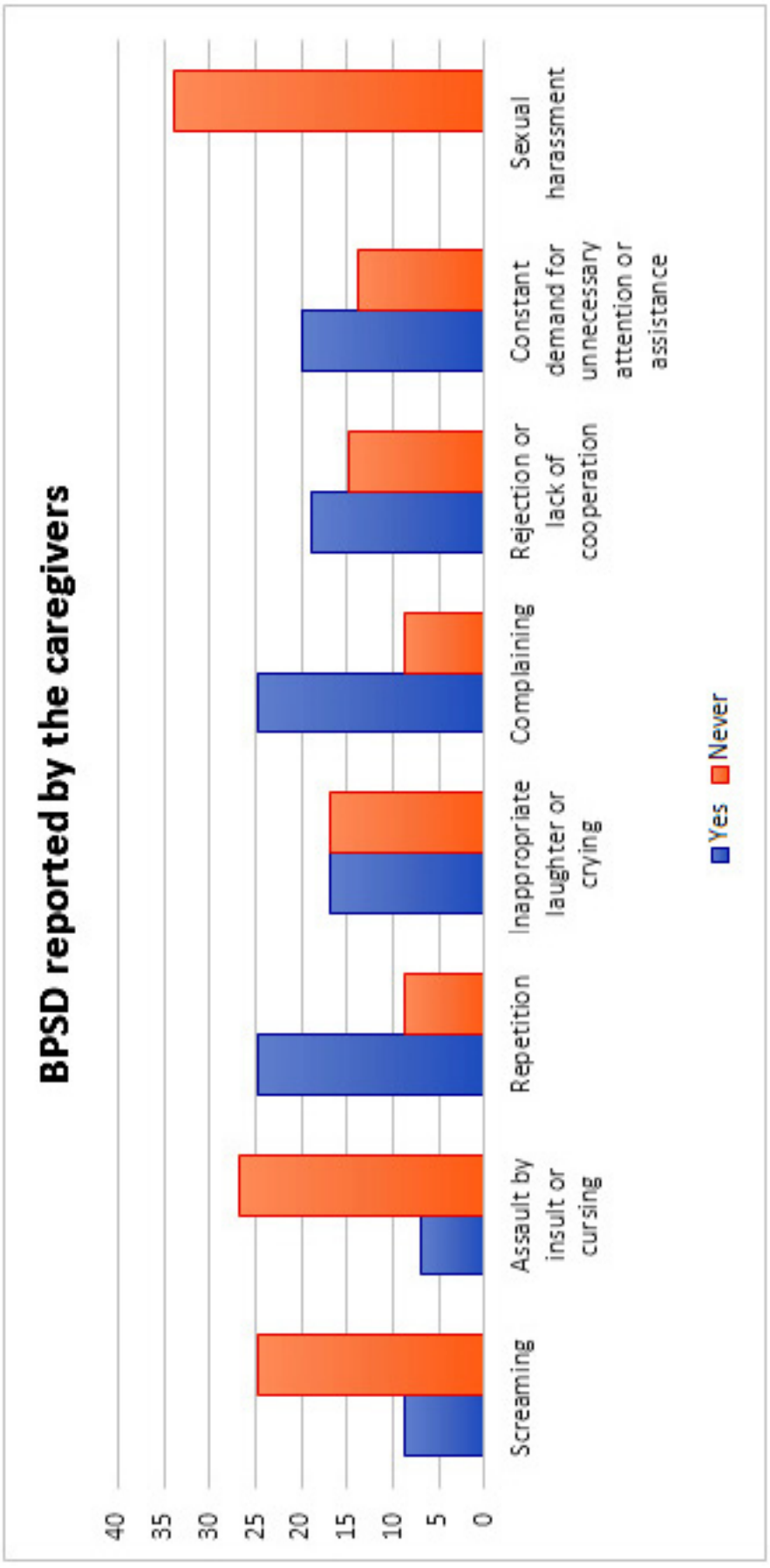



**Table 3: Perceived actions by the caregivers towards the BPSD.**

| Caregiver action | Never (%) | Yes (%) |
|---|---|---|
| Attempt to find reasons to explain the patient`s behavior | 56 (83.6 %) | 11 (16.4%) |
| Attempt to know what the patient likes and does not like to avoid recurrence of this behavior | 39 (58.2 %) | 28 (41.8%) |
| Ask other relatives about this behavior | 58 (86.6 %) | 9 (13.4 %) |
| Attempt to find organic causes of the behaviors such as (pain, infection, constipation, etc.) | 57 (85%) | 10 (15%) |
| Discuss the patient`s behavior with different medical subspecialities | 55 (82%) | 12 (18%) |
| Document/record the patient`s behavior | 60 (89.6%) | 7 (10.4%) |
| Distract the patient from the behavior by changing the subject | 60 (89.6%) | 7 (10.4%) |
| Do some activities that contribute to memory stability | 49 (73.1%) | 18 (26.9%) |
| Do a therapeutic massage to improve patient`s mood and behavior | 53 (79.1%) | 14 |
| Try to improve the level of movement and physical activity of the patient as much as possible such as walking, exercising, physical therapy session, etc. | 50 (76.9%) | 17 |
| Distract the patient from the behavior by singing | 62 (92.5%) | 5 (7.5%) |
| Use aromatherapy | 62 (92.5%) | 5 (7.5 %) |
| Adjust the daily schedule according to the needs of the patient | 41 (61.2%) | 26 (38.8%) |
| Dealing with aggressive behaviors by humor | 61 (91 %) | 6 (9%) |
| Try to reassure and calm the patient down | 39 (58.2%) | 28 (41.8%) |
| Learn and apply self-control techniques (likes breathing exercise, place changes, etc.) towards the patient | 55 (82%) | 12 (18%) |

**Figure 2: BPSD reported by the caregivers.** (Change page view)



## Discussion

Neuropsychiatric symptoms in demented patients have a significant impact over the caregivers. Finding the correct approach to identify and evaluate these symptoms is a crucial part of the management plan [1].

When reviewing the literature, the prevalence of BPSD in patients with dementia was noted to be significantly higher than in bedridden patients without dementia, as demented patients' prevalence was 67% in comparison to non-demented group. The ratio is of more than twice compared to the non-dementia patients which was 38% [7]. In another study, it was found that almost 75% of dementia patients had at least one behavioral or psychological symptom [2]. Apathy, aggressiveness, depressed thoughts and hallucinations were the most prevalent among inpatients, while aggressive behavior, sleep disruption, activity disruption, and anxiety were reported to be the most common through emergency departments [8].

Our study showed that over 50.7% of dementia patients developed BPSD toward their caregivers. In other studies, designed for residents at nursing homes, BPSD was observed in 67% of the patients with moderate dementia, and 88% of those with severe dementia [7][ 9].

C Mühler et al., highlighted that patients with continuous mental distress were more likely to show aggression via screaming. In comparison to our study, screaming was found to be more associated with female gender group [10]. Repetition of sentences or questions was also found with similar rate, 73.5%, in comparison to other previous studies. [10][11][12].

A significant relationship between dementia and other comorbidities such as diabetes and cardiovascular disorders was found, as patients with these comorbidities were more likely to develop BPSD [13][14].

Diabetes mellitus has a proven association with BPSD. It has an impact on some components of cognitive functions like intellectual ability, cognitive training and flexible thinking, especially in the elderly which can lead to significant BPSD among patients [15].

Health-related quality of life (HRQOL) is a useful indicator of overall health, as it captures information on the physical and mental health status of individuals and the impact of health status on quality of life [16]. Multiple studies have found that these neuropsychiatric symptoms, as well as patients' cognitive decline, have massive impact on caregivers' HRQOL, mainly on the caregivers' mental health [17][18][19]. 40 % of the caregivers in our study have had to adjust their daily schedules according to the patient's demands. BPSD are considered incredibly challenging for caregivers and most of them experience a sense of decline in the relationship between them and the patient [20].

The study is unique, as it is conducted toward prevalence of BPSD in the community of Jeddah, Saudi Arabia, and to our knowledge it is the first on this subject.

The study is a cross-sectional study with typical design limitations. Therefore, no clear temporal association between caregivers' burden and BPSD was measured.

## Conclusion and Recommendation

BPSD's prevalence in patients with dementia in the community is found to be 50.7%. Family education, non-pharmacological approach and attending psychiatric visits might help to overcome the caregivers` burden and to improve the quality of life for the patients and their caregivers. This study will help in a better understanding of BPSD from the caregiver's point of view.

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# Knowledge and practices of health practitioners toward pulmonary tuberculosis in Saudi Arabia

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Received: February 2023 Accepted: March 2023; Published: April 1, 2023.
Citation: Manal Alotaibi et al. Knowledge and practices of health practitioners toward pulmonary tuberculosis in Saudi Arabia. World Family Medicine. March 2023; 21(3): 13-18 DOI: 10.5742/MEWFM.2023.95256068

## Abstract

Background: Appropriate TB knowledge and good practice attitudes are substantial particularly among health care personnel because of great occupational risks during their daily activities. Therefore, TB prevention and control have become an important issue on training courses. This study mainly aimed to assess the level knowledge and practices of health practitioners toward pulmonary tuberculosis in Saudi Arabia. In addition we aim to assess the perception of health practitioners toward the role of CXR.

Methodology: This is a cross-sectional online questionnaire-based study conducted in Al-imam medical clinics Saudi Arabia during 2022.

Results: A total of 95 participants responded to our survey. Almost two thirds of the sample were general practitioners (n = 67, 70.5%). A total of 27 physicians (28.4%) reported seeing a positive result of pulmonary tuberculosis and 43 participants (45.3%) agreed on doing CXR with/without Microbiologic testing to investigate a suspected pulmonary TB patient. Almost half of the participants (n = 47, 49.5%) reported referring to isolation as the next step for positive cases.

Conclusion: Generally speaking, there was a good understanding of TB and clinical knowledge among medical students and physicians which is particularly important for early detection, management and protective measures. Our results showed moderate knowledge regarding TB investigations and excellent knowledge in terms of dealing with positive or suspected cases.

Key words: pulmonary tuberculosis, health practitioners, Saudi Arabia

## Introduction

TB (caused by Mycobacterium tuberculosis) is considered to be the ninth leading cause of death worldwide. As per the World Health Organization (WHO), 10.4 million cases were detected in 2016, and 1.4 million deaths were reported to be caused by TB in 2020 (1-2). Tuberculosis is not an area of concern for an individual but for national public health it is devastating and contagious. It is communicable disease caused by a special type of bacteria known as Mycobacterium tuberculosis, which cannot be detected by the formal gram staining method. The disease predominantly affects the lungs of an individual (90% of the cases), but it can also affect many different organs of the body (1). Multiple screening methods are now available to detect Mycobacteria, among which the most common is Chest X-ray, a relevant and rapid method to detect pulmonary changes in pulmonary TB (3). The best cost-effective, compliant, and easy method is CXR, but still, it has been discouraged for TB diagnosis due to its limitations of not being capable of diagnosing smear-negative TB (4). TB has contributed to a significant disease burden and economic loss worldwide. Early identification of TB infection has been challenging. This study aimed to assess the level of knowledge and practices of health practitioners toward pulmonary tuberculosis in Saudi Arabia, in addition to assessing the perception of health practitioners toward of role of CXR.

## Methodology

This was a cross-sectional online questionnaire-based study conducted in Al-imam medical clinics Saudi Arabia during 2022. After obtaining ethical approval from Imam medical center, Imam Mohammad Ibn Saud Islamic University No. 292/2022. The self-administered questionnaire was distributed randomly among medical physicians in different specialties, intern doctors, and medical students. The questionnaire was designed to assess knowledge and practices of medical practitioners toward pulmonary tuberculosis. Additional questions related to the role of CXR were added to the survey. The questionnaire was distributed in the English language. Those who were non-health practitioners were excluded.

## Results

**Characteristics of responders**

A total of 95 participants responded to our survey. Almost two thirds of the sample were general practitioners (n = 67, 70.5%); where 40% of the participants were medical students and 30.5% intern doctors. However, family medicine doctors were the highest from medical specialties with an estimated 6.3% compared to internal medicine (5.3%) and emergency medicine (4.2%). The majority of participants had experience of less than 5 years (n = 79, 83.2), however, 11 participants had experience more than 10 years (11.6%). More than half of the sample reported working in a hospital other than Imam Medical Center (n = 53, 55.8%). (Table 1)

**Assessment of clinical knowledge**

A total of 27 physicians (28.4%) reported they had seen a positive result of pulmonary tuberculosis. Among them, 22 have seen one to five cases, however, three physicians saw five to ten cases and only two physicians reported seeing more than ten cases. Further, 13 of those who had seen positive cases were general practitioners; either medical students or intern doctor.

Regarding the investigation advised for suspected pulmonary TB patients, 43 participants (45.3%) agreed on CXR with/without Microbiologic testing and 40 participants (42.1%) agreed on Microbiologic testing with/without CXR. More than half of the sample (53.7%) reported microbiologic testing as a confirmatory test for pulmonary TB patients, compared to 33.7% who reported CXR. A total of 12 participants (12.6%) were not sure about the investigation for suspected pulmonary TB and the confirmatory test.

In terms of role of CXR in pulmonary TB cases, most participants (n= 35, 36.8%) agreed on its role as a screening tool to detect active TB, followed by being a faster tool (28.4%) and high availability (22.1%). However, 13 physicians agreed in all items (13.7%) for being available, cheaper, faster and as a screening tool to detect active TB.

A total of 80% of responders reported engaging a radiologist to read the CXR, and 42.2% agreed to use CXR to follow up the patients. Cavitation was the most frequent reported lesion expected to be seen in case of pulmonary TB by CXR reported by the vast majority of participants (n = 81, 85.26%), followed by enlarged hilar lymph node (n = 72, 75.8%), pleural effusion (n = 68, 71.6%) and consolidation (n = 62, 65.3%). However, one participant reported tumor, space occupied lesions as an extra lesion to the abovementioned lesions. (Table 2).

Almost half of the participants (n = 47, 49.5%) reported referring to isolation as the next step for positive cases; 31 participants (32.6%) reported referring to pulmonologist. Meanwhile, 13 participants thought ordering additional investigation and only four suggested medications prescription as a next step. (Figure 1).

**Table 1: characteristic of included participants**

| Items | N | % |
|---|---|---|
| Medical specialty | | |
| Emergency medicine | 4 | 4.2 |
| ENT | 1 | 1.1 |
| Family medicine | 6 | 6.3 |
| General surgery | 5 | 5.3 |
| Intern doctor | 29 | 30.5 |
| Internal medicine | 5 | 5.3 |
| Medical student | 38 | 40.0 |
| Neurology | 1 | 1.1 |
| Ob/gyn | 1 | 1.1 |
| Pediatrics | 4 | 4.2 |
| Psychiatry | 1 | 1.1 |
| Years of experience | | |
| 5 - 10 years | 5 | 5.3 |
| Less than 5 years | 79 | 83.2 |
| more than 10 years | 11 | 11.6 |
| Have you worked in a hospital other than Imam medical center? | | |
| Yes | 53 | 55.8 |
| No | 42 | 44.2 |

**Figure 1: What is the next step for positive cases?**

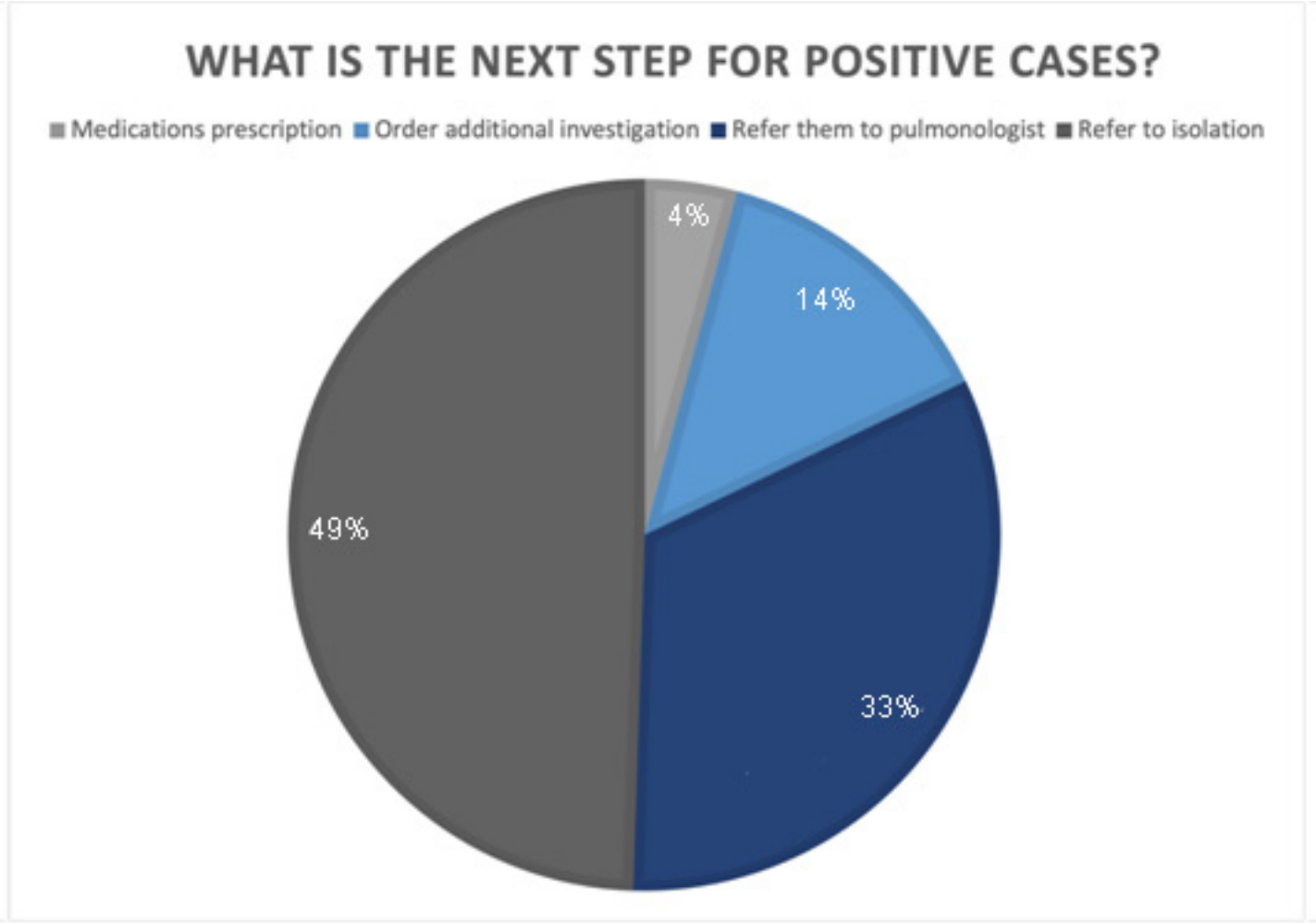

**Table 2: The level of knowledge and practices of physicians**

| Item | N | % |
|---|---|---|
| Have you ever seen a positive result of pulmonary tuberculosis? | | |
| No | 68 | 71.6 |
| Yes | 27 | 28.4 |
| Approximately how many cases you ever seen? | | |
| +10 cases | 2 | 2.1 |
| 1 - 5 cases | 22 | 23.2 |
| 6 - 10 cases | 3 | 3.2 |
| None | 68 | 71.6 |
| Investigation advised for suspected pulmonary TB patient? | | |
| CXR with/without Microbiologic testing | 43 | 45.3 |
| Microbiologic testing with/without CXR | 40 | 42.1 |
| Not sure | 12 | 12.6 |
| Confirmatory test for pulmonary TB patient? | | |
| CXR | 32 | 33.7 |
| Microbiologic testing | 51 | 53.7 |
| Not sure | 12 | 12.6 |
| Role of CXR in pulmonary TB cases? | | |
| Availability | 21 | 22.1 |
| Cheaper | 6 | 6.3 |
| As screening tool to detect active TB | 35 | 36.8 |
| Faster | 27 | 28.4 |
| Not sure | 12 | 12.6 |
| All | 13 | 13.7 |
| What is the next step for positive cases? | | |
| Medications prescription | 4 | 4.2 |
| Order additional investigation | 13 | 13.7 |
| Refer them to pulmonologist | 31 | 32.6 |
| Refer to isolation | 47 | 49.5 |
| Do you engage a radiologist to read the CXR? | | |
| No | 19 | 20.0 |
| Yes | 76 | 80.0 |
| CXR can be used to follow up with patient | | |
| No | 34 | 35.8 |
| Not sure | 21 | 22.1 |
| Yes | 40 | 42.1 |
| What is expected to be seen in case of pulmonary TB by CXR? | | |
| Cavitation | 81 | 85.26 |
| Hilar lymph node | 72 | 75.8 |
| Plural effusion | 68 | 71.6 |
| Consolidation | 62 | 65.3 |
| Tumor, space occupying lesions | 1 | 1.1 |

## Discussion

Appropriate TB knowledge and good practices and attitudes are substantial particularly among health care personnel because of the great occupational risks during daily activities. Therefore, TB prevention and control have become an important issue on training courses [5]. One of the United Nations Millennium Development Goals (MDGs) was to decrease the TB incidence by 2015 and target TB control [6]. Our findings revealed that the percentages of diagnostic knowledge, awareness of radiological findings, and appropriate clinical management of suspected cases were satisfactory among our sample. In our study, approximately 45% of participants had adequate knowledge regarding the investigation advised for suspected cases and about 50% had accurate knowledge regarding the confirmatory test of TB. Our results come higher than percentages found in Bangalore city where adequate knowledge was reported by 30% only [7]. In the USA, a self-reported survey was provided for students in The National Tuberculosis Curriculum Consortium (NTCC) schools prior to the availability of NTCC-developed educational course to evaluate the baseline level of knowledge about TB. Most students thought TB education was important to their academic program and their career path. However, 40% of the respondents reported that they were unconfident about their level of TB knowledge for their career needs [8]. This emphasizes the need to establish effective and sufficient TB educational programs worldwide.

Concerning the appropriate management step after diagnosing TB, in a study done in Japan in 2002 among physicians in 80 medical school hospitals, about 89.3% of doctors believed the necessity of isolation for TB patients and about 70.5% reported offering anti TB drugs for patients with any complications [9]. Conversely, in our study almost half of the participants reported referring to isolation as the immediate next step for positive cases, and only four suggested medications prescription.

In Brazil, a cross-sectional survey was conducted among 1,094 undergraduate medical students in early and late clinical years. Many students did not have sufficient knowledge regarding the main routes of TB infection and protective measures of using face mask during examination of an active TB case [10]. In Italy, the results from a cross-sectional survey among the fifth medical year students (n=183) showed that around half of the sample had correct answers regarding TB knowledge (56.5% ± 11.6%), epidemiology and prevention (63.5% ± 16.3%), diagnosis (54.1% ± 12.4%), and treatment (45.7% ± 20.4%) [11].

According to meta-analysis, PBL in medical education was found to have favorable outcome on student medical knowledge and acquired skills [12]. The majority of our sample were medical students or intern doctors and showed a satisfactory knowledge of TB similar to that found with students in the final or graduation medical year from Canada, India, and Uganda who had significant basic knowledge and practice competency[13]. In this context, Kilicaslan et al. showed that TB related questions in pulmonology exam for undergraduates did not meet the learning objectives by WHO covering only nine objectives [14].

According to the Centers for Disease Control Core Curriculum, all health care professionals should have adequate knowledge of TB burden, screening, prevention, and BCG vaccination [15]. For instance, in a survey conducted among nursing students, average knowledge about the sputum smear examination being diagnostic was 50% [16].

There are other aspects challenging TB knowledge and control issues and it is important to raise the awareness of these obstacles. The social stigma of TB was mainly because of fear of infection, physical frailty, and association with human immunodeficiency virus/acquired immune-deficiency syndrome (HIV/AIDS) [17]. Further, several infection control measures have been recommended to reduce TB transmission including adequate ventilation, triage and isolation of patients with cough which might be unavailable in lesser facilities [18]. The new generation screening tool, QuantiFERON-TB test, has excellent utility and accuracy, especially in BCG-vaccinated populations and immunocompromised patients that might be difficult to obtain due to the high cost [19]. Furthermore, according to systematic review with 37 included studies, there were reasonable numbers of inappropriate TB regimens prescription including type, dose, frequency of dosing and combination in 67% of the studies, despite the quality of reporting studies being low The authors recommended the need to improve implementation of the WHO treatment guidelines. On the other hand, patient education is important as much as health workers, especially in high-risk groups. For instance, employed patients were more likely to adopt adequate infection control strategies [20].

There are some limitations to our study; firstly, the small sample size who responded to our survey. Secondly, the majority of respondents were medical students or intern doctors who have minor clinical experience with TB patients and who did not accurately assess the clinical practice. Thirdly, the results were based on self-reports by the participants which may be biased to present themselves in a positivemanner. Fourthly, we could not assess the knowledge of drug regimen for TB. Nevertheless, the strength of the study is that the findings highlight the level of knowledge in our sample in terms of clinical management of suspected cases, diagnostic tools and radiological findings that were not assessed by other published surveys

## Conclusion

Generally speaking, there was good understanding of TB and clinical knowledge among medical students and physicians are particularly important for early detection, management and protective measures. Our survey outlined TB knowledge among our sample, in which, medical students and intern doctors were the majority. Our results showed moderate knowledge regarding TB investigations and excellent knowledge in terms of dealing with positive or suspected cases.

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# Collagen-Based Grafts and Autologous Dura Replacement in Patients with Dura Abnormalities: A Retrospective Comparative Evaluation

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Received: February 2023; Accepted: March 2023; Published: April 1, 2023.
Citation: Zahra Mannan Waheed et al. Collagen-Based Grafts and Autologous Dura Replacement in Patients with Dura Abnormalities: A Retrospective Comparative Evaluation. World Family Medicine. March 2023; 21(3): 19-23
DOI: 10.5742/MEWFM.2023.95256069

## Abstract

Introduction: Accidental spinal anomalies of the spinal dura mater are the source of cerebrospinal fluid (CSF) leakage. Typically, dura abnormalities are identified in 3 percent of endoscopic lumbar discectomy cases.

Objective: The purpose of the current research was to evaluate the results of autologous dura replacement versus collagen-based grafts in individuals with dura deformities.

Methods: The Institute of Neurosurgery at Liaquat National Hospital Karachi undertook this randomized evaluation to identify the most effective therapy for dura mater defects. Employing non-probability random selection, 82 cases among both sexes were selected. Participants were divided randomly into two subgroups i.e. Group 1A received an autologous graft for dura restoration, whereas Group 2B received a semi-synthetic dura replacement. A skilled surgeon led a medical team of six people who completed the entire process.

Results: The operation duration for semi-synthetic collagen was significantly reduced. There was a 40 minute variation in total time spent by the two groups. Autologous grafts showed ideal tightness and better flexibility and fair workability on the other hand semi-synthetic collagen showed better tightness and workability and ideal flexibility. Postoperative hospital stays were seen to be 26 + 2.5 hours in Group 1A whereas they were 23 + 2.5 hours for Group B.

Conclusion: According to the aforementioned findings, an accessible, secure, and efficient substitution for an autologous graft for dura restoration in dura abnormalities is the use of a semi-synthetic collagen substitute.

Keywords: semi-synthetic collagen substitute, cerebrospinal fluid, dura abnormalities, autologous graft.

## Background

Accidental spinal anomalies of the spinal dura mater are the source of cerebrospinal fluid (CSF) leakage [1]. As a result of sudden intracranial hypotension (SIH), patients with spontaneous CSF leakage frequently report with orthostatic headaches [2]. Dura abnormalities and a drop in CSF levels occur in around 20% of thoracic myelopathy individuals [3]. Typically, dura abnormalities were identified in 3 percent of endoscopic lumbar discectomy cases [3,4]. These flaws can result in adhesive arachnoiditis, headaches, post-operative diseases, adhesive CSF pseudocysts and cerebrospinal meningitis [5]. After neurosurgery operations, dural abnormalities must be sealed to block the flow of CSF and minimise the risk of perioperative disorders [6].

Due to factors such as coagulation-induced dura contraction or renounce, surgical resection of the dura (resection of meningiomas), or dural damage after trauma, main closure is extremely difficult in a number of surgical situations. As a result, the dural defect must be repaired using a replacement [7,8]. There are several dura alternatives on the market right now. Solely dura grafts formed of semi-synthetic collagen seem encouraging among all these dura replacements because they are designed to consistently present a physical barrier, contain non-toxic, biodegradability biological material with antimicrobial properties, and have been established in terms of effectiveness and insulative properties. They are also assumed to maintain a matrix for in growth and subsequent replacement by endogenous connective tissue [9,10].

Due to their nontoxicity, quick integration into native tissues, flexibility, strength, ease of suturing, and lack of immunological or inflamed responses, autologous grafts like galea-pericranium or fascia lata serve as the ideal framework for dural transplants [11,12]. However, employing such tissues for an autograft is rarely effective [13]. The benefits of autologous grafts are their low cost, fairly widespread access, and bio-compatibility with the patient [14]. The disadvantages involve patient requiring a second surgical incision, an extended recovery duration, an upsurge in operating theatre time required for further tissue collection, and higher patient pain [15].

The purpose of the current research was to evaluate the results of autologous dura replacement versus collagen-based grafts in individuals with dura deformities.

## Material and Methods

The Institute of Neurosurgery at Liaquat National Hospital Karachi undertook this randomized evaluation to identify the most effective therapy for dura mater defects. Employing non-probability random selection, 82 cases among both sexes were selected. Participants over the age of 18 who needed a dura replacement during supratentorial surgical treatment were included. Expectant mothers, individuals having weak immune systems, all spine damage instances, and untreated wounds were all eliminated. Following the hospital ethics panel's clearance, the research was performed. The participant's caregivers also provided signed consent permission.

Participants were divided randomly into two subgroups i.e. Group 1A received an autologous graft for dura restoration, whereas Group 2B received a semi-synthetic dura replacement. A skilled surgeon led a medical team of six people who completed the entire process. Following surgery and dural replacement by auto-graft or semi-synthetic grafts, CSF drainage and disease were detected. Following that, the participants experienced routine follow-up and examinations every 3 weeks for 6 months. One set of patients undergoing supratentorial brain surgery received an autologous dura transplant.

At the intersection of the top and central thirds of the upper leg, a 4 to 6 cm long incision was made to remove the fascia lata from the medial thigh. In the superficial area of the abdominal portion, a bone flap was transplanted. All participants underwent preoperative medication, and surgical drains inserted surgically were eliminated two days following the surgery. Semi-synthetic dura grafts in the dimensions of 3.5x3.5 cm, 4x4 cm, and 6.5 cm x 6.5 cm were employed in the group 2B.

In order to do the statistical study, SPSS version 21 was used. The two subgroups underwent a Student's t-test to compare variables, and the results were deemed statistically meaningful at p value greater than 0.05.

## Results

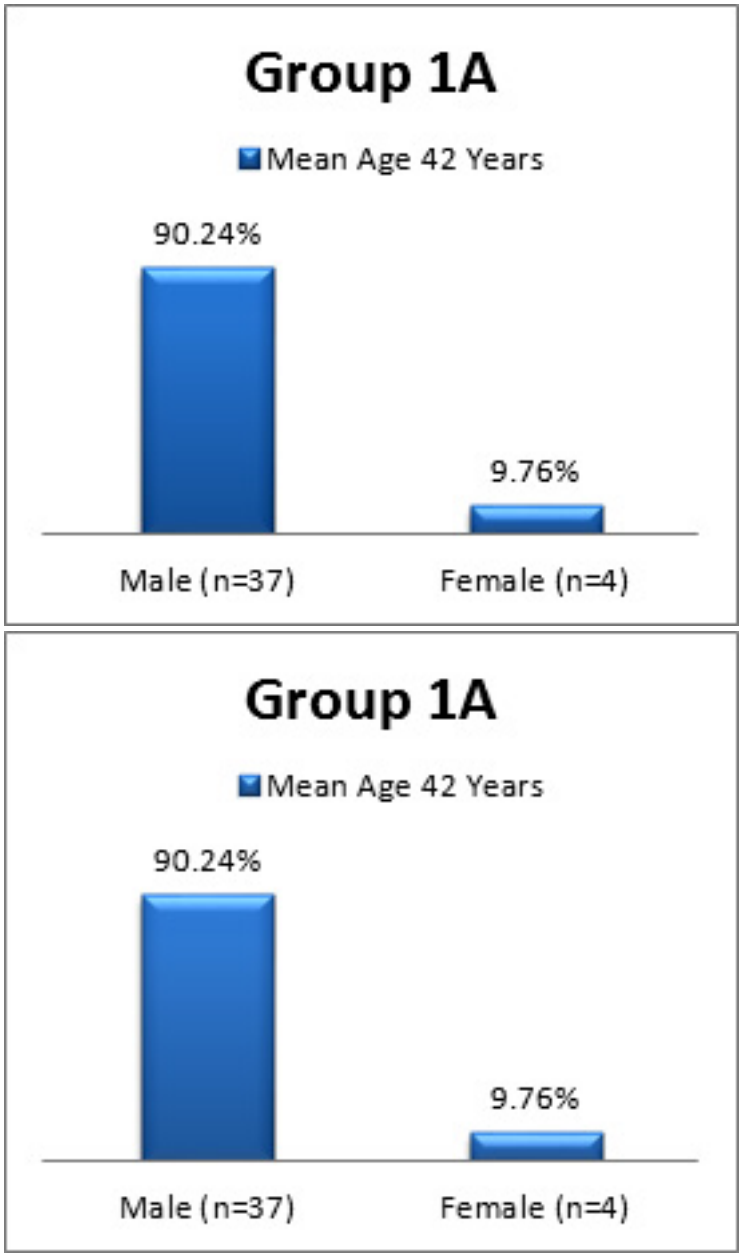
Eighty-two individuals with an average age of 38.46±6.4 years were included in this retrospective comparative evaluation. Group 1A (autologous graft ) and Group 2B of patients were randomly assigned to each category (semisynthetic collagen). Group 1A's patients had an average age of 42 whereas group 2B's patients had an average age of 34. Participants in both groups were more likely to be men than women. Four women (9.76%) and 37 men (90.24%) made up Group 1A, whereas nine women (21.96%) and 32 men (70.04%) made up Group 2B (Figure 1).

The average surgical time in group 1A was significantly longer than in group 2B (170.02±4.5 minutes vs. 120.12±4.5 minutes), with a mean difference of 40 minutes. By adopting a semi-synthetic collagen graft rather than an autologous graft, considerable time might be saved, according to the time factor. However, both groups noted statistically significant variations in the length of the surgery (< 0.002) (Table 1).

Compared to semi-synthetic collagen (6%), autologous surgery took 19% longer to complete. In neither group was an infection case noted. Post treatment, all individuals had intensive care unit (ICU) monitoring and underwent anti-epileptic drugs (AEDs) and therapies for oedema. Autologous grafts displayed ideal tightness,

better flexibility, and fair workability, while semi-synthetic collagen displayed better tightness, workability, and ideal flexibility (Figure 2). In Group 1A, the post - operative hospital stay was seen to be 26 + 2.5 hours, whereas Group 2B was 23 + 2.5 hours. There was no discernible change in the number of days the patient stayed in the hospital (Figure 3).

**Figure 1: Gender distribution of patients with mean age.**

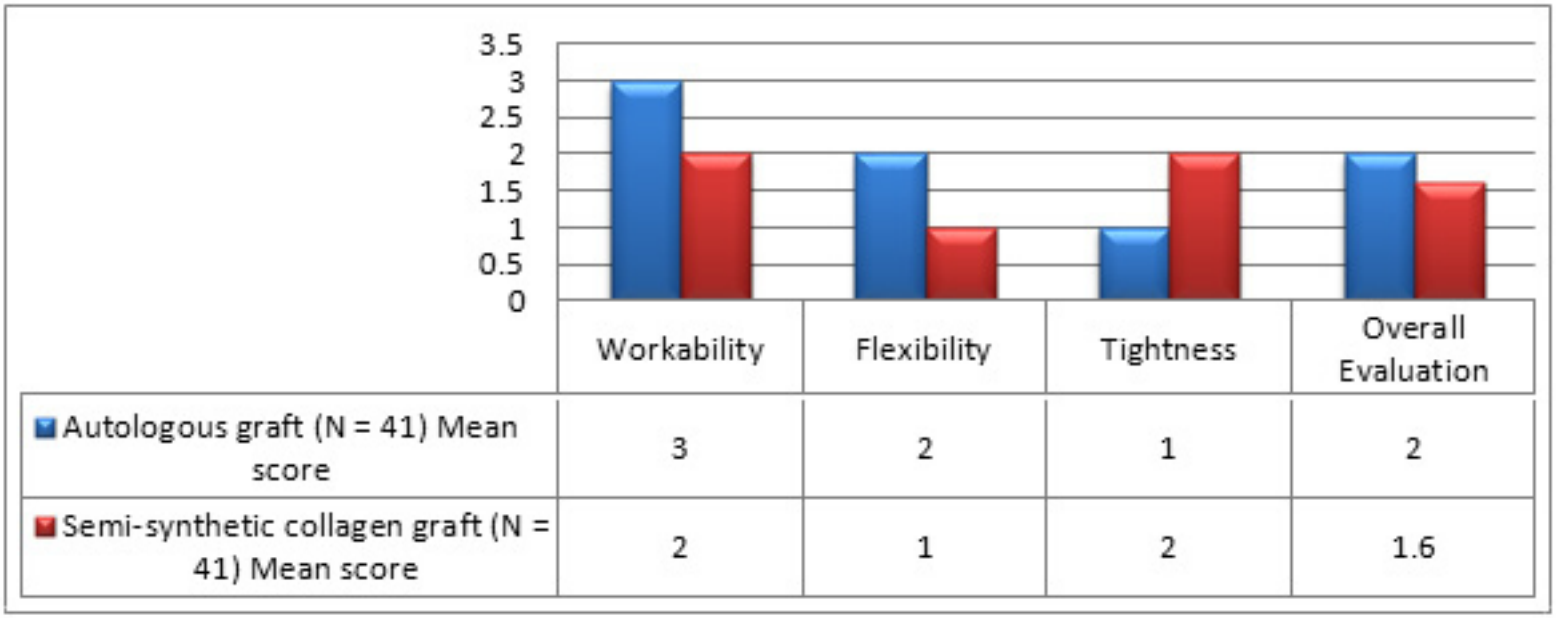



Group 1A
Mean Age 42 Years
90.24%
9.76%
Male (n=37)
Female (n=4)

**Table 1: Statistical evaluation of dura restoration**

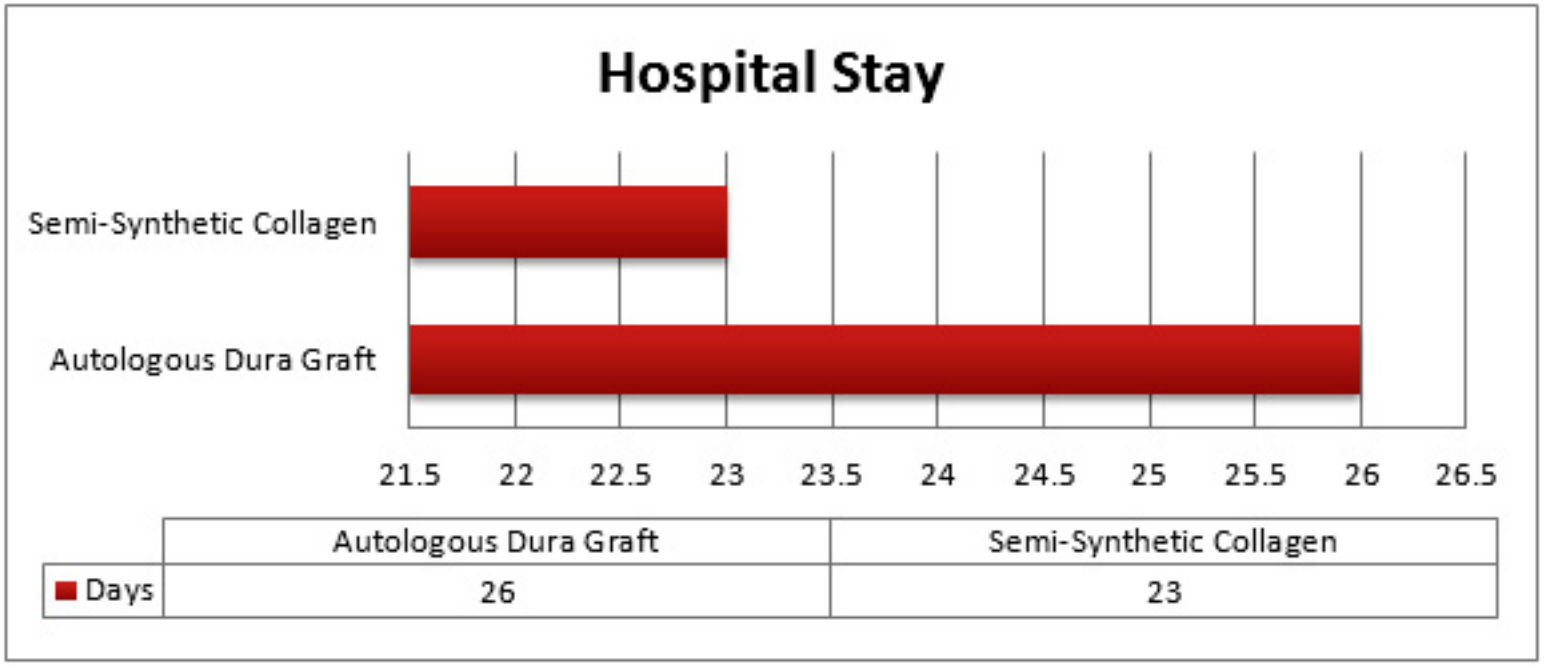
| | Materials | Mean | Standard deviation | Typical Error of the Mean |
|---|---|---|---|---|
| **Minutes spent doing the surgery** | Autologous graft | 170.02 | 3.53 | 0.78 |
| | Semi-synthetic Collagen | 120.12 | 4.53 | 1.02 |

**Figure 2: Parameter evaluated post operatively (1 = Ideal, 2 = Better, 3 = Fair, 4 = poor, 5 = incredibly bad).**




| | Workability | Flexibility | Tightness | Overall Evaluation |
|---|---|---|---|---|
| Autologous graft (N = 41) Mean score | 3 | 2 | 1 | 2 |
| Semi-synthetic collagen graft (N = 41) Mean score | 2 | 1 | 2 | 1.6 |

**Figure 3: Hospital stay time of both groups (autologous dura graft and semi-synthetic collagen).**




| | Autologous Dura Graft | Semi-Synthetic Collagen |
|---|---|---|
| Days | 26 | 23 |

## Discussion

In current research, the effectiveness of autologous vs semisynthetic collagen-based grafts in individuals with dura mater defects was compared. The current research demonstrated that the operation duration for semi-synthetic collagen was significantly reduced. There was a 40 minute variation in total time spent by the two groups. These findings are consistent with the earlier investigation of Dash et al. [16]. Our autologous research group had CSF leaking as a result of the use of surgical dissection, prolonging the hospital stay. These findings are consistent with the earlier investigation of Ransom et al. [17].

In the current investigation, restorations were completed without the usage of stitches, and no CSF leaking was noticed throughout the follow-up period. According to studies, fixing dura abnormalities that cannot be fixed with standard reattachment techniques requires the use of autologous grafts as a quick and efficient strategy. Collagen matrix was shown to be a good method for anterior fossa in a research by Narotam et al. (18), during which it was used as a graft without employing stitches and causing any difficulty [18]. By attaching to the holes in the collagen matrix, the fibroblast acts as a framework for additional collagen. Collagen matrix is fully immersed and is replaced by a fresh dura mater at the end of seven weeks. Consequently, this method is simple to apply and has an effective safety record [19].

Autologous grafts showed ideal tightness and better flexibility and fair workability; on the other hand semi-synthetic collagen showed better tightness and workability and ideal flexibility. Additionally, postoperative hospital stays were seen to be 26 + 2.5 hours in Group A whereas they were 23 + 2.5 hours for Group B. Concerning the number of days the patient remains in the hospital, there wasn't any discernible difference. These results are consistent with research by Muhammad et al. [20].

## Conclusion

Considering the aforementioned results, our research came to the conclusion that an easy, secure, and efficient replacement for an autologous graft for dura restoration in dura abnormalities is the use of a semi-synthetic collagen substitution. Comparing semi-synthetic collagen graft to autologous graft for dura restoration, there is a considerable reduction in operative time, surgical trauma, and the amount of time individuals remain hospitalized.

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# Prevalence and characteristics of Nocturnal Enuresis (NE) in affected children aged 5-18 years in Saudi Arabia

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Received: February 2023 Accepted: March 2023; Published: April 1, 2023.
Citation: Saleh Mohamed Alrajihi at al. Prevalence and characteristics of Nocturnal Enuresis (NE) in affected children aged 5-18 years in Saudi Arabia. World Family Medicine. March 2023; 21(3): 24-33 DOI: 10.5742/MEWFM.2023.95256067

## Abstract

Background: Nocturnal enuresis (NE) is involuntary urination that happens while you're asleep after a certain age when you should be able to control your bladder at night. Depending on when the condition first appears, enuresis is divided into primary and secondary categories. Families shouldn't be concerned about it, but we must be mindful of the effects it may have on the family and the child. This study aims to determine the prevalence and to reveal the characteristics of Nocturnal Enuresis (NE) in affected children aged 5-18 years in Saudi Arabia.

Materials and Methods: A cross-sectional descriptive study was carried out among 458 Saudi parents/caregivers, whose children were aged from 5 to 18 years. It was conducted during the period from July 2022 to November 2022. An electronic questionnaire was designed using a Google form distributed among parents/caregivers in Saudi Arabia. Ethical approval was obtained from KFMC. Data were analyzed using Statistical Package for Social Sciences (SPSS) version 26.

Results: 75% of children suffering from NE were males and 51.9% had an age ≥ 10 years with a mean age of 8.78± 3 years. In this study 34% of the children with NE experienced 2-4 bouts of bedwetting, per week. The most common procedure done for management was Behavioral Stimulation Therapy (75.9%) and 55.6% reported improvement of the child after the intervention. Male children, and those with an age <10 years had a significantly higher percentage of daily NE (p=<0.05). Children who were circumcised and those who drink a lot of water or any other beverage had a significantly higher percentage of having daily NE (p=<0.05). At the same time, children who had UTI had a significantly higher percentage of having daily NE (p=<0.05).

Conclusion: NE occurs among children in various Saudi Arabian regions. Male gender, aged 5 to 10 and suffering from weakness of bladder muscles, chronic constipation, worry and depression was associated with NE and UTI. Families and caregivers utilize effective therapies such as alarm and behavioral stimulation, however, they do not look for medical assistance.

Keywords: Nocturnal Enuresis, Children, Characters, Prevalence

## Introduction

Nocturnal enuresis (NE) is the involuntary urination that occurs while asleep after an age when bladder control at night is expected (involuntary urination that happens during the day is known as diurnal enuresis (1).

It is grouped into two types: primary and secondary. Primary nocturnal enuresis occurs when a patient has never achieved continence for at least 6 months, whereas secondary nocturnal enuresis is onset of symptoms after a patient had achieved continence of at least 6 months (2,3). Age, male gender, daytime incontinence, encopresis, social anxiety, delayed walking age, positive parental history of enuresis, and sibling history of enuresis are all risk factors associated with NE (4). Nocturnal enuresis can cause low self-esteem, a sense of failure, chronic stress, and social problems for children. It has been linked to a variety of behavioral, psychological, and social issues. As a result, it is critical to identify at risk children and take therapeutic steps (5).

The universal incidence of Nocturnal enuresis in children 6-12 years of age was shown to be 15%-25% in one study, while a study in Saudi Arabia showed an incidence of 31.2% among children aged 3-12 years (2,6).

Enuresis is a prevalent clinical condition that affects both students and their parents' quality of life as a result of the disorder's impact on social life, and emotional and learning issues arise (7).

Therefore, our aim of the study is to determine the prevalence and to reveal the characteristics of Nocturnal Enuresis (NE) in affected children aged 5-18 years in Saudi Arabia.

## Subjects and Methods

**Study Design, setting and time frame:** a cross-sectional study was done at KFMC from August to November 2022.

**Study participants:** the inclusion criteria were guardians of children aged 5-18 years' old who are residents in Saudi Arabia. And the exclusion criteria: was any participant with chronic diseases such as (Mental defect, paralysis, diabetes mellitus, sickle cell disease, congenital defect, epilepsy or other neurological defect).

**Sample size:** by using Raosoft online sampling with margin of error of 5% and confidence level of 95% and according to the most recent study that was conducted in Saudi Arabia measuring the prevalence of NE among children, our estimated sample size is 330

**Study instrument:** an electronic pre-designed questionnaire in a Google form was distributed among parents in Saudi Arabia through social media platforms (What's App) and through the community, in public places to target the General population. A brief introduction and the aim of the study was written and consent was obtained from the parents. Questions were adapted from a previous literature review (8). Two expert reviewers edited the questionnaire and modification was done based on feedback from reviewers. The last version of the questionnaire contained three sections. The first section included items to collect the children's demographic characteristics and the 2nd section had multiple questions regarding sleep pattern and involuntary urination types. The 3rd section was about the consequent effects on the family with 4 response options.

**Data collection:**
An electronic questionnaire designed using Google form was distributed among parents/caregivers in Saudi Arabia. It was distributed through social media platforms (What's App groups, emails) and through the community in public places to target the General population. A brief introduction and the aim of the study was written and consent was obtained from the parents/caregivers. Questions were adapted from previous literature review [8]. Two expert reviewers edited the questionnaire, and modification was done based on feedback from reviewers. The final version of the questionnaire contained three sections. The first section gathered demographic data of the child and the parent/caregivers. The second section had multiple questions regarding sleep pattern and involuntary urination types. The third section enquired about the scale of consequential effects on the family with 4 response options (large degree, medium degree, small degree, not at all). To enhance validity and clarity of the questionnaire the final form was piloted on 10% of the sample.

**Ethical consideration:**
Ethical approval was obtained from KFMC. The link only opened if participants selected 'agree to participate'. The questionnaire had a brief introduction explaining its aim and purpose and informing participants that participation is entirely voluntary. No names were recorded in the surveys, neither date of birth nor address was collected. All answers were kept confidential and safe.

**Statistical analysis:**
Data analysis: data was analyzed using SPSS version 26. To investigate the association between the variables, the Chi-squared test ($\chi 2$) was applied to qualitative data that was expressed as numbers and percentages. Quantitative data was expressed as mean and standard deviation (Mean ± SD) and a p-value of $< 0.05$ was considered significant.

## Results

(Figure 1) illustrates that of the studied guardians, 108 (76.8%) reported that they have a child or children who suffer from nocturnal enuresis (NE).

**Figure 1. Percentage distribution of guardian according to having a child or children suffering Nocturnal Enuresis (NE) (No.: 465)**

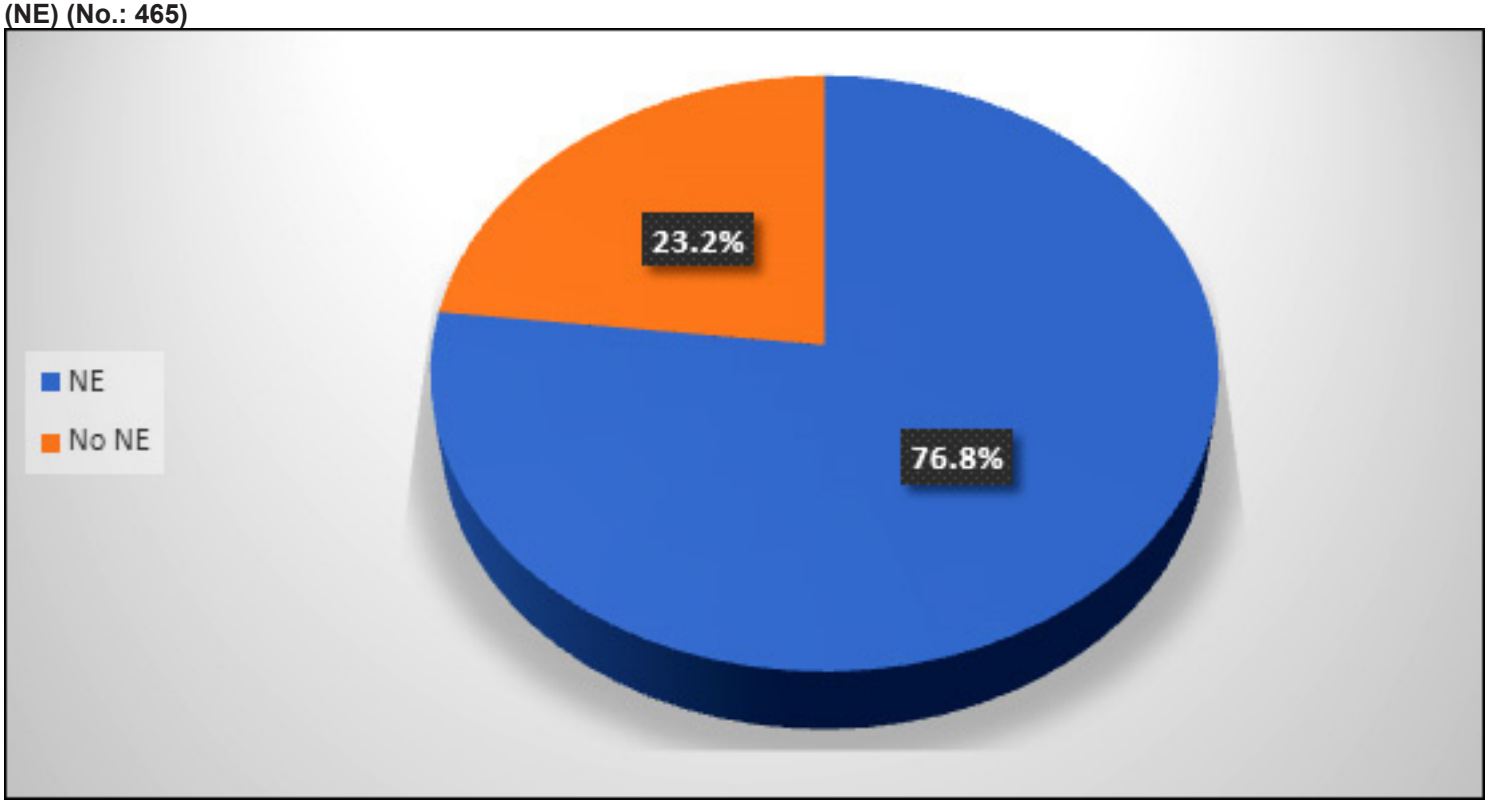



Table 1 shows that 75% of children suffering from NE were males and 51.9% had an age ≥ 10 years with a mean age of 8.78± 3 years. Of them, 90.8% were of Saudi nationality, 44.6% were from the Central region of KSA, 45.5% had a monthly family income <10000 SR and the mean number of family members with father and mother was 6.69 ± 6.37. Most children (90.9%) were living with their parents, and the mean order of the child among his siblings was 3.06 2.23 rank. The mean number of children the guardian has with nocturnal enuresis was 1.47±0.98 children. The most common health problems the NE children suffered were: worry (23.1%) and hyperactivity(22.2%). Only 8.3% were suffering from UTI.

Table 2 shows that most children (79.6%) were delivered through normal delivery, 72.2% had a 9th gestational age at birth, 25.1% had both parents and 29.65 had a sibling suffer from bedwetting during childhood. For 34.1% the frequency of NE was once a month, while 15.7% had daily NE. The condition of the child during sleep was difficult for 64.9% of children, 51% had NE a long time after sleep and 52.8% were 6 months or more without bedwetting. Of them, 75% were circumcised and 72.3% drink a lot of water or any other beverage.

**Table 1. Distribution of children with NE according to their demographics, child order, other children with NE and associated disorders (No=108)**

| Variable | No. (%) |
|---|---|
| The gender of the child? | |
| Female | 27 (25) |
| Male | 81 (75) |
| How old is the child? | |
| <10 years | 52 (48.1) |
| ≥10 years | 56 (51.9) |
| (mean ± SD) | 8.78 ± 3 |
| The nationality of the child? | |
| Saudi | 98 (90.8) |
| Non-Saudi | 10 (9.2) |
| Where you live? | |
| South | 2 (1.8) |
| East | 41 (37.9) |
| North | 8 (7.4) |
| West | 9 (8.3) |
| Central | 48 (44.6) |
| Family income | |
| <10000 SR | 49 (45.5) |
| 10000-30000 SR | 40 (37) |
| >30000 SR | 19 (17.5) |
| Mean number of family members with father and mother | 6.69 ± 6.37 |
| Who does the child live with? | |
| Father only | 2 (1.8) |
| Mother only | 7 (6.4) |
| Parents | 98 (90.9) |
| Between mother & father | 1 (0.9) |
| What is the order of the child among his siblings? | 3.06 ± 2.23 |
| How many of your children have or have had nocturnal enuresis? (mean ± SD) | 1.47 ± 0.98 |
| Does the child suffer from any of the following? (n=108) | |
| Intellectual disabilities | 3 (2.7) |
| Physical paralysis | 1 (0.9) |
| Diabetes | 7 (6.4) |
| Sickle cell fracture | 6 (5.5) |
| Birth defects | 7 (6.4) |
| Epileptic or neurological disease | 5 (4.6) |
| Does the child suffer from any of the following ? | |
| Autism | 1 (0.9) |
| hyperactivity | 24 (22.2) |
| Snoring | 15 (13.8) |
| Apnea at night | 5 (4.6) |
| Urinary tract infection | 9 (8.3) |
| Weakness of the bladder muscles | 4 (3.7) |
| Chronic constipation | 6 (5.5) |
| Worry | 25 (23.1) |
| Depression | 4 (3.7) |

**Table 2. Distribution of children with NE according to their pregnancy and childbirth conditions, family history of NE and NE pattern (No=108)**

| Variable | No. (%) |
|---|---|
| What is the type of child's birth? | |
| Normal | 86 (79.6) |
| CS | 22 (20.4) |
| What is the gestational age when the child is born? | |
| 7th | 22 (20.4) |
| 8th | 8 (7.4) |
| 9th | 78 (72.2) |
| Did one or both parents suffer from bedwetting during childhood? | |
| No | 66 (61.1) |
| Yes, Father | 6 (5.5) |
| Yes, Mother | 9 (8.3) |
| Yes both | 27 (25.1) |
| Did any of the child's siblings suffer from bedwetting during childhood? | |
| No | 69 (64) |
| No siblings | 7 (6.4) |
| Yes | 32 (29.6) |
| If yes, how many siblings are affected? (mean ± SD) | 0.71 ± 0.1.1 |
| Rate of nocturnal enuresis | |
| Daily | 17 (15.7) |
| Once / week | 20 (18.5) |
| 2-4 times / week | 34 (31.4) |
| Once / month | 37 (34.4) |
| The condition of the child during sleep? | |
| Easy | 38 (35.1) |
| Difficult | 80 (64.9) |
| What time does bedtime urination occur? | |
| Any time after sleep | 44 (40.7) |
| Shortly after sleep | 9 (8.3) |
| Long time after sleep | 55 (51) |
| Has the child been 6 months or more without bedwetting? | |
| No | 51 (47.2) |
| Yes | 57 (52.8) |
| Was the child circumcised? | |
| No, a female child | 22 (20.4) |
| No | 5 (4.6) |
| Yes | 81 (75) |
| Does the child drink a lot of water or any other beverage? | |
| No | 30 (27.7) |
| Yes | 78 (72.3) |
| In the case of a urinary tract infection, how often? (mean SD) | 1.83 1.58 |

Table 3 shows that the most common factor that surrounds the child at the beginning of the symptoms of bedwetting was family problems inside the house. Of the Guardians, 40.8% reported that the child's NE causes embarrassment or social shame for the child. The most common procedure done for management was Behavioral Stimulation Therapy (75.9%) and 55.6% reported improvement of the child after the intervention.

**Table 3. Distribution of children with NE according to factors surrounding child at beginning of NE, effect on family and management (No=108)**

| Variable | No. (%) |
|---|---|
| The factors surrounding the child at the beginning of the symptoms of bedwetting: | |
| Having a newborn child (smaller than the child who suffers from urination) | 21 (19.4) |
| The family has moved to another city | 12 (11.1) |
| There are family problems inside the house | 23 (21.2) |
| Separation of father and mother | 8 (7.4) |
| The death of a relative | 7 (6.4) |
| There are financial problems in the family that cause tension inside the home | 12 (11.1) |
| Did the problem cause embarrassment or social shame for the child? | |
| No | 64 (59.2) |
| Yes | 44 (40.8) |
| Have you done one of the following procedures to get rid of bedwetting in the child ? | |
| Behavioral Stimulation Therapy | 82 (75.9) |
| Bedwetting alarm | 4 (3.7) |
| Exercises to strengthen the bladder muscles | 8(7.4) |
| Ease of medicines | 8 (7.4) |
| Surgery | 2 (1.8) |
| If you used one of the previous procedures, did the child's condition improve after that? | |
| No | 48 (44.4) |
| Yes | 60 (55.6) |

Table 4 shows that most of the guardians (49.1%) reported that the child with bedwetting takes a lot of the carer's time . While 59.4% reported that this experience never made them more connected to religious and spiritual matters and never caused them to understand the things that should be valued in life (23.1%). The majority (63.2%) reported that NE never caused additional financial burdens, but bedwetting has never improved their relationship with their husband/wife (69.6%). Almost a third (30.5%) reported that chronic stress in the family is never a consequence of having a child with bedwetting and only 6.4% reported that NE experience never helped them realize that every child has a unique personality and unique talents. The majority (64%) reported that a child with bedwetting never made them postpone or cancel some big vacation plans and 45.4% reported that family members become a little bit more tolerant of differences in other people, and more receptive to mental or physical differences between people. For 68.7%, NE never reduced the time parents spend with their friends and for 31.8% the child's condition never caused positive personal development, or the personal strength of the father or mother. For 76.1%, NE never made parents reluctant to call friends or acquaintances by phone. For 66.7% it never caused tension and tension between the spouses and for 69.5% NE never postponed any major purchases. 42.5% reported that raising a child who has difficulty makes life a little bit more meaningful for family members.

**Table 4. Distribution of guardians of children with NE according their thoughts about family implications of having a child with bed-wetting (No=108)**

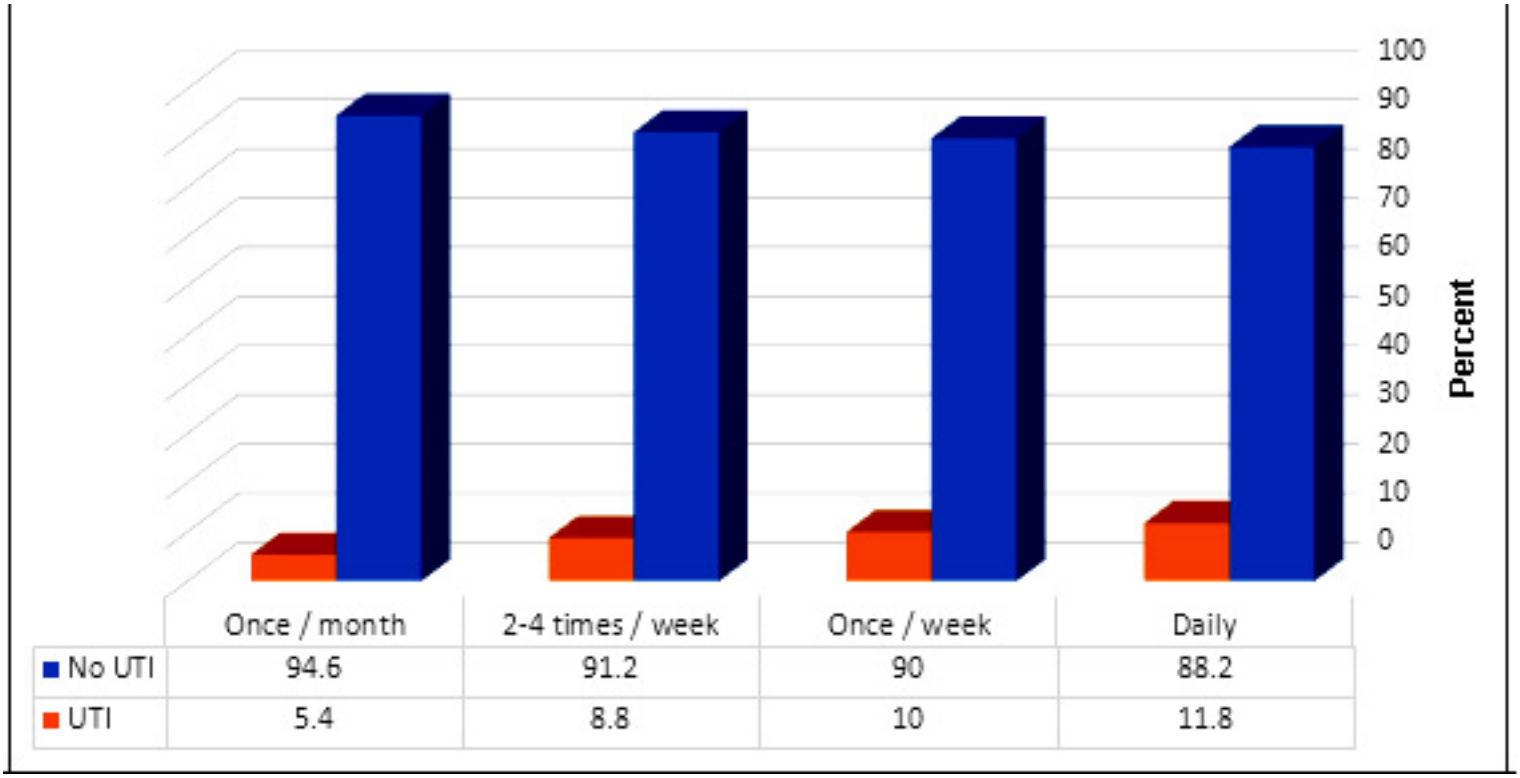
| Variable | Never | Little | Moderate | Much |
|---|---|---|---|---|
| Caring for a child with bedwetting takes a lot of time | 8 (7.4) | 20 (18.5) | 27 (25) | 53 (49.1) |
| Having a child with bedwetting caused unwanted disruptions in the normal family routine | 20 (18.5) | 47 (43.5) | 29 (26.6) | 12 (11.1) |
| This experience (having a child with bedwetting) made us more connected to religious and spiritual matters | 63 (59.4) | 13 (12) | 16 (14.8) | 15 (13.8) |
| Having a child with bedwetting has caused additional financial burdens | 68 (63.2) | 23 (21.2) | 10 (9.2) | 7 (6.4) |
| Family members do more things for each other than they do for themselves | 27 (25) | 27 (25) | 39 (38) | 13 (12) |
| Having a child with bedwetting has improved my relationship with my husband/wife | 75 (69.6) | 21 (19.4) | 5 (4.6) | 7 (6.4) |
| Having a child with bedwetting reduced social contact outside the home | 72 (66.8) | 16 (14.8) | 11 (10.1) | 9 (8.3) |
| This experience (having a child with bedwetting) made us come to understand the things that should be valued in life | 25 (23.1) | 29 (28.8) | 40 (37) | 12 (11.1) |
| Chronic stress in the family is one of the consequences of having a child with bedwetting | 33 (30.5) | 19 (17.5) | 38 (35.4) | 18 (16.6) |
| This experience (having a child with bedwetting) helped me realize that every child has a unique personality and unique talents | 7 (6.4) | 19 (17.5) | 40 (47.4) | 31 (28.7) |
| Having a child with bedwetting made us postpone or cancel some big vacation plans | 68 (64) | 22 (20.4) | 7 (6.4) | 10 (9.2) |
| Family members become more tolerant of differences in other people, and more receptive to mental or physical differences between people | 27 (25) | 48 (45.4) | 20 (18.5) | 12 (11.1) |
| This condition (having a child with bedwetting) has reduced the time parents spend with their friends | 73 (68.7) | 17 (15.7) | 7 (6.4) | 10 (9.2) |
| The child's condition has caused positive personal development, or the personal strength of the father or mother | 61 (31.8) | 18 (16.6) | 19 (17.5) | 9 (8.3) |
| Because of this condition, parents are reluctant to call friends or acquaintances by phone | 81 (76.1) | 15 (13.8) | 6 (5.5) | 5 (4.6) |
| This experience has made family members more aware of people's needs and suffering of having a child with bedwetting | 25 (23.1) | 22 (20.4) | 40 (38) | 20 (18.5) |
| This situation caused tension and tension between the spouses | 71 (66.7) | 22 (20.4) | 6 (5.5) | 8 (7.4) |
| This experience taught me that there are so many blessings when having a child who has a difficulty/problem | 15 (13.8) | 21 (19.4) | 42 (40) | 29 (26.8) |
| Due to circumstances related to the child's condition, many major purchases have been postponed | 74 (69.5) | 16 (14.8) | 8 (7.4) | 9 (8.3) |
| Raising a child who has difficulty making life more meaningful for family members | 28 (28.9) | 46 (42.5) | 15 (13.8) | 16 (14.8) |

Table 5 shows that male children, with an age <10 years had a significantly higher percentage of having daily NE (p=<0.05), while children who had NE 2-4 times / week had a significantly higher percentage of having any of the following medical conditions (Autism, hyperactivity , snoring, apnea at night, weakness of bladder muscles, chronic constipation, worry, depression) (p=<0.05). Children who were circumcised and those who drink a lot of water or any other beverage had a significantly higher percentage of having daily NE (p=<0.05). At the same time, children who had UTI had a significantly higher percentage of having daily NE (p=<0.05) (Figure 2).

**Table 5. Relationship between NE frequency and children demographics, medical conditions, circumcision and drinking a lot of water or beverage**

| Variable | Rate of nocturnal enuresis | | | | χ2 | p-value |
|---|---|---|---|---|---|---|
| | Daily No. (%) | Once / week No. (%) | 2-4 times / week No. (%) | Once / month No. (%) | | |
| The gender of the child? | | | | | | |
| Female | 5 (29.4) | 6 (30) | 10 (29.4) | 6 (16.2) | 4.98 | <0.001 |
| Male | 12 (70.6) | 14 (70) | 24 (70.6) | 31 (83.8) | | |
| How old is the child? | | | | | | |
| <10 years | 9 (52.9) | 15 (75) | 22 (64.7) | 6 (16.2) | 4.77 | <0.001 |
| ≥10 years | 8 (47.1) | 5 (25) | 12 (35.3) | 31 (83.8) | | |
| Does the child suffer from any of the following ? | | | | | | |
| Autism | 0 (0.0) | 0 (0.0) | 1 (2.9) | 0 (0.0) | 4.45 | <0.001 |
| Hyperactivity | 6 (35.3) | 4 (20) | 12 (35.3) | 2 (5.4) | 13.20 | <0.001 |
| Snoring | 3 (17.6) | 3 (15) | 8 (23.5) | 1 (2.7) | 9.99 | <0.001 |
| Apnea at night | 0 (0.0) | 0 (0.0) | 5 (14.7) | 0 (0.0) | 14.12 | <0.001 |
| Weakness of bladder muscles | 1 (5.9) | 1 (5) | 2 (5.9) | 0 (0.0) | 7.5 | <0.001 |
| Chronic constipation | 0 (0.0) | 1 (5) | 3 (8.8) | 2 (5.4) | 7.34 | <0.001 |
| Worry | 2 (11.8) | 6 (30) | 13 (38.2) | 4 (10.8) | 5.96 | <0.001 |
| Depression | 1 (5.9) | 0 (0.0) | 3 (8.8) | 0 (0.0) | 6.17 | <0.001 |
| Was the child circumcised? No, a female child | | | | | | |
| No | 0 (0.0) | 1 (5) | 3 (8.8) | 1 (2.7) | 8.27 | <0.001 |
| Yes | 12 (70.6) | 14 (70) | 24 (70.6) | 31 (83.8) | | |
| Does the child drink a lot of water or any other beverage? | | | | | | |
| No | 7 (41.2) | 5 (25) | 13 (38.2) | 5 (13.5) | 6.01 | <0.001 |
| Yes | 10 (58.8) | 15 (75) | 21 (61.8) | 32 (86.5) | | |

**Figure 2. Relationship between NE frequency and having UTI**




| | Once / month | 2-4 times / week | Once / week | Daily |
|---|---|---|---|---|
| No UTI | 94.6 | 91.2 | 90 | 88.2 |
| UTI | 5.4 | 8.8 | 10 | 11.8 |

N.B.: ($\chi 2 = 8.27$, p-value = <0.001)

## Discussion

Around the world, nocturnal enuresis (NE) is a frequent childhood condition that can be problematic for both children and their families. This study calculated the prevalence of nocturnal enuresis among children aged 5 to 18 in several Saudi Arabian locations, along with some factors, including demographics, child order, and associated disorders. It also provides description of the thoughts of guardians of children with NE. Finally, it explored the relationship between NE frequency and children's medical conditions, circumcision and drinking a lot of water or beverages.

In various parts of Saudi Arabia, the prevalence of having a child with NE was around 22.1%, with a higher prevalence among boys (68.8%). The prevalence is increased over the years, which required more attention by the specialized clinical provider. At tertiary military hospital, where the study by Alshahrani et al., 2018 was conducted, a frequency of NE was (18.5%), with a higher prevalence among boys [9]. Later in 2020 a country-wide survey comprising 2,148 replies, indicated a higher prevalence rate of (31.4%) [2].

Published local research showed, that prevalence of NE differs according to child's age with strong correlation between enuresis prevalence and age [1]. Alhifthy et al. (2021) reported, that the prevalence was highest in age group 5-7years (36.6%) and dropped as age increased, with a slight rise in prevalence in children aged 16–18 years (9.3%) compared to those aged 13–15 (8.9%) [8]. This is similar to our findings, as the prevalence was highest in children aged 5 to 10 (76.3%), and it reduced, reaching a low of (23.8%) in children older than 10 years. This distribution was also observed by Alshahrani et al. (2018) [9].

In contrast, some studies, showed that older age group had the highest prevalence [11], while others, found no appreciable variation in the prevalence of NE with age [10].

Regarding distribution of guardians of children with NE, common thoughts were caring for a child with bedwetting takes a lot of time and that this child is special.

Regarding the frequency of bedwetting, in this study 34% of the children with NE experienced 2-4 bouts of bedwetting, per week. Those who experienced a frequency of bedwetting episodes more than twice per week, were commonly reported by children with NE [13], [14].

The frequency of bedwetting could be affected by many factors. For example, this study showed that children who were circumcised and those who drink a lot of water or any other beverage had a significant higher percentage of having daily NE. However, there is no scientific evidence about the association between that circumstance and bedwetting.

Medical profile of a child, can affect the sleep quality [15]. Conditions including, autism, hyperactivity, snoring, apnea at night, weakness of bladder muscles, chronic constipation, worry, and depression were significantly associated with NE 2-4 times per week. The frequency was also associated with the UTI.

Moreover, families and caregivers had to some extent a positive response to the NE. Finding a solution is proof of admitting NE is a health issue. The common methods utilized by families and caregivers in our sample, were behavioral stimulation therapy (55, 68.8%), followed by medication and exercises to strengthen the bladder muscles (8.8%). Only 3.8% employed bedwetting alarms.

Other researchers observed a negative response towards NE. Alhifthy et al. (2021), reported that the majority of respondents (64.3%) did not try any therapy to manage their child's NE [8]. According to Pandey et al. (2019), just 13.2% of parents had implemented behavioral interventions for their children, while 79% had not [13]. Hamed et al. (2017) discovered that behavioral treatment was employed in 16.7% of instances and that families didn't intervene in the majority of a sample [14].

Seeking a medical consultation, is an early intervention that could prevent NE from developing as a chronic condition. However, a lower percentage of households used medical care, as only 29% of the participants received pharmaceutical care.

The effectiveness of the used therapies, was not evaluated or reported by local researchers. There is a need for depth interview and a clinical evaluation scale to measure which therapy is more effective for controlling NE among Saudi Children. As resolved by randomized trials of NE; alarm therapy and the use of desmopressin have been shown to be effective [15].

In addition, the different attitude toward early treatment of NE might be due to different socioeconomic status. A number of parents who had a higher education and income act positively toward child's urinary incontinence. As a result, it did not reflect on their quality of life. Most of participants thought that NE never had a negative impact on their quality of life.

Socioeconomics according to early evidence, determined the awareness and mindset for dealing with a health condition. However, the importance of seeking medical consultation is at a lower grade of parental knowledge [2,8]. Saudi parents usually prefer to deal with PNE themselves than to seek professional help. Similar behavior was observed in eastern countries, such as China and Korea [16].

**Limitation**

To our knowledge there was no similar studies which show or discuss this point. The study covered many aspects of NE which we believe strength the methods The study has some limitations. The researchers did not assess daytime functional bladder among children, and the study only interviewed parents regarding nocturnal enuresis. In patients with findings of overactive bladder, besides urotherapy, anticholinergic drugs may be useful.

## Conclusion

NE occurs among children in various Saudi Arabian regions. Male gender, aged 5 to 10 and suffering from weakness of bladder muscles, chronic constipation, worry and depression were associated with NE and UTI. Families and caregivers utilized effective therapies such as alarm and behavioral stimulation, however, they do not look for medical assistance.

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# Concerns of parents of students with autism spectrum disorders (ASD) towards the safety of COVID-19 Vaccination in Saudi Arabia (SA)

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Received: February 2023 Accepted: March 2023; Published: April 1, 2023.
Citation: Ibraheem M. Alsawalem, Khalaf A, Alotaibi, Omar A. Alsamani. Concerns of parents of students with autism spectrum disorders (ASD) towards the safety of COVID-19 Vaccination in Saudi Arabia (SA). World Family Medicine. March 2023; 21(3): 34-41 DOI: 10.5742/MEWFM.2023.95256070

## Abstract

Background: Although previous scientific studies have confirmed that vaccinations are safe and do not result in harm to students with and without disabilities, some parents of students with autism spectrum disorders (ASD) had concerns that vaccines might cause potential medical issues for their children. These concerns may have an impact on these parents' decision to vaccinate their students against COVID-19. Therefore, this study aims to explore and understand the concerns of parents of students with ASD about the safety of the COVID-19 vaccination and to what extent these concerns can diminish the willingness of parents of students with ASD to vaccinate their children against COVID-19 in Saudi Arabia (SA).

Methods: a qualitative design was adapted through a developed semi-structured interview. Participants included eight parents of students aged 12 years and over with ASD, who were enrolled in two male state-funded institutions that provide educational services to those with developmental disabilities, including ASD in Riyadh, SA. The study was conducted between 17th of September and the 15th of November 2022.

Results: The results indicated that parents had several concerns regarding the safety of the COVID-19 vaccines. However, their concerns have not diminished their willingness to vaccinate their children. To increase parents' knowledge and relieve their concerns, several recommendations should be applied such as strict penalties being imposed on parents who refuse to have their children vaccinated, because they put their children in a risky position and the authorities in this matter and using the media to convince the community of the importance of the vaccine and the necessity of addressing it.

Conclusion: The current study emphasized the need to provide more care and support for parents with children with disabilities. An urgent intervention should be provided for children with ASD because they are more likely to be at a higher risk of COVID-19 illness due to the increased prevalence of underlying health conditions, suboptimal vaccination rates, and systemic inequities.

Keywords: COVID-19, vaccines, autism, Saudi Arabia

## Introduction

COVID-19 has affected communities worldwide, including people with disabilities. At the beginning of 2020, most countries enforced lockdowns that required people to stay in their homes or institutions, withdrawn from freedom of movement and communication with others. At the beginning of 2021, governments represented by the Ministry of Health announced that vaccinations have been made and are ready to be used for human beings. The demand from disabilities organizations in the USA, providing vaccines for students with developmental disabilities such as autism spectrum disorder (ASD) was an urgent priority due to their specific circumstances [22].

ASD is a neurodevelopmental disorder characterized by deficits in social communication along with restricted, repetitive patterns of behaviour, interests, or activities. The reported prevalence of ASD has continued to increase in recent years, with current estimates now being 1 in 54 children in the United States (USA) [20]. While in SA, there is no exact percentage, however, there are about 53,282 students who have been diagnosed with ASD [26].

Students with developmental disabilities such as ASD may be at an increased risk of contracting COVID-19 or experiencing more severe illness if infected because of their health conditions. In a cross-sectional study of >64 million US patients of all ages, COVID-19 incidence was three times higher among students with ASD than in those without disabilities. Among those with COVID-19, twice as many students with ASD, were hospitalized, admitted to the Intensive care units (ICU), or died, compared to those without disabilities [22].

Decreased immunization reduces an individual's protection from vaccine-preventable diseases. Individuals with ASD were nine times more likely to be hospitalized following COVID-19 infection and were nearly six times more likely to have an elevated length of hospital stay compared to those without ASD. These findings point to prioritizing access to vaccines to prevent COVID-19 infection and morbidities [12,16].

**Statement of the problem:**
Even though an increasing number of academic studies have focused on vaccine concerns and hesitancy in the last few years [18], little is known about the concerns regarding the safety of COVID-19 vaccination of children with developmental disabilities such as ASD [15,22]. Furthermore, the authors reviewed the related literature, and they found a lack of studies that discussed this issue in the Saudi context, which gives this study great scientific value. They also noticed that most of the studies focused on the hypothesised relationship between vaccines and ASD for parents with children without disabilities. Based on that, this is the first paper we know of that explores the concerns of parents of students with ASD regarding the safety of COVID-19 Vaccination in SA.

Keeping this in mind, the main objective of this study is to capture the whole picture by exploring the concerns of parents of students with ASD about the safety of COVID-19 Vaccination and to what extent these concerns can reduce the willingness of parents of students with ASD to vaccinate their children against COVID-19 in SA. Investigating these two matters will offer a deeper understanding of parents' concerns as to who is responsible for healthcare in SA such as the Ministry of Health. In addition, this is particularly relevant in the current situation of the COVID-19 pandemic, where high rates of vaccine hesitancy are observed disproportionately in communities at greater risk of more severe COVID-19 morbidity and mortality [14]. By understanding the parents' concerns, appropriate support can be provided to the students with ASD and their families.

## Literature review

In the 18th century, concerns about the safety of vaccines appeared first in the USA over the first smallpox immunization campaigns. Over time, the communities' specific concerns have changed as new vaccines have been developed and research into vaccine safety has been conducted. Public health strategies to control vaccine-preventable diseases rely on a critical percentage of the population being vaccinated. The efforts of the national research community, play a significant role in highlighting parents' concerns regarding the safety of the vaccine [12,16]

A previous study confirmed that vaccines in general are safe and important for students, especially those with ASD. They also confirmed that there are no links between vaccines and developmental disabilities, such as ASD [5, 6]. However, other studies indicated that parents had some concerns about vaccine safety, which included causing autism, diabetes, developmental delays, hyperactivity, and attention-deficit disorders or the child's immune system being weakened by vaccinations, serious diseases to be prevented by vaccines and vaccines are not tested enough [7,17].

Another study, [12] found that a quarter of the parents who participated in the study had refused at least one recommended vaccine due to a serious adverse effect. This allegation was initially ignited by a publication suggested by Andrew Wakefield and colleagues in The Lancet in February 1998. The article described those 12 children with inflammatory bowel conditions and regressive developmental disorders, which is a symptom of ASD. In eight of the 12 cases, the children's parents or paediatricians believed that the mumps and rubella (MMR) vaccine might have contributed to the onset of behavioural problems because this onset followed shortly after vaccination. The study's authors hypothesized that the MMR vaccine may have been responsible for bowel dysfunction, which subsequently resulted in neurodevelopmental disorders.

The high vaccination coverage in SA stems from the bylaws that mandate completion of the vaccination schedule before issuing birth certificates or admitting children into schools. In fact, the efforts of the Ministry of Health in SA have translated to nearly achieving 100% of the vaccination rate by educating the community and raising awareness about vaccines [23]. Regarding COVID-19 vaccines, citizens in SA are not allowed to attend their jobs, universities, schools, or any private and public institutions without being vaccinated with two shots of a vaccine approved by the health department in SA.

The earlier argument justifies the published studies which generally indicated that parents have a high level of knowledge and awareness about vaccination regarding the preventive measures and importance of vaccination, which resulted in positive attitudes and practice patterns among most of them. However, they simultaneously showed concerns, which included fear of weakening the child's immunity and non-necessity of some vaccinations, and based on that, they prevented compliance with vaccinations [1].

The literature review showed that the concern of parents of children with ASD about the safety of COVID-19 vaccination is not well investigated, especially in SA; however, parents' hesitancy towards vaccination and confidence in vaccines has been discussed broadly in several studies. Parents hesitated in getting their children vaccinated because of some concerns and fears they had, which resulted in a delay in vaccination or not getting vaccinated at all. Therefore, to increase the rates of COVID-19 vaccinations, healthcare providers should adopt best practices that are recommended by the global scientific research.

This conclusion raises a red flag about the provided support and intervention to children with ASD because they are more likely to have a higher risk of developing COVID-19 illness due to the increased prevalence of underlying health conditions, suboptimal vaccination rates, and systemic inequities [22]. Other reasons reported by the parents for their concern about vaccinating their children were the beliefs that vaccines are unnecessary, inadequate, and information of the duration of immunity is unknown. This concern developed conspiracy theories and distrust in the government and healthcare professionals, creating more doubts and objections to vaccinations [19].

Confusion due to the constant circulation of false news influences and increases the public's fear of the side effects related to COVID-19 vaccines, raising additional questions and concerns about the vaccines [10]. Therefore, parents emphasized that transparent information surrounding vaccine development, efficacy, and safety must be provided by the national public health authorities so that they can make informed decisions about vaccination [3]. This was important after the incident when various European countries suspended the use of the Oxford/AstraZeneca vaccines supported by deaths arising from blood clots on 15th March 2021 [8, 11].

To conclude, different studies showed a decrease in vaccine acceptance, either directly through quantitative results in SA, for example [21] or indirectly through reduced turnout for scheduled vaccinations in Ecuador. The exact reason for not showing up for the vaccinations is also unclear, which justifies the importance of studying the parents' concerns about the safety of COVID-19 vaccinations.

**Research questions**

**1.** What are the concerns of parents of students with ASD regarding the safety of COVID-19 Vaccination?

**2.** To what extent can the COVID-19 Vaccine safety concerns diminish the willingness of parents of students with ASD to vaccinate their children?

## Method

**Participants and Setting**

The study used a qualitative design to explore the concerns of parents of students with ASD regarding the safety of the COVID-19 vaccine. A semi-structured interview was developed to better explore their vaccine safety concerns and to understand to what extent these concerns can diminish the willingness of parents of students with ASD to vaccinate their children against COVID-19. The target population of the current study were all parents of students with ASD, who were enrolled in either of the two male state-funded institutions that provide educational services to those with ASD in Riyadh, SA.

These two institutions serve 88 students with ASD, aged between 6–22 (Department of Education in Riyadh, 2021). The students' ages of the parents involved in the current study had to be between 12–22 years so that they would be qualified to receive the vaccines, according to the Ministry of Health [23]. The Saudi authority announced that students aged 12 years and over can be vaccinated with two doses of Pfizer or Moderna, which are approved and recommended by both the food and drug administration in the USA and SA [24]. The study was conducted between 17th of September and the 15th of November 2022 in Riyadh, SA.

The participants in the present study were eight parents of students with ASD (4 males and 4 females) from two male institutions that provide educational services to those with ASD. (See Table 1 for participant demographics). The participants were aged from 39 to 50 years and the majority had a high school certificate, except three participants who had a bachelor's degree as their highest academic qualification. The age of students with ASD ranged from 12 to 18 years, with an average age of 14 years. Four of the 10 students were vaccinated with Pfizer vaccine, and four were not.

**Procedure:**

Before the study was conducted, ethical approval from Hail University and permission from the Ministry of Education was obtained. The authors communicated with the principals of both institutions and explained to them the aims and procedures of the study. The principals

**Table 1. Parent Participant Demographics**

| Number | Gender | Parent's age | Academic qualification | Student's age | Vaccination status of the students |
|---|---|---|---|---|---|
| 1 | Male | 43 | Bachelor | 15 | Yes (Pfizer) |
| 2 | Male | 50 | High school | 18 | No |
| 3 | Male | 45 | High school | 13 | Yes (Pfizer) |
| 4 | Male | 41 | Bachelor | 16 | Yes (Pfizer) |
| 5 | Female | 49 | High school | 17 | No |
| 6 | Female | 40 | High school | 14 | No |
| 7 | Female | 39 | Bachelor | 12 | No |
| 8 | Female | 50 | High school | 19 | Yes (Pfizer) |

agreed to play a role in the study by contacting the parents in both institutions by sending an SMS to the parent's phone numbers that included an online link containing the invitation, information about the study, and a consent form, which they could fill-in if they agreed to participate in the interviews.

A total of 12 questions were developed to obtain in-depth data including demographic questions. All questions were open, and parents were asked to express their beliefs as completely and deeply as possible until they had nothing more to say. These questions were derived from the research questions and the review of the literature [13,14,15,19,18].

To establish confidence in the validity of the interview questions, a Saudi panel of four people who hold a PhD in special education and the medical field were invited to review the interview questions and make sure that each was relevant to the aims of the study and that all were clearly worded. Each interview was privately conducted by the authors in person, according to the participants' preferences. The interview questions were presented in Arabic, were verified by all authors, and were then provided to the participants before the interview.

**Data analysis:**
Due to the importance of increasing the consistency of the findings of qualitative studies [9], the study followed a model (4) for the analyzing process. The reason for using this model was for adding more information to sort data. The function of this comprehensive framework was to develop a thematic analysis by following the six steps given by [4].

## Results

Developed themes have emerged through the recursive analysis of the transcripts of the interviews with the eight parents of students with ASD. The four key themes that are reported below are: parents' concerns about the safety of COVID-19 vaccines, beliefs surrounding the safety of COVID-19 vaccines, the relationship between ASD and COVID-19 vaccines, and to increase the parents' knowledge and relieve their concerns.

**Theme (1): Parents' concerns about the safety of COVID-19 vaccines:**
Participants expressed their concerns regarding the safety of COVID-19 vaccines. They feel that giving the vaccine to their children who are under 18 years is not easy. To be more specific, their concern about the vaccine is not related to the vaccine itself, but instead about vaccinating those under 18 years.

*Giving it to anyone under the age of 18 should be cancelled because of its uncontrollable symptoms. Where the vaccine may affect the level of development of the child at this age and make him vulnerable to other diseases (P2)*

Another response determined that the negative side effects of the vaccine on those under 18 years such as having a stroke were a great concern for the parents. Parent 7 said: *"The negative side effects on the growth and mental abilities of my son, which include poor memory, distraction, and some motor problems. The great concern is the stroke. I heard about a person, one of his sons under 18 years, who had blood clots, and it was kept secret before it was officially published."*

In relation to parents' concerns, the type of vaccine determined to what extent they were concerned about the side effects. Parent 3 explained: "*It is true that I gave my son a dose of the Corona vaccine, but I am frankly afraid of the side effects of this vaccine, even though he got Pfizer, which is considered a high reputation in terms of mild side effects. However, as my son developed a high fever after taking the first dose, he was hospitalized for a week. The side effects that come after the first dose are my biggest fear about corona vaccines. I also think that other vaccines have worse side effects, such as the Moderna vaccine".*

Respondents also reported that the foundation of these kinds of concerns is rumoured. One respondent stated: *"rumours about the futility of the vaccine and whether it is successful or not. Such as: causing infertility, memory loss and negative impact on the vital functions of the body (P5). She also reported the reason that makes these rumours believable according to her: "The speed of the vaccine industry is one of the main concerns affecting parents. And the feeling that it is a conspiracy hatched in secret to eliminate humanity" (P5).*

**Theme (2): Beliefs surrounding the safety of COVID-19 vaccines:**

Even though parents completed their children's vaccination schedule, they were not convinced about its benefits, and they still needed to take it. This is because they were being forced to take it or had lost faith in its benefits, Parent 6 reported: *"No, I did not refuse to receive any vaccines for my son, despite my conviction that it is useless, but I am obligated to it towards my children, as they will not be able to obtain an academic or job seat until after completing all the doses".* Another parent mentioned an interesting comment, which questions the benefit of the vaccine: *"The effectiveness of the vaccine has not been proven, and the reason is you will still be infected by the virus even if you had two shots of the vaccine. Also, the vaccine contains modern techniques that have not been used before, which gives an indication to do something new (P7)"*

However, one of the parents refused to show up in the hospital to give his son a vaccine due to the adverse effects: Parent 1 said "*I had previously refrained from going after my child received the measles vaccine, which affected him to the point where he was admitted to the hospital, which made me refrain from giving it to my next son until I discussed this problem with the pediatrician, who explained to me its importance and the reason for the appearance of some accompanying symptoms, which are considered justification for the case and eventually was given to him on time. My son's failure to go to the health center previously was a precautionary measure to ensure the safety of the vaccine for use for my son's condition and to avoid any side effects.*

Regarding vaccination safety, there is disagreement between the parents. Some of them believed that the vaccine is safe for several reasons. For instance:

*"I believe that the vaccine is safe, and the reason is because the whole world got it and it was approved by official bodies, with the exception of vaccines that were stopped because of their effect on the body. Why isn't it safe? (P1, P4 and P8)"*

However, others believe that the vaccine is useless and not effective because it was produced very fast. Parent 5 commented: *"No, it's not safe because the speed of vaccine production was fast and illogical, despite many diseases like cancer which are old and still exist with no vaccines being available for them so far". In addition, Parent 6 said: "I think that vaccine is useless and has no benefit that can be mentioned, but it is a commodity sold for business purposes only".*

**Theme (3): Relationship between ASD and COVID-19 vaccines:**

Most of the parents believed that there is a link between ASD and all types of vaccines. Parent 5 reported: *"Without a doubt vaccine causes the main reason for having ASD in vaccines. ASD rates rise due to the increase in the number of vaccinations worldwide, despite the disappearance of the diseases that these vaccines target, such as German measles".* They also doubted the study's outcomes and believe that there is no link between them: Parents 6 and 7 said *"without official confirmation of this, doubt remains. ASD has not yet known its causes, and studies that deny this accusation have not presented the causes of autism".*

However, some parents disagreed with this assumption, and they believed that the cause of ASD "*is not yet clear (P1 and P3)" or it is "caused by genetics, not by vaccines (P4)"*. Parent 8 added that the reason for linking ASD to vaccines was that *"the emergence of autism coincided with the beginnings of the production and administration of the vaccine".*

Even though the parents believed that vaccines at an early age can cause ASD, they did not believe that COVID-19 vaccines would cause ASD in normal children because they received it when they were at least 12 years old.

*"Yes, vaccines cause ASD. The studies are supposed to be highly credible in this matter and come out with results confirming the relationship of ASD when children take vaccines at an early age. There is also ambiguity in the results related to the relationship of the vaccine to autism. And we all know that drug companies and vaccine factories cannot confirm this because they will lose their reputation and money if they declare this (P2)"*

**Theme (4): Practice to increase parents' knowledge and relieve their concerns:**

Parents' knowledge regarding COVID-19 vaccines was poor, according to them. They believed that official authorities did not have enough time to educate people about the importance of taking the vaccine and that it is safe and does not cause any future problems. Parent 2

indicated the reason for not having enough time to educate people saying, "*The speed of manufacturing the vaccine and its adoption in a short period has not happened before. The Ministry of Health also did not clarify its position towards giving people who do not suffer from health or physical problems such as ASD and the extent to which they are negatively affected by taking the vaccine. This gave families an opportunity to refuse the vaccine and not accept it completely".*

Responses associated the lack of parents' knowledge toward the importance of vaccines to the lack of specialists in the field of disability in general and ASD in particular. Parent 3 reported: *"The services for people with disabilities has a full back and the lack of specialists in the field of disability in general and ASD in particular at the top of the pyramid, which gives this group the necessary attention and care in everything related to their affairs, especially with regard to vaccination".*

Generally, parents believed that the shortage of time to overcome this crisis justified stakeholders to force people worldwide including SA to take vaccines without questions. They suggested, *"increasing the level of efforts by targeting people with disabilities because of their individual differences, which make them distinguished in their health, physical and psychological conditions (P4 and 5)". Another suggestion is "they should focus on people with disabilities in the daily press conference when they talk about the virus and the vaccines (P8)".*

With regard to practice that increases parents' knowledge and relieves their concerns, one respondent recommended *"taking the vaccine by influential people in society (and this was activated by the Saudi government), Strict penalties being imposed on those who refuse to be vaccinated, not giving the parents, who refused the authorities in this matter and using the media to convince the community of the importance of the vaccine and the necessity of addressing it (P1,2 and 3)".*

More importantly, parents highlighted the need for guidance in this matter. They think that parents with disabilities should receive more care regarding the case of vaccinations.

*"There is a need for direct guidance to families with children with ASD so they can be supported by health centers and receive all the information that can convince them of the feasibility of the vaccine. Communicating with the families of people with disabilities to give them additional support in this matter is significant. This is because they may be unaware of their children's needs for the vaccine, especially when the disability is severe and prevents communication with others, such as ASD (P7 and 8)".*

## Discussion and Conclusion

The current study aims to identify and understand the concerns of parents of students with ASD regarding the safety of COVID-19 vaccination in SA and to understand to what extent these concerns can diminish the willingness of parents of students with ASD to vaccinate their children against COVID-19 in SA. The findings indicate that most of the participants had several concerns regarding the safety of COVID-19 vaccines. One of their great concerns was not about the vaccine itself, but about the vaccine being administered to those who have not completed 18 years. An interesting result was that some of the parents feel that Pfizer is the only available safe vaccine that they can give their children, not only in SA but in the world, . This is an interesting outcome after the incident when various European countries suspended the use of the Oxford/ AstraZeneca vaccines, supported by deaths arising from blood clots on 15th March 2021[11].

Participants also reported that the foundation of these concerns is rumours, which are believable, according to them. These concerns developed conspiracy theories and distrust in government or healthcare professionals, thus creating more doubts and objections to vaccination [19]. The qualitative results indicated that most of the participants completed their children's vaccination schedule. However, they were not convinced about its benefits but still had to take it. This is because they were forced to take it. This is because citizens in SA had to complete the vaccination schedule for their children if they wanted to issue birth certificates or admit their children into schools.

The study also showed that some of the parents refused to show up in the hospital to give their children a vaccine due to the adverse effects. This is consistent with another study [4], which mentioned that some of the parents refused at least one recommended vaccine due to a serious adverse effect. This may be related to the consequences that their children may have if they received the vaccine.

Regarding vaccination safety, there is disagreement between the parents. Some of them believed that the vaccine is safe, and others believed that the vaccine is useless and ineffective because it was produced very fast. This indicated the important role of parents' knowledge and awareness about vaccination regarding the preventive measures and importance of vaccination, which results in positive attitudes and practice patterns among most of them [1,2].

Most of the parents believed that there is a link between ASD and all types of vaccines. They also doubted the studies' outcomes and believe that there is a link between them. This conflicts with many studies that confirmed that there are no links between vaccines and developmental disabilities such as ASD [5,6]. However, the outcomes of the current study were consistent with other studies, which indicated that parents had some concerns towards that vaccine safety such as causing autism [7,17].

Nevertheless, some parents disagreed with the assumption that vaccines cause ASD, and they believed that the cause of ASD is not yet clear, or it may be caused by genetic reasons. Moreover, they did not believe that the COVID-19 vaccines caused ASD in normal children because they received it when they were at least 12 years old. This is an interesting result that confirmed the lack of studies that focus on the causes of ASD based on the perceptions of parents of children with ASD.

Parents' knowledge regarding COVID-19 vaccines was found to be poor. They believed that official authorities did not have enough time to educate people about the importance of taking the vaccine and that it is safe and does not cause any future problems. Therefore, stakeholders worldwide including SA, forced people to take vaccines without question. This made people confused due to the constant circulation of false news influences and increased the public's fear of side effects related to COVID-19 vaccines, raising additional questions and concerns about the vaccines [10].

With regards to practices that increase the parents' knowledge and relieve their concerns, respondents recommended several practices, which included influential people in the society being vaccinated, strict penalties being imposed on those who refuse to be vaccinated, not giving the parents, who refused, the authorities in this matter and using the media to convince the community of the importance of the vaccine and the necessity of addressing it. These results show there is a need to address the parents' concerns regarding vaccinating their children with ASD since they will be the ones making decisions to vaccinate their children [15,22].

More importantly, parents highlighted the need for guidance in this matter. They think that parents with children with disabilities should receive more care regarding the case of vaccinations. This conclusion raises a red flag about the support and intervention provided to children with ASD because they are more likely to be at a higher risk of COVID-19 illness due to the increased prevalence of underlying health conditions, suboptimal vaccination rates, and systemic inequities [22].

**Limitations of the Study**

Several limitations have been identified in the present study. For instance, the study took place in two male state-funded institutions that provide educational services to those with developmental disabilities, which included ASD in Riyadh, SA. Even though the selection of these two institutions has been justified, the reliability and generalizability may have increased if other institutions and schools in multiple cities were explored.

Another limitation was the study did not include female students in state-funded institutions that provide educational services to those with developmental disabilities, which included ASD. The reason for this limitation is related to the ages of the female students, which was lower than 12 years. However, including female students may change the outcomes of the current study.

**Implications for Practice**

The most important implications are increasing the parents' knowledge and relieving their concerns by following the best practices. This can be done by giving the parents with children with ASD more care and support regarding the case of vaccinations. Authorities should give the parents the time to understand the whole process so they can decide positively and solve any problems or confusion that the parents had before and after receiving the vaccines for their students.

Having influential people publicly advertise the importance of vaccines to encourage hesitant parents and imposing strict penalties on those who refuse to be vaccinated, not giving the parents who refused the authorities in this matter and using the media channels to convince the community of the importance of the vaccine and the necessity of addressing it are suggested solutions to increase the rates of COVID-19 vaccinations in SA.

**Implications for Future Studies**

Future research should concentrate on the investigation of other disabilities such as intellectual disability. An investigation of the concerns of parents of children with intellectual disabilities will add great scientific value to the literature. The outcomes of the current study shed light on having more consideration for the parents' concerns regarding vaccinating their children with ASD since they are making decisions on behalf of them [15,22]. Future studies should investigate more in this matter.

**Acknowledgment**

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Scientific Research Deanship at the University of Ha'il, KSA [grant number RG-22 008].

***Conflict of Interest Statement***

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Funding Acknowledgments**

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Scientific Research Deanship at the University of Ha'il, KSA [grant number RG-22 008].

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# Post COVID 19 vaccination symptoms among the health care workers in Egypt

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Received: February 2023 Accepted: March 2023; Published: April 1, 2023.
Citation: Hala A. Hussein et al.. Post COVID 19 vaccination symptoms among the health care workers in Egypt. World Family Medicine. March 2023; 21(3): 42-49 DOI: 10.5742/MEWFM.2023.95256071

## Abstract

Background: Vaccines are the most important strategy to overcome the global pandemic of COVID 19. Although the vaccine's protective effectiveness is commonly addressed, little is known regarding the adverse effects after vaccination. Therefore, this study's primary objective was to study the prevalence of different COVID-19 vaccine side effects among the early vaccinated healthcare workers in Egypt.

Methods: A cross-sectional observational study was done to assess the post vaccination symptoms among the health care workers who were vaccinated with COVID vaccine in Egypt.

Results: One hundred and ninety-two health care workers (HCWs) responded to this questionnaire. The most common symptoms reported after the 1st dose of vaccination were pain at injection site (81.7%), followed by tiredness (70.7%) then myalgia and bone pain (62.8%). The most reported distressing symptoms after the 2nd dose were local pain at injection site (18.8%), tiredness (13.6%) and headache (10.5%).

Conclusion: We concluded that post vaccination symptoms among health care workers were mild, short symptoms, and there were no serious adverse effects after the first dose as well as the second dose. The majority of participants did not report COVID-19 infection after vaccination which confirms the efficacy and safety of the vaccine.

Key words: Covid vaccine, healthcare workers, Egypt

## Introduction

The global pandemic of COVID-19 has affected about 517,648,631 confirmed cases including 6,261,708 deaths, reported to World Health Organization (WHO) so Emergency Approval of COVID-19 virus vaccines were launched by WHO with a total of 11,655,356,423 vaccine doses having been administered (1).

The best defense against COVID-19 infection is the successful development and implementation of vaccinations. The decrease in infection rates with the introduction of vaccines, together with measures to mask and socially isolate those with Coronavirus, boosted hopes that it can be contained (2).

Response to a viral infection is either innate or an adaptive immune response. When adaptive immune cells (B cells and T cells) come into contact with the same virus for the second time, they clear it out before infection occurs. Immune memory is used in vaccines to defend against diseases caused by prior infection or an effective vaccine. Vaccination functions by simulating natural immunity. The first dose activates the immune system's first memory, while the second dose paralyses it (3).

In clinical trials and real-world effectiveness studies, COVID-19 vaccines have shown high levels of efficacy in older adults, healthcare workers, and the general population, with 50–70 percent protection against infection or mild disease and 75–85 percent protection against hospitalization or death. After two doses, effectiveness against infection or moderate disease is 65–90%, and against severe disease is 90–100% (4).

However, the success of a vaccination program to provide 'herd immunity' (the proportion of subjects with immunity in each population) remains dependent on a high proportion of the population being vaccinated. Vaccines' potential negative effects were the most common reason for vaccine hesitation among people (5).

Although the vaccine's protective effectiveness is commonly addressed, little is known regarding the real-world experience after vaccination outside of scientific trials. Knowledge of what to expect following vaccination will aid in public education, dispelling myths, and reducing vaccine apprehension (6).

Therefore, this study's primary objective was to study the prevalence of different COVID-19 vaccine side effects among the early vaccinated healthcare workers in Egypt.

## Methods

The global pandemic of COVID-19 has affected about 517,648,631 confirmed cases including 6,261,708 deaths, reported to World Health Organization (WHO) so Emergency Approval of COVID-19 virus vaccines were launched by WHO with a total of 11,655,356,423 vaccine doses having been administered (1).

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Therefore, this study's primary objective was to study the prevalence of different COVID-19 vaccine side effects among the early vaccinated healthcare workers in Egypt.

## Results

One hundred and ninety-two health care workers (HCWs) responded to the questionnaire, all of whom received the first dose of vaccine but only 60 respondents received the second dose. The mean age of the participants was 34.54± 8.02; the majority of them were females (74.3%), non-smoker (94.8%), and the most common shared specialty was Internal medicine and its specialties (36.6%) Most were working in Ministry of Health hospitals (54.4%); the most common documented chronic medical illness was Eczema or previous allergic history (18.8%). About 32.3% confirmed past history of COVID-19 infection before vaccination (Table 1).

**Table 1: The basic characteristics of the participants (N=192)**

| Item | | N | % |
|---|---|---|---|
| **Age** | **Mean ±SD** | **34.54± 8.02** | |
| **Gender** | Female | 142 | 74.3% |
| | Male | 50 | 25.5% |
| **History of medical disease** | DM | 2 | 1% |
| | Hypertension | 14 | 7.3% |
| | Heart disease | 1 | 0.5% |
| | Bronchial asthma | 12 | 6.3% |
| | Autoimmune disease | 9 | 4.7% |
| | Eczema or previous allergic history | 36 | 18.8% |
| | Other medical diseases | 17 | 9.8% |
| **Smoking** | Current | 3 | 1.6% |
| | Ex-smoker | 7 | 3.6% |
| | Non-smoker | 182 | 94.8% |
| **Specialty** | General surgery and surgical specialties | 11 | 5.7% |
| | Internal medicine, its specialties, | 70 | 36.6% |
| | Critical care Emergency Anesthesia | 10 | 1.9% |
| | Ophthalmology | 10 | 1.9% |
| | Infection control | 1 | 0.5% |
| | Radiology | 14 | 7.3% |
| | Clinical and chemical pathology | 5 | 2.6% |
| | House officers | 31 | 16.2% |
| | Gynecology, obstetric and Family planning | 8 | 4.1% |
| | Pediatrics | 15 | 7.8% |
| | Academic | 16 | 8.3% |
| | General medicine | 8 | 4.1% |
| **Work place during COVID** | University hospitals | 78 | 40.6% |
| | Educational hospitals | 10 | 5.2% |
| | Ministry of Health hospitals | 104 | 54.4% |
| **Working or previously worked in isolation hospitals** | | 42 | 21.9% |
| **Past history of COVID-19 infection before vaccination** | Yes | 62 | 32.3% |
| | Maybe | 47 | 24.5% |
| **No of vaccinations received** | 1st dose | 192 | 100% |
| | 2nd dose | 60 | 31.4% |

The most reported symptoms after the 1st dose were local pain at injection site followed by tiredness and myalgia or bone pains. The most reported distressing symptoms after the 2nd dose were local pain at injection site, tiredness and headache. About 70.7% of participants needed medications for symptoms relief after the 1st dose while only 11.5% of them needed that after the 2nd dose. The minority of participants (9.4% and 4.7%) did not have any symptoms after the 1st dose and after the 2nd dose respectively (Table 2).

**Table 2: Frequency of different symptoms after 1st and 2nd dose**

| Symptoms | After 1st dose | | After 2nd dose | |
|---|---|---|---|---|
| | No | % | No | % |
| Tiredness | 135 | 70.7 | 26 | 13.6 |
| Myalgia or bone pain | 120 | 62.8 | 18 | 9.4 |
| Fever | 85 | 44.5 | 8 | 4.2 |
| Headache | 88 | 46.1 | 20 | 10.5 |
| Local pain at injection site | 156 | 81.7 | 36 | 18.8 |
| Joint pain | 53 | 27.7 | 10 | 5.2 |
| Nausea | 24 | 12.6 | 3 | 1.6 |
| Diarrhea | 11 | 5.8 | 2 | 1.0 |
| Sore throat | 19 | 9.9 | 1 | 0.5 |
| Insomnia | 28 | 14.7 | 2 | 1.0 |
| Allergic rash | 5 | 2.6 | 1 | 0.5 |
| Chills or rigors | 40 | 20.9 | 4 | 2.1 |
| Vomiting | 2 | 1.0 | 2 | 1.0 |
| Syncope | 2 | 1.0 | 1 | 0.5 |
| Cough | 9 | 4.7 | 3 | 1.6 |
| Chest tightness | 17 | 8.9 | 5 | 2.6 |
| Redness at injection site | 53 | 27.7 | 10 | 5.2 |
| None | 18 | 9.4 | 9 | 4.7 |
| Need medication for symptom relief | 135 | 70.7 | 22 | 11.5 |

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The onset of symptoms after the 1st dose was 14 hours and lasted for 24 hours while after the 2nd dose the symptoms appeared after 6 hours and lasted for 14 hours (Table 3).

**Table 3: Onset of appearance, duration of symptoms and Number of COVID infected participants after vaccination**

| | 1st dose | 2nd dose |
|---|---|---|
| Onset of appearance of symptoms in hours | 14.05±53.03 | 6.55± 7.60 |
| Duration of symptoms in hours | 24.94±24.43 | 14.97± 19.80 |
| Number of COVID infected participants after vaccination | 13 | 6.8 % |

There was no statistically significant difference between different age groups regarding different symptoms after the 1st dose apart from tiredness, local pain at injection site, nausea and cough. There is astatistically significant difference between different age groups regarding receiving the 2nd dose of vaccine, as older patients were more keen on completing the doses than younger participants (Table 4).

**Table 4: Relation between different symptoms and different age groups after 1st dose**

| Symptoms | Age groups | | | | |
|---|---|---|---|---|---|
| | 25-34 | 35-45 | More than 45 | X2 | P value |
| Tiredness | 20(90.9%) | 73(73.0%) | 42(60.9%) | 7.809[a] | **.020** |
| Myalgia or bone pain | 16(72.7%) | 61(61.0%) | 43(62.3%) | 1.074[a] | .585 |
| Fever | 12(54.5%) | 48(48.0%) | 25(36.2%) | 3.305[a] | .192 |
| Headache | 8(36.4%) | 48(48.0%) | 32(46.4%) | .987[a] | .611 |
| Local pain at injection site | 21(95.5%) | 84(84.0%) | 51(73.9%) | 5.930[a] | **.052** |
| Joint pain | 3(13.6%) | 30(30.0%) | 20(29.0%) | 2.491[a] | .288 |
| Nausea | 6(27.3%) | 14(14.0%) | 4(5.8%) | 7.396[a] | **.025** |
| Diarrhoea | 0(0.0%) | 696.0%) | 5(7.2%) | 1.636[a] | .441 |
| Sore throat | 4(18.2%) | 11(11.0%) | 4(5.8%) | 3.116[a] | .211 |
| Insomnia | 1(4.5%) | 18(18.0%) | 9(13.0%) | 2.835[a] | .242 |
| Allergic rash | 0(0.0%) | 1(1.0%) | 4(5.8%) | 4.354[a] | .113 |
| Chills or rigors | 4(18.2%) | 25(25.0%) | 11(15.9%) | 2.138[a] | .343 |
| Vomiting | 1(4.5%) | 0(0.0%) | 1(1.4%) | 3.764[a] | .152 |
| Syncope | 1(4.5%) | 1(1.0%) | 0(0.0%) | 3.331[a] | .189 |
| Cough | 1(4.5%) | 8(8.0%) | 0(0.0%) | 5.821[a] | .054 |
| Chest tightness | 2(9.1%) | 8(8.0%) | 7(10.1%) | .233[a] | .089 |
| Redness at injection site | 8(36.4%) | 26(26.0%) | 19(27.5%) | .968[a] | .616 |
| None | 2(9.1%) | 9(9.0%) | 7(10.1%) | .066[a] | .968 |
| Inconvenience to routine work on the next day | 13(59.1%) | 52(52.0%) | 34(49.3%) | .646[a] | .724 |
| Need of any medication for symptom relief | 14(63.6%) | 72(72.0%) | 49(71.0%) | .615[a] | .735 |
| Did you receive the 2nd dose | 3(13.6%) | 29(29.0%) | 28(40.6%) | 6.188[a] | **.045** |

There is no statistically significant difference between different age groups regarding different symptoms after the 2nd dose apart from vomiting, syncope, cough and redness at injection site. There is a statistically significant difference between different age groups regarding feeling more confident to work after COVID-19 vaccination. The majority of the participants (93.2%) did not report COVID-19 infection symptoms after vaccination. Only 7.14% of people who received AstraZeneca and 5.5% of people who received Sinopharm reported post vaccine COVID infection (Table 5).

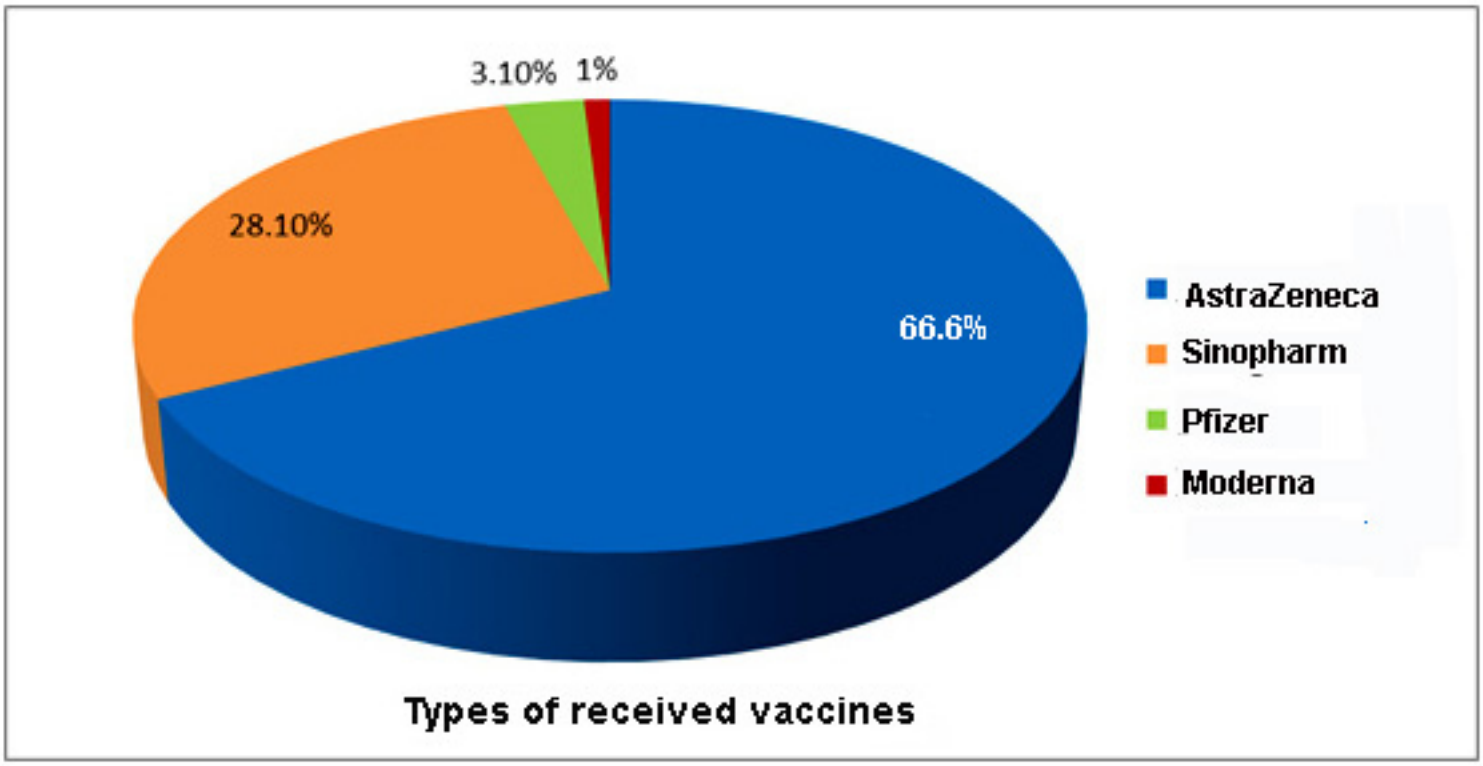
The most commonly received vaccine (66.6) was AstraZeneca while the least commonly received (1%) was Moderna (Figure 1).

AstraZeneca vaccine showed the highest proportion of received vaccines 66.6%, while Sinopharm, Pfizer and Moderna types received by little portion.

**Table 5: Relation between different symptoms and different age groups after 2nd dose**

| Symptoms | Age groups | | | | |
|---|---|---|---|---|---|
| | 25-34 | 35-45 | More than 45 | X2 | P value |
| Tiredness | 2(9.1%) | 12(12.0%) | 12(17.4%) | 6.522[a] | .163 |
| Myalgia or bone pain | 0(0.0%) | 10(10.0%) | 8(11.6%) | 7.037[a] | .134 |
| Fever | 0(0.0%) | 3(3.0%) | 5(7.2%) | 7.236[a] | .124 |
| Headache | 1(4.5%) | 9(9.0%) | 10(14.5%) | 6.344[a] | .175 |
| Local pain at injection site | 3(13.6%) | 15(15.0%) | 18(26.1%) | 8.097[a] | .088 |
| Joint pain | 0(0.0%) | 5(5.0%) | 5(7.2%) | 6.492[a] | .165 |
| Nausea | 0(0.0%) | 2(2.0%) | 1(1.4%) | 6.615[a] | .158 |
| Diarrhoea | 0(0.0%) | 1(1.0%) | 1(1.4%) | 6.240[a] | .182 |
| Sore throat | 0(0.0%) | 1(1.0%) | 0(0.0%) | 7.342[a] | .119 |
| Insomnia | 0(0.0%) | 1(1.0%) | 1(1.4%) | 6.240a | .182 |
| Allergic rash | 0(0.0%) | 0(0.0%) | 1(1.4%) | 7.465[a] | .113 |
| Chills or rigors | 0(0.0%) | 2(2.0%) | 2(2.9%) | 6.297[a] | .178 |
| Vomiting | 0(0.0%) | 1(1.0%) | 1(1.4%) | 6.240a | .182 |
| Syncope | 0(0.0% | 0(0.0%) | 1(1.4%) | 7.465[a] | .113 |
| Cough | 0(0.0% | 2(2.0%) | 1(1.4%) | 6.615[a] | .158 |
| Chest tightness | 0(0.0% | 2(2.0%) | 3(4.3%) | 6.647[a] | .156 |
| Redness at injection site | 0(0.0% | 5(5.0%) | 5(7.2%) | 6.492[a] | .165 |
| None | 0(0.0% | 6(6.0%) | 3(4.3%) | 7.619[a] | .107 |
| Need of any medication for symptom relief | 0(0.0% | 11(11.0%) | 11(15.9%) | 7.067[a] | .132 |
| Feeling more confident to work after vaccination | 14(63.6% | 34(34.0%) | 27(39.1%) | 6.642[a] | .036 |
| Were you infected with COVID after vaccination | 0(0.0% | 8(8.0%) | 5(7.2%) | 1.852[a] | .396 |

**Figure 1: Frequency of different types of vaccines received**



## Discussion

It's critical to understand all of the symptoms that follow COVID-19 vaccination because this will help raise public understanding about the vaccine's safety and lessen vaccine apprehension.

The current study is a descriptive study and used a self-administered questionnaire which includes demographic variables and experience related to COVID-19 vaccination aimed to assess the post COVID-19 vaccination symptoms among healthcare workers in Egypt.

It was shown that most participants in the current study were females (74%). This agreed with Das et al, 2021 (7) who studied post COVID-19 vaccination symptoms among recipients in Dadra and Nagar Haveli, as the majority of participants in that study were also females (67.5%) as females are usually easily motivated to be safe.

In our study, the most common symptoms reported after the 1st dose of vaccination were pain at injection site (81.7%), followed by tiredness (70.7%) then myalgia and bone pain (62.8%). About 70% of participants needed medication for symptoms relief.

This was consistent with the study of Das et al, 2021 (7) as the most common symptoms reported by the beneficiaries were fever (65%) and pain at local site (64.6%).

Also these findings were in line with Lakhanpal et al, 2021 (8) who did a multicenter survey in India and concluded that the most common symptoms post vaccination among recipients was pain at the vaccination site (54.21%) followed by generalized malaise which was present in 36.4% HCWs, but Lakhanpal et al, 2021 (8) stated that 25% of the participants took medication for pain relief which was different to the finding in the current study as 70 % of participants needed medication for pain relief.
This was against Jayadevan et al, 2021 (6) whose study reported local pain at injection site (27%), joint pain (12%), while tiredness and myalgia were more common (45%, 44%).

There was no statistically significant difference between different age groups regarding different symptoms after the 1st dose apart from tiredness, local pain at injection site, nausea and vomiting. Also in the current study there was no statistically significant difference between different age groups regarding different symptoms after the 2nd dose. These symptoms are more reported in the younger age than the older one, which was also a finding by Jayadevan et al, 2021 (6) who reported in the youngest age group (20-29 years) 81.3% developed symptoms, while only 7.4% of those over 80 years reported any symptom suggesting that Vaccine reactogenicity declines with age.

There was a statistically significant difference between different age groups regarding receiving the 2nd dose of vaccine, as older participants were more keen on completing the doses than younger participants.

Regarding psychological symptoms after vaccination, more than thirty percent of our participants were feeling more confident to work after vaccination. This was in agreeance with Das et al, 2021 (7) as almost the same percentage was feeling more confident to work after vaccination.

Regarding the type of received vaccine, AstraZeneca vaccine in the current study showed the highest portion of received vaccines (66.6%), while Sinopharm, Pfizer and Moderna types were received by a small portion of respondents.

This was in agreement with the study carried out by Jayadevan et al, 2021 (6), as among the respondents, (95%) had received Covishield, (3.3%) received Covaxin, while (0.8%) each had received Pfizer-Biontech and Sinopharm vaccine from other nations.

The current study reported that the majority of the participants (93.2%) did not report COVID-19 infection after vaccination, while only 7.14% of people who received AstraZeneca and 5.5% of people who received Sinopharm reported post vaccine COVID-19 infection.

While the study done by Cucunawangsih et al, 2021 (9) in Indonesia stated that of 1,040 HCWs who had received two doses of the COVID-19 vaccine only 1.25% tested positive for SARS-CoV-2 RNA between 2 and 11 days after the second vaccination.

The study was limited by the number of participants in the survey as we need larger numbers to be able to generalize the results and this study's main focus was on the short term symptoms of the vaccine.

## Conclusion

We concluded that post vaccination symptoms among health care workers were mild short symptoms. There was no serious adverse effects after the first dose as well as the second dose. The majority of participants did not report COVID-19 infection after vaccination which confirms the efficacy and safety of the vaccine.

**Recommendations**
More studies on post vaccination adverse effects on larger groups of people and after different periods of time are needed to completely cover the incidence of the adverse effects after vaccination.

**Acknowledgment**
We would like to thank all the healthcare workers who participated and provided useful data for the present study

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# Vaccine hesitancy and COVID-19 vaccine acceptance in Makkah Al-Mukarramah, Saudi Arabia

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Received: February 2023 Accepted: March 2023; Published: April 1, 2023.
Citation: Mohammad Alkot, Abdurahman Hassan-Hussein et al.. Vaccine hesitancy and COVID-19 vaccine acceptance in Makkah Al-Mukarramah, Saudi Arabia. World Family Medicine. March 2023; 21(3): 50-56 DOI: 10.5742/MEWFM.2023.95256073

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## Abstract

Background: Lack of knowledge, resources and community feedback could play a great role in developing vaccine hesitancy among populations. This study aimed to determine the prevalence of vaccine hesitancy and to assess the acceptance of COVID-19 vaccine during the ongoing MERS-CoV-2 pandemic in Makkah, Saudi Arabia.

Methods: A cross-sectional study was conducted during March 2020 on the local population (n=262) of Makkah Al-Mukarramah. A pre-tested electronic questionnaire was used to obtain participants' demographic data, knowledge base and attitudes.

Results: Of 262 participants, 76% were adults (18 to 60-years-old), and 24% were parents. Around 62% of participants were keen to take the flu vaccine. Regarding vaccine knowledge and the source of the knowledge, 92% had heard of the influenza vaccine from their health care provider, health awareness campaign, social media, relatives or friends, at 45%, 29%, 16%, and 11%, respectively. A significant interaction was found between participant's age group and willingness to accept the introduction of a new vaccine against novel corona virus (P = 0.00).

Conclusion: Currently, vaccine hesitancy in Makkah is high (38%) compared to previous findings. It is recommended that improved measures should be taken to create more awareness through increased communal educational campaigns. Moreover, continuing education about the importance of vaccinations should be conducted by health care providers. Additional studies are needed in Makkah to assess the vaccine hesitancy movement.

Keywords: Vaccine hesitancy, Influenza, prevalence, Saudi Arabia, MERS-CoV2, COVID-19

## Introduction

Up to the middle of the last century, people of all ages died from diseases that could be prevented by vaccines, hence they are called vaccine-preventable diseases (1). Infants, in particular, were contributing to the high mortality rates due to their weak developing immune systems. For instance, deaths from polio infection reached 1904 cases in 1950 in the United States (1). Other diseases such as measles, diphtheria, smallpox, and pertussis secured top positions on the list of childhood killers.

Nevertheless, most of these diseases were contained with the discovery of vaccinations. Smallpox infection, for example, has been eradicated (1). Immunization is the process whereby a person is made immune or resistant to an infectious disease, typically by the administration of a vaccine (2). Immunity to a disease is achieved when the body synthesizes specific proteins, called antibodies, which act against a particular disease; antibodies are thus disease specific.

Immunity is of two types, active immunity, and passive immunity. With passive immunization, the body is exposed to less virulent particles of the target pathogen, creating an infection alert; the vaccine tricks the immune system and urges it to synthesize the antibodies. With active immunization, antibodies are generated readily from pathogens of the outer environment. Active immunity has more benefits than passive immunity as it lasts longer, in some cases for a lifetime (2,3).

Vaccine hesitancy is defined as the refusal of people to take vaccines or a delay in vaccine acceptance despite vaccination offers from health authorities (3). Hesitancy is widely prevalent and includes people who have not yet rejected vaccination (4). Several factors contribute to vaccine hesitancy, mainly, complacency, convenience, confidence, belief related, and low socioeconomic status. This could lead to parental doubts about vaccine safety, side effects, effectiveness, and its components. Some parents believe that pediatric illnesses are part of the child's development (5).

In Saudi Arabia, the Saudi immunization coverage showed that basic vaccines coverage ranged between 96-98% (6). However, it is noticeable that vaccine hesitancy is a growing trend, which has contributed to the re-emergence of vaccine-preventable diseases. Considering such a trend, it is rational to suspect a possible hesitancy toward future vaccines against the novel corona virus (SARS-CoV2). This virus emerged near the end of 2019 after its initial identification from Wuhan, China (7). Within a few months, it spread across the globe and became one of the major health concerns worldwide and was labeled a pandemic by the World Health Organization (7).

Only a few studies have been conducted to address the concern about vaccine hesitancy in Saudi Arabia. One of these studies is a study at King Abdul-Aziz Medical City, Riyadh, Saudi Arabia, to determine the prevalence of influenza vaccine hesitancy and the effect of vaccine awareness campaigns on vaccine acceptance. It revealed low influenza vaccination hesitancy (17%). However, common reasons for hesitancy included that the vaccine has no effect and is considered unnecessary. The sources of information about influenza vaccination were awareness campaigns and health education provided by medical staff (8).

Another study among medical students in central Saudi Arabia showed knowledge and uptake of influenza vaccination were inadequate. The main reasons given were lack of risk of influenza infection (37.90%), worry about side effects (28.90%), doubt of vaccine effectiveness (14.50%), and difficulties in scheduling the time for getting the vaccine (11.03%) (4). Worldwide, influenza results in significant morbidity and represents a public health problem with considerable socioeconomic implications (9).

Many studies have been performed previously to assess vaccine hesitancy in different populations, yet none of these took place in Makkah. This study aimed to determine the prevalence of vaccine hesitancy and to assess the acceptance of COVID-19 vaccine during the ongoing MERS-CoV-2 pandemic in Makkah, Saudi Arabia.

## Subjects and Methods

A cross-sectional study was conducted in Makkah city, Saudi Arabia in partnership with Umm Al-Qura University (UQU) during March 2020 among adult residents found on the most-popular social media applications (WhatsApp, Twitter and Snapchat).

The sample size was collected based on a population of 1,000,000 in Makkah with 262 participants recruited at a 95% confidence interval (CI) and a 5% margin of error. Adults 18 to 60-year-old living in Makkah city with online access were included in the study. Whereas, residents who were <18 or >60-year-old, living outside Makkah and who did not have online access were excluded.

Data were recorded by a Google form questionnaire via the social media applications. The participants were subjected to a well-structured, Arabic-based, validated questionnaire (8). The questionnaire was an internet-based tool that consisted of five sections. The first section had demographic information (age, sex, educational level, economic status, chronic illnesses, and nationality). Section two was concerned with the knowledge of the participant's perceptions regarding vaccinations and their source of knowledge. In the third section, participants were asked to state their attitudes towards vaccination. Section four focused on compliance with vaccinations. The last section concentrated on reasons for hesitancy, if present.

Statistical Package for the Social Sciences (SPSS), version 21.0 was used to analyze the questionnaire. Section one of the questionnaire was analyzed using the descriptive statistics to assess frequency distribution of the data. The last four sections were analyzed using the cross tabulations and ANOVA test to assess the interactions between the participant's perception regarding vaccinations and their hesitancy if present.

## Results

Of the 262 participants, 76% were adults (18 to 60-year-old), and 24% were parents with 51 male and 211 female participants (Table 1).

**Table 1: Characteristics of study participants (n=262)**

| Characteristics | Frequency | Percentage (%) |
|---|---|---|
| **Participants:** | | |
| Adult | 199 | 76.0 |
| Parent | 63 | 24.0 |
| **Gender:** | | |
| Male | 51 | 19.5 |
| Female | 211 | 80.5 |
| **Nationality:** | | |
| Saudi | 253 | 96.6 |
| Non-Saudi | 9 | 3.4 |
| **Educational Level:** | | |
| Secondary | 49 | 18.7 |
| Intermediate | 3 | 1.1 |
| Bachelor | 198 | 75.6 |
| Higher education studies | 12 | 4.6 |
| **Marital Status:** | | |
| Single | 162 | 61.8 |
| Married | 100 | 38.2 |

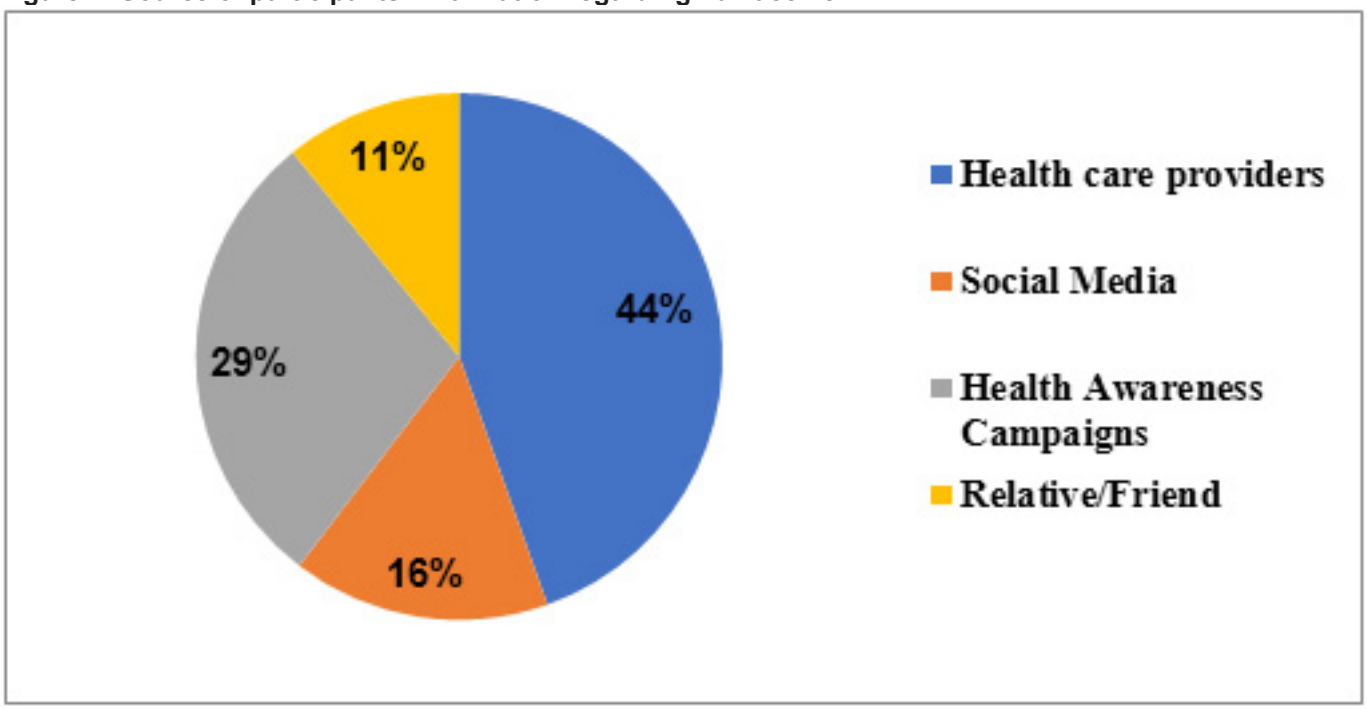
Knowledge, attitude, practice, and the future hesitancy after the outbreak of COVID-19 was also measured and it was found that 96.95% participants agreed on vaccination safety and 87.40% support seasonal flu vaccination (Table 2).

**Table 2: Knowledge, attitude and practice of participants regarding non-obligatory vaccines**

| S/N | Variables | Yes N (%) | No N (%) |
|---|---|---|---|
| 1 | Do you think Vaccination is safe? | 254 (96.95) | 8 (3.05) |
| 2 | Have you ever heard of seasonal influenza vaccine? | 241 (91.98) | 21 (8.02) |
| 3 | Do you support vaccination against seasonal flu? | 229 (87.40) | 33 (12.60) |
| 4 | Is there a possibility that you will take the seasonal flu vaccination after outbreak of Corona Virus (COVID 19) | 175 (66.79) | 87 (33.21) |
| 5 | If there is a new vaccine against the new Corona virus (COVID 19), will you take it? | 227 (86.64) | 35 (13.36) |

The participants' information about flu vaccine was found to be versatile, where, 45% reported that they had heard information from their health care providers and 29% from health awareness campaigns (Figure 1).

**Figure 1: Source of participants' information regarding flu vaccine**




Around 2.67% participants believed that there is no need to be vaccinated at almost any age (Table 3).

**Table 3: Participants beliefs regarding age groups who needed to take vaccines**

| | Frequency | Percentage (%) |
|---|---|---|
| Children till 18 years | 26 | 9.92 |
| Adult till 65 years | 13 | 4.96 |
| Elderly > 65 years | 3 | 1.15 |
| All age groups | 213 | 81.30 |
| Nobody | 7 | 2.67 |
| Total | 262 | 100.0 |

Moreover, it was demonstrated that 7.36% participants believed that no one is in need of vaccination regardless of their health situation (e.g. chronic disease, or pregnancy) and only 62% participants were keen to take the vaccine (Table 4).

**Table 4: Participants belief regarding people most in need of vaccination for Seasonal Flu**

| | Frequency | Percentage (%) |
|---|---|---|
| Everyone | 167 | 64.73 |
| Everyone with chronic diseases | 63 | 24.42 |
| Pregnant ladies | 6 | 2.33 |
| I think no one really needs them | 19 | 7.36 |
| Others | 3 | 1.16 |
| Total | 262 | 100.0 |

Around 25.19% participants would never adhere to taking the flu vaccine regardless of the time of the year and despite if they were asked by a health care provider or not (Table 5).

**Table 5: Practice of participants regarding flu vaccination**

| | Frequency | Percentage (%) |
|---|---|---|
| Annually | 55 | 28.63 |
| Sometimes | 75 | 20.99 |
| When I am Asked by Healthcare provider | 66 | 25.19 |
| I do not take the vaccine | 66 | 25.19 |
| Total | 262 | 100.0 |

The first most common reason was the lack of perception of need (n=16, 32.7%), whereas the second most common reason was the perception of ineffectiveness (n=8, 16.4 %) (Table 6).

**Table 6: Cross tabulation: Frequency of reasons that lead to flu vaccination hesitancy**

| The reasons for vaccine hesitancy | Frequency | Percentage |
|---|---|---|
| I do not need it | 16 | 32.7 |
| I don't think it is useful or effective | 8 | 16.4 |
| it hurts | 4 | 8.2 |
| A friend or relative advised me not to take it | 4 | 8.2 |
| It causes side effects | 3 | 6.1 |
| It causes diseases like autism | 2 | 4 |
| I don't care | 2 | 4 |
| I am allergic to seasonal flu vaccine | 1 | 2 |
| Better for immunity not to take it | 1 | 2 |
| Others | 8 | 16.4 |
| Total | 49 | 100 |

Approximately, 18.7% out of 33.2% parents do not give their children the flu vaccine. Furthermore, 13.36% participants are not willing to take COVID-19 vaccine if it would exist in the future (Table 7).

**Table 7: Do you give your child the seasonal flu vaccine?**

| | Frequency | Percentage |
|---|---|---|
| Yes | 38 | 14.50 |
| No | 49 | 18.70 |
| I don't have children | 175 | 66.80 |
| Total | 262 | 100 |

## Discussion

Vaccinations are among the most effective public health interventions against infectious diseases. Vaccine hesitancy is a continuum of behaviors ranging from delay in receipt to vaccination refusal. The World Health Organization (WHO) identified vaccine hesitancy as one of the top ten global health threats in 2019 (10).

Vaccine hesitancy is one of the reasons identified for the Global Vaccine Action Plan to miss its goals by 2020 (11). This study was conducted to determine the prevalence of vaccine hesitancy in Makkah Al- Mukarramah, Saudi Arabia. The study included 262 individuals and it was found that the overall vaccine hesitancy was high in Makkah population (38%). The most common reasons for refusal were lack of perception of need (32.7%), and perception of ineffectiveness (16.4 %).

The current study hypothesis stated that vaccine hesitancy is more prevalent than the previous literature conducted outside Makkah, which was supported by the results found. Since this study took a different approach to measure vaccine hesitancy from the previous literature, the comparison of results between this study and the results of the literature would be based on the closest and the most similar measures, which is in this case was the willingness to take the flu vaccine.

In the current study, 38% ultimately refused to take the influenza vaccine. This result is higher than the reported flu vaccine hesitancy rate in Alabbad et al., in Riyadh, Saudi Arabia 2017 (8). A common selected reason for this hesitancy was, "I don't think it is useful or effective". In Alabbad et al, 21.5% of the 17% who were hesitant responded this way, while in this study, it was 4.58% of the 38% who gave the same response (8).

The response choice "I don't need it because I am healthy" was selected by 17.6% of the 17% who were hesitant in Alabbad et al, while in this study it forms 10.69% of the 38% who were hesitant. The response choice "it causes side effects" was selected by 13.7% of the 17% in Alabbad et al., [8] while in this study, it was chosen only by 2.67%.

Regarding vaccine knowledge and the source of the knowledge, in Alabbad et al., 89% of the participants knew about the influenza vaccine, with the knowledge source being medical staff, health awareness campaign, and social media, at 25%, 24%, and 20%, respectively (8). In this study, 91.98% were aware of the influenza vaccine, with their source of knowledge being the medical staff, health awareness campaign, social media, relatives or friends, at 45%, 29%, 16%, and 11%, respectively.

The current study had some limitations. First, assessing the knowledge, attitude, and practices toward vaccines was from a self-reported questionnaire. Second, convenience sampling was adopted that was restricted to one city; therefore, this study has limited generalizability. On the other hand, there were many studies performed to assess vaccine hesitancy in different populations of Saudi Arabia and the Middle East North Africa region, yet none of these took place in Makkah; additionally, local attitudes toward COVID-19 were assessed right at the beginning of the outbreak to measure the possible future hesitancy against any expected COVID19 vaccine.

## Conclssion

Currently, vaccine hesitancy in Makkah is high (38%) compared to previous findings. It was recommended that improved measures should be taken to create more awareness through increased communal educational campaigns. Moreover, continuing education about the importance of vaccinations should be conducted by health care providers. Additional studies are needed in Makkah to assess the vaccine hesitancy movement.

**Authors' contributions**

All author contributed equally to literature search, figures, study design, data collection, data analysis, data interpretation, writing.

**List of abbreviations:**

Confidence Interval (CI)
Statistical Package for the Social Sciences (SPSS)
Umm Al-Qura University (UQU)
World Health Organization (WHO)

**Conflict of Interest:**
The authors declare that there is no conflict of interest regarding the publication of this article.

**Funding:**
None

**Consent for publication:**
Written informed consent was obtained from all the participants

**Ethical Approval:**
Ethical approval was obtained from the Biomedical Ethics committee, approval No: HAPO-02-K-012-2020-03-368, dated: 9-03-2020

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# The impact of vitamin D deficiency on gestational COVID-19 infection

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Received: February 2023 Accepted: March 2023; Published: April 1, 2023.
Citation: Kader Mutluer, Juwairia Hashmi. The impact of vitamin D deficiency on gestational COVID-19 infection. World Family Medicine. March 2023; 21(3): 57-62 DOI: 10.5742/MEWFM.2023.95256074

## Abstract

Background: A worldwide pandemic infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 2020 caused an outbreak of the disease called COVID-19 infection. Multiple researchers investigated the effect of serum Vitamin D levels in preventing and treating infectious respiratory syndromes. Vitamin D is a steroid hormone and fat-soluble vitamin which helps preserve a strong immune system and is frequently taken as supplements for the prevention of viral and bacterial illnesses. The serum Vitamin D levels in pregnant women have led to discussions on the severity of the clinical outcomes and its possible role in preventing a COVID-19 infection by treating Vitamin D deficiency with supplements. The purpose of this study is to describe the most recent studies on the impact of vitamin D levels on pregnant women with COVID-19 infection.

Methods: This is a narrative literature review in which PubMed, Medline, ScienceDirect, Cochrane and Google Scholar database were used to select the most relevant research published in English before December 2022 and available to the authors.

Results and Conclusion: Although lower serum vitamin D levels are associated with a higher chance of contracting a serious disease caused by several respiratory viruses like SARS-CoV-2, they are not associated with a higher possibility of COVID-19 occurring in expecting women.

Key words: COVID-19, SARS-CoV-2, Vitamin D, Vitamin D deficiency, pregnant women

## Introduction

In March 2020, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that caused the coronavirus disease 2019 (COVID-19) outbreak was classified as a pandemic (1). Despite intense international attempts, the spread of COVID-19 infection has caused more than 700 million confirmed illnesses and more than 6.5 million fatalities globally as of January 2023 (2).

Compared to SARS-CoV-1 and the Middle East Respiratory Syndrome (MERS), SARS-CoV-2 has increased transmissibility and infectivity, but had a lower fatality rate (3).

SARS-CoV-2 is mainly transmitted through respiratory droplets and binds to pulmonary epithelial cells via membrane-bound angiotensin-converting enzyme 2 (ACE-2), resulting in its down-regulation (4). Based on current knowledge, the host immune system plays a significant role in the elimination of SARS-CoV-2. Consequently, alterations in the immunological state during conditions like pregnancy could substantially impact the course of COVID-19 and its clinical outcomes (5).

Discussions about the advantages of normal serum vitamin D levels in preventing and treating infectious respiratory syndromes have been sparked by COVID-19. Numerous researchers have investigated how vitamin D supplementation and serum levels relate to the likelihood and severity of respiratory virus infection (6, 7). There is currently insufficient evidence to conclusively link vitamin D concentration to COVID-19 risk and consequences.

COVID-19 infection symptoms in pregnant women are comparable to those in the general population. However, compared to non-pregnant women, pregnant women are more likely to need treatment in the intensive care unit (ICU) when they exhibit clinical signs of cough, chills, headache, malaise, and shortness of breath (8). The availability of studies on vitamin D's function in expectant mothers who have COVID-19 is limited.

The aim of this narrative literature review is to present the current state of knowledge on the influence of vitamin D levels in pregnant women with COVID-19.

## Methods and Search Strategy

We performed electronic searches using PubMed, Medline, ScienceDirect, Cochrane and Google Scholar databases for literature published in English before December 2022. The keywords used for the literature search were: COVID-19, SARS-CoV-2, pregnant women, Vitamin D, and Vitamin D deficiency. The results were further screened by heading and abstract. Finally, the screened full-text articles were evaluated by both authors and included in this review.

## Results and Discussion

**1. Covid-19 and vitamin D**

Micronutrients, which include vitamins and minerals, are important for preserving a strong immune system and are frequently taken as supplements for the prevention of viral and bacterial illnesses. Anti-infective, anti-inflammatory, and immunomodulatory properties are properties of vitamin D. Vitamin D is a steroid hormone and fat-soluble vitamin that is created on the skin as a result of UV radiation. It can also be acquired exogenously through food sources or dietary supplements.

It helps to maintain the integrity of the physical barrier of the cell and boosts the activity of T cells, macrophages, and monocytes, which are part of the innate immune system (13).

Tekin et al. have suggested that vitamin D's immunomodulatory and anti-inflammatory properties are the potential mechanisms for the vitamin's positive effects on the treatment of a SARS-CoV-2 infection. It is thought that vitamin D can diminish inflammatory responses connected to a cytokine storm in COVID-19 and slow down the SARS-CoV-2 replication (14).

Low vitamin D levels (i.e., deficiency) were found to be significantly linked with worse patient outcomes and prognoses in a meta-analysis involving a total of 1,368 COVID-19-positive patients (15). Vitamin D deficiency plays an independent causal role in the expression of illness severity, remaining untouched by potential "confounders" like age, gender, or concomitant disorders. Notable was the marginally evident variation in vitamin D levels between individuals who survived versus not survived as a result of COVID-19 (15).

The COVID-19 pandemic has sparked debates over vitamin D's potential for both preventing and treating the illness. This is due to the fact that adequate blood vitamin D levels enable the immune system to work well, which can aid in a positive cellular response and defend against the severity of infections brought on by microorganisms (16).

**2. COVID-19 and pregnant women**

There is currently little information on the impact of SARS-CoV-2 infection on the mother or fetus in pregnant women. However, pregnant women are known to be more prone to experiencing severe symptoms when they contract viral respiratory disease due to the physiological changes typical during pregnancy, especially in the immune system (immunosuppression) and the cardiopulmonary system. Studies of other viruses conducted in the past have contributed to the knowledge regarding the effects of SARS-CoV-2 infection on pregnant women and the fetus. For example, only 1% of women who contracted influenza A H1N1 in 2009 were pregnant, but they were responsible for 5% of infection-related mortality (9).

In a very small study of 12 patients during the SARS-CoV pandemic in 2002 and 2003, women infected during their first trimester had a high miscarriage rate (57%). Women who were in their second and third trimesters developed intrauterine growth restriction (40%), and preterm delivery (80% [one spontaneous and 3 induced by maternal condition]) and 3 women died during pregnancy (25%) (10).

Another study found that of 11 MERS-CoV-infected pregnant patients, nine (91%) had adverse outcomes, six (55%) were admitted to the neonatal intensive care unit, and three (27%) died (11).

According to data so far from the Wuhan SARS-CoV-2 outbreak, the infection seems to affect pregnant women less severely than it did during earlier SARS-CoV and MERS-CoV outbreaks (9). It is essential to mention the small sample sizes of these studies, which could raise the risk of bias and low power.

There were very few cases of confirmed SARS-Cov-2 pneumonia in the first and second trimesters and a lot of cases in the third trimester (31). As a result, more data should be gathered from a bigger group of pregnant women who are infected with the virus.
To understand the effects of the novel coronavirus infection on the expectant mother, the fetus, and the course of pregnancy, follow-up studies of infected pregnant women with coronavirus during the first and second trimesters should be encouraged (12).

**3. Vitamin D and Pregnancy**
The serum calcifediol concentrations of many pregnant women around the world are relatively low, and this has been linked to an elevated risk for the mother's health, the health of the fetus or neonate, and even on later health events of the progeny. More than 10% of pregnant women in the majority of Mediterranean nations had mean serum Vitamin D levels < 10 ng/mL (17).

Another cohort study (18) indicated that pregnant women from various ethnic groups frequently have vitamin D deficiency: 26% in Sub-Saharan Africa, 40% in the Middle East, and 45% in South Asia
.
Numerous other cross-sectional investigations also produced similar findings. A review of 54 observational studies from around the world found that mothers with serum 25OHD concentrations below 12 ng/mL had a higher risk of having babies who were small for gestational age (OR 1.59) and a lower birth weight (mean difference—88 g) (19). This risk persisted (OR 1.43) in mothers with serum 25OHD concentrations below 20 ng/mL compared to mothers with higher serum calcifediol levels.

In a Cochrane review, Palacios et al. analysed 22 RCT's involving 3,725 women and reached similar findings. According to the result of this meta-analysis vitamin D supplements lower the risk of pre-eclampsia (RR 0.48), gestational diabetes mellitus (RR 0.51), and low birth weight (RR 0.55)—all statistically significant (20).

Another meta-analysis evaluated 24 RCTs which included 5,405 participants, and it concluded that vitamin D supplementation decreased the risk of being small-for-gestational-age (OR significant at 0.72) but not for perinatal mortality. Vitamin D supplementation slightly increased the mean birth weight by 75g (21).

A large RCT in Bangladesh involving primarily mothers with severe vitamin D deficiency (mean blood 25OHD of 10ng/ml) did not discover any positive effects of vitamin D supplementation (starting at 20 weeks of gestation) on their offspring either at birth or at age 1 (no effects of body length, weight, or head circumference) (22).

However, pregnancy-related problems and rates of caesarean sections decreased, according to the evaluation of the effects of high doses of vitamin D beginning before 16 weeks of gestation (23,24).

According to a study conducted in India, where the majority of pregnant women had mild vitamin D insufficiency, taking vitamin D supplements reduced the risk of preterm labour, pre-eclampsia, and gestational diabetes by almost 50% (25).

A meta-analysis studied 11,082 participants who received vitamin D supplementation during their pregnancy in doses ranging from 800 IU daily to 50,000 IU weekly (Liu et al. 2022). The risk of fetal death was considerably decreased by supplementation, as shown by the RR of 0.690 (95% CI, 0.482-0.985; P =.04). Preterm delivery, small for gestational age, and low birth weight were not significantly linked with the vitamin D supplementation intervention. The regulation of immunomodulation at the maternal-fetal interface, lung development, and vitamin D's effects on the genome are thought to be the mechanisms underlying its effects (26,27).

**4. Vitamin D deficiency in COVID-19-positive pregnant women**
Most recently a systematic review and a meta-analysis were conducted by Mazaheri-Tehrani et al. A case-control approach was employed in five of the seven studies that were included (13,14,28,29, 30) a retrospective cohort analysis was used in one study (31) and a cross-sectional design was used in another study (32).

The included studies included a total of 1799 pregnant women, 886 of whom were healthy, and 913 of whom had been diagnosed with COVID-19. A retrospective cohort research with 34 participants had the smallest sample size, while a case-control study with 491 people had the largest sample size. While several research studies accepted participants regardless of gestational age, three solely evaluated pregnant women in the third trimester. All studies considered quantities above 30 ng/ml of vitamin D to be within the normal range, with the exception of one conducted in Turkey by Tekin et al., who deemed levels above 50 ng/ml to be an ideal blood level.

Serum vitamin D levels were shown to be considerably lower in SARS-CoV-2-infected pregnant women compared to healthy subjects in five studies (13,28,29,31,32).

Tekin et al. discovered that pregnant women diagnosed with COVID-19 had no difference in serum vitamin D levels than controls (12.52 ± 8.28 ng/ml vs. 14.64 ± 10.72 ng/ml). Additionally, the blood vitamin D status of cases (21.28 ± 9.52 ng/ml) and controls (18.54 ± 8.04 ng/ml) in a case-control research conducted in Spain did not show any discernible differences (30).

Even though the mean serum vitamin D level was 2.55 ng/ml lower in the COVID-19 group compared to the healthy group (WMD = 2.55 ng/ml, 95% CI: 6.85 - 1.74), the combined results of five studies (14,28,29,30,31) did not demonstrate a significant difference between infected women and the non-infected group.

In December 2022 Vásquez-Procopio et al. published a retrospective study that involved 165 pregnant women in the third trimester.

By RT-qPCR, 86 people (52%) tested positive for SARS-CoV-2, while 79 people (48%) tested negative. 32 (19%) of the positives had no symptoms, 44 (27%) had just minor symptoms, and 10 (6%) had severe COVID-19 symptoms. The serum vitamin D levels were lower in SARS-CoV-2-infected women than in healthy, pregnant controls. Women who had severe symptoms also had considerably lower levels, which is consistent with the progression of the condition.

Three observational studies found a link between vitamin D deficiency and the severity/mortality of COVID-19 (16,34,35,36) however, four other studies did not find a link (37,38,39,40).

It is important to keep in mind that vitamin D status varies significantly depending on factors including age, ethnicity, place of residence, and sun exposure. Therefore, the association between low vitamin D status and severe COVID-19 is still debatable.

## Conclusion

Most of the studies indicate a connection between the severity of COVID-19 infection and vitamin D deficiency in pregnant women. Moreover low serum vitamin D levels are a risk factor for the development of severe COVID-19 in pregnant women which supports the use of Vitamin D supplements to prevent worse COVID-19 outcomes during pregnancy. According to the available data, vitamin D has a critical function in immune regulation and has a connection to the prevention of respiratory infections and local inflammation at the pulmonary level. Vitamin D helps to prevent illnesses and reduces the severity of illness caused by several respiratory viruses, such as influenza and respiratory syncytial virus.

Although lower serum vitamin D levels are linked to a greater risk of developing a serious illness, serum vitamin D levels are not linked to the likelihood of COVID-19 occurrence in expectant women. The relationship between vitamin D levels and COVID-19 in pregnant women should be better researched by additional studies, comparing participants with adequate vitamin D status to those with vitamin D deficiency. These discoveries might be useful for newly discovered viral illnesses in the future.

**Declaration of Competing Interest**

The authors declare that they have no relationships or financial conflicts that could have seemed to affect the results presented in this study.

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# Prevalence of Computer Vision Syndrome among undergraduate medical students in Riyadh, Saudi Arabia: A multi-university cross-sectional study

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Received: February 2023 Accepted: March 2023; Published: April 1, 2023.
Citation: Khalid A. Bin Abdulrahman et al. Prevalence of Computer Vision Syndrome among undergraduate medical students in Riyadh, Saudi Arabia: A multi-university cross-sectional study.. World Family Medicine. March 2023; 21(3): 63-74
DOI: 10.5742/MEWFM.2023.95256075

## Abstract

Background: Computer Vision Syndrome (CVS) is a group of eye and vision-related symptoms resulting from prolonged and extensive use of electronic devices. Such symptoms include blurry vision, dry eyes, watery eyes, headaches, fatigue, and neck pain. This study aimed to measure the prevalence of CVS and the frequency of exercising ergonomic practices among undergraduate medical students attending several medical colleges in Riyadh, Saudi Arabia.

Methods: A cross-sectional study surveyed 1,014 undergraduate medical students from several medical colleges in Riyadh. Data collection was held for four weeks throughout July-August 2021. Data were analyzed using IBM SPSS Statistics Version 21. CVS-Q manual was implemented as the scoring system.

Results: Out of the total surveyed medical students, 85.5% reported using electronic devices for educational purposes. Neck pains (42.5%), headaches (39.4%), and eye dryness (38.6%) were the most frequent symptoms. 60.8% of students were found CVS-positive. Male students were significantly less predicted to have CVS than female students (P<0.001). Brightness levels of screens correlated substantially with the risk of CVS (P=0.035) as more students who used bright backlight were found CVS-positive compared to those who did not.

Conclusion: CVS and its associated symptoms were relatively common among medical students. Future studies are necessary to measure CVS across larger samples. Further awareness and routine ophthalmic assessments are imperative to mitigate this issue and promote ocular health.

Keywords: Computer Vision Syndrome, Medical Students, Saudi Arabia, Electronic Devices.

## Introduction

In this era of advanced technology, medical students are presented with various opportunities to pursue their academic learning in more personalized and convenient manners. The use of digital devices has become an integral part of a student's learning process. Nevertheless, the continuous use of such technological gadgets for extensive durations is inevitably bound to instigate vision-related problems.

Computer Vision Syndrome (CVS), or Digital Eye Strain, is an umbrella term that refers to various ocular and non-ocular symptoms related to extensive, prolonged use of digital devices, such as smartphones, tablets, and computers. These symptoms comprise ocular manifestations like blurry vision, dry eyes, redness, itchiness, excessive tearing, and non-ocular manifestations such as headaches, neck pain, and shoulder pain. It is further explained by the American Optometric Association (AOA) as a group of vision-related symptoms that result from prolonged use of computers, tablets, or cellphones and are experienced either during periods of usage or persisting after [1].

Learning through digital and electronic devices has become standard practice for students. However, whether for educational purposes or research work, the consequences of such educational advancement have raised significant health concerns. A study at the University of Birmingham Medical School in England found that 70% of medical students use smartphones to facilitate their medical education [2]. A local study conducted at King Saud Bin Abdulaziz University for Health Sciences (KSAU-HS) in Jeddah, Saudi Arabia, described that 97.3% of its participants had reported at least one symptom of CVS [3]. Similarly, another study in Jeddah at King Abdulaziz University concluded that 90% of its participants expressed CVS symptoms, with the most reported symptoms being excessive tearing, dryness, and itching [4].

The symptoms of CVS generally manifest with prolonged hours of use. A study conducted in Pune, India, demonstrated that 39.9% of students who presented with CVS symptoms spent an average of 6-8 hours of computer use [5]. Another study on Qassim University medical students in Saudi Arabia reported that most students with CVS complaints spent more than 8 hours on computers or some visual display monitor [6]. In consequence, the syndromic symptoms (extra-ocular symptoms) begin to manifest. A study done on Bahria University students in Karachi revealed that out of all its medical students complaining of ocular CVS symptoms, 38% experienced fatigue, and 21.8% experienced neck and shoulder pain [7].

The presence of these symptoms can disrupt daily activities if left untreated. Subsequently, preventive measures and ergonomic practices are sought after for symptom relief. A Malaysian-based study conducted across five universities demonstrated that taking breaks amidst working was the most common practice performed by students for symptom relief (68.8%), followed by looking at far-away objects and massaging eyes [8]; while in another study, the two most common practices were adjusting brightness level according to surrounding lighting and taking breaks while using devices at 82% and 66%, respectively [3].

During the Covid-19 pandemic, the imperative transition from traditional lecture halls to virtual classrooms due to mandatory e-learning to maintain public health safety has significantly affected university students' vision [9]. Consequently, this study aimed to measure the prevalence of Computer Vision Syndrome and its associated habitual risk factors among undergraduate medical students in Riyadh, Saudi Arabia, during this period, as well as the frequency of ergonomic practices exercised by the students.

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## Methods

A cross-sectional study was conducted on 1,014 undergraduate medical students attending four medical colleges in Riyadh, Saudi Arabia, from July-August of 2021. Respondents included were required to be undergraduate medical students attending medical colleges in Riyadh, irrespective of gender and age. The study involved four major public medical colleges from governmental universities in Riyadh: King Saud University (KSU), King Saud bin Abdulaziz University for Health Sciences (KSAU-HS), Imam Mohammed Ibn Saud Islamic University (IMSIU), and Princess Nourah Bint Abdulrahman University (PNU). Five academic levels are included in this study, aside from the preparatory year (as it is not a legitimate medical year as per governmental requirements). Exclusion criteria included students who do not use electronic devices for academic purposes, interns, other health sciences majors, and students outside the Riyadh region.

The data collection process was held for four weeks from July-August 2021. Respondents were asked to fill out a self-administered online questionnaire. The sampling technique was based on non-probability (convenience) random sampling, and the expected sample size was estimated to be 377 with a 95% confidence interval (CI) and a 5% margin of error.

The validated Computer Vision Syndrome Questionnaire (CVS-Q) was adapted and developed from previous literature [4, 5, 10]. It was implemented as a data collection tool divided into three sections: Section 1 comprised questions regarding demographic data, ophthalmological medical history, and whether electronic devices were used for academic purposes and/or studying. Section 2 detailed questions regarding study habits using electronic devices and behavioral practices such as time spent using such devices, lighting source, posture, and other study habits. Section 3 included the 18-item CVS-Q questionnaire, the frequency of exercising ergonomic practices to reduce symptoms, and whether the symptoms have exacerbated since the mandatory transition to virtual classrooms amid the Covid-19 pandemic.

Participation in this research was optional. All respondents consented to partake and engage.

Respondents were not required to give out names, student IDs, or other personal information. All records were kept confidential and used carefully, and respondents' data were only accessible to the researchers. Ethical approval was obtained through the ethical committee of the Institutional Review Board (IRB) of Imam University (IMSIU) Medical College.

Regarding statistical analysis, the mean and standard deviation (SD) were used to describe continuously measured variables, and the frequency and percentages were used for categorically measured variables. The chi-squared ($\chi 2$)-test of independence was used to assess the correlations between categorically measured variables, and the independent samples t-test was used to determine the statistical significance of mean differences on metric variables across the levels of categorical binary outcomes.

CVS-Q scoring manual was followed to estimate students' total CVS scale score with a cutoff value of six (6 points), which was used to classify students' final CVS risk into positive versus negative states. The Multivariate Binary Regression analysis was used to assess the statistical significance of the predictors of students' odds of having CVS. The association between students' odds of having CVS with sociodemographic and other relevant predictor variables was expressed as an Odds Ratio (OR) with an associated 95% confidence interval (CI). The alpha significance level was considered at 0.050 level. The IBM SPSS Statistics Version 21 statistical analysis software program was used to analyze the data.

## Results

**Sociodemographic Data**

One thousand and fourteen (1014) university students attending four medical colleges in Riyadh enrolled themselves electively into the study and completed an online questionnaire. The majority of students were females (59%), whereas the remainder of the students were males (40.3%). The academic year of study was as follows: 175 (17.3%) students were in their first study year, 167 (16.5%) students in their second year, 239 (23.6%) students in their third study year, 261 (25.7%) students in their fourth year, and 172 (17%) students in their fifth year.

Asked to indicate their affiliated universities, 274 (27%) students were attending KSAU-HS, 272 (26.8%) students were attending IMSIU, 251 (24.8%) students were attending KSU, and 217 (21.4%) students were attending PNU. Out of 1,014 total students, 865 (85.3%) enrolled in the study reported using electronic devices for educational and academic purposes [Table-1].

**Students' Study Habits**

Regarding students who use electronic devices (n=865), their study habits were assessed. The time spent using electronic devices was measured: 22 (2.5%) students used electronic devices for less than an hour per day, 62 (7.2%) students used devices for about 1-2 hours per day, 271 (31.3%) students used electronic devices for 3-4 hours per day, and 591 (59%) students used electronic devices for more than 4 hours per day.

**Table-1: Demographic and Academic Characteristics (n= 1014)**

| | Frequency | % |
|---|---|---|
| **Gender** | | |
| Female | 605 | 59.7 |
| Male | 409 | 40.3 |
| **Year of Study** | | |
| 1st Year | 175 | 17.3 |
| 2nd Year | 167 | 16.5 |
| 3rd Year | 239 | 23.6 |
| 4th Year | 261 | 25.7 |
| 5th Year | 172 | 17 |
| **University** | | |
| Imam Mohammad ibn Saud Islamic University | 272 | 26.8 |
| King Saud bin Abdulaziz University for Health Sciences | 274 | 27 |
| King Saud University | 251 | 24.8 |
| Princess Nourah bint Abdulrahman University | 217 | 21.4 |
| **Use of Electronic Devices for Academic Purposes** | | |
| No | 149 | 14.7 |
| Yes | 865 | 85.3 |

About taking breaks, 765 (88.4%) students reported taking short breaks from electronic devices while studying, of which the frequency was as follows: 191 (22.1%) students had breaks every 30 minutes or less, 414 (47.9%) students had breaks every 30-60 minutes, and 260 (30.1%) students had breaks every 60 minutes or more.

Asked to indicate the distance they keep their eyes away from the screens of laptops/tablets, 362 (41.8%) students keep a distance greater than a forearm length, whereas 503 (58.2%) students keep a distance less than a forearm length. Moreover, 311 (36%) students reported they keep their screen level parallel to their eye level, 522 (60.3%) students keep it below the level of their eyes, and 32 (3.7%) students keep it above the level of their eyes.

Furthermore, students were asked to indicate the brightness of their devices: 60 (6.9%) students preferred a dark screen, 289 (33.4%) students preferred a flat screen, 424 (49%) students preferred brightly lit screens, and 92 (10.6%) students preferred very bright screens. As for using anti-glare screen filters, only 225 (26%) students reported the use of anti-glare screen filters. The remaining findings are showcased in Table-2.

**Frequency of CVS Manifestations**

Students were asked to rate the frequency and intensity of eighteen CVS manifestations using Likert-like scales. The top nine most experienced CVS symptoms, which were reported as often/always, were as follows: Neck, shoulder, and back pains (42.5%), headaches (39.4%), eye dryness (38.6%), tearing (22%), itching (21.6%), burning (20.5%), eye redness (20.5%), feeling that sight is worsening (20.3%), and increased sensitivity to light (20.1%). Regarding symptom intensity, the top nine symptoms reported as intense were as follows: Neck, shoulder, and back pains (20.3%), headaches (18.3%), eye dryness (17.5%), eye redness (10.9%), itchiness (9.2%), increased sensitivity to light (9.1%), eye pain (8.3%), numbness of fingers (7.9%), and feeling that sight is worsening (7.7%). Table-3 summarizes the remainder of the findings.

**Ergonomic Practices**

Students coping methods with their experienced symptoms were assessed in Table-4. Students' mean self-rated frequency of practicing recurrent blinking and eye massaging as the ergonomic practice was measured with 2.5/5 points, suggesting that they blink and massage their eyes to relieve CVS symptoms between rarely to occasionally on average. Additionally, students were asked to rate how often they practice the 20-20-20 rule using a Likert-like scale; their collective mean rate was measured with 2.41/5 points, indicating they perform such practice rarely to occasionally on average. The students' rate of using anti-glare screens for their electronic devices was measured with 1.95/5 points, denoting students use anti-glare screens between never to rarely on average. Asked to rate how often they adjust their brightness levels to match their surrounding conditions to relieve eye strain, students' collective mean rate was measured with 2.95/5, indicating they adjust brightness levels occasionally to often on average.

**CVS-Positive Bivariate Analysis**

Of 865 students who used electronic devices for academic purposes, 526 (60.8%) were considered CVS-positive. [Table-5].

Students who use electronic devices were analyzed for statistically significant associations between their demographic characteristics, study habits, and performing ergonomic practices to gain insight into why they may have a higher or lower risk of CVS. The resulting findings (Table-6) showed that male students were found to be significantly less predicted to have CVS compared to female students ($P<0.001$), according to the Chi-squared test of independence. Year of study and affiliation to a particular university showed no association with risk of CVS as P-value was statistically insignificant ($P>0.05$).

Regarding study habits, students' daily use of electronic devices correlated significantly with their CVS risk. Students who use their devices for >4 hours per day were found to be substantially more predicted to have CVS compared to those who use their devices for <4 hours per day ($P<0.001$).

Moreover, students' rate of taking these breaks correlated significantly with their risk of CVS ($P=0.020$); students who take breaks every 60 minutes or more were found to be considerably more predicted to have CVS than those who take breaks less than every 60 minutes.

Additionally, bivariate results showed that students who kept a shorter distance between their eyes and their screens (less than the length of a forearm) were found to be significantly more predicted to have CVS ($P<0.001$) than those who kept a long distance (more than the length of a forearm). The students' posture while using electronic devices did not correlate significantly with their risk of having CVS ($P=0.323$). However, the level at which they stationed these screens relative to their line of sight has considerably converged on their risk of CVS; those students who stationed their screens at one aligned level with their line of sight were found to be significantly less inclined to have CVS compared to students who kept it below or above their line of sight ($P<0.001$).

The source of room illumination did not correlate with their risk of having CVS, albeit the brightness levels of their screens did indeed correlate significantly with their risk of CVS ($P=0.035$), as students who set their screen backlight as dark were found to be considerably less predicted for CVS. In contrast, students who set their screen backlight as bright were significantly more predicted to risk CVS than those who used different screen-brightness settings.

**Table-2: Students' Study Habits & Electronic Device Use Conditions. (n=865)**

| | Frequency | % |
|---|---|---|
| **1. Time spent studying using a laptop/tablet:** | | |
| Less than an Hour per day | 22 | 2.5 |
| 1-2 hours per day | 62 | 7.2 |
| 3-4 hours per day | 271 | 31.3 |
| > 4 hours per day | 510 | 59 |
| **2. Taking breaks during studying using a laptop/tablet** | | |
| No | 100 | 11.6 |
| Yes | 765 | 88.4 |
| **3. Frequency of taking breaks during studying using a laptop/tablet** | | |
| Every 30 minutes or less | 191 | 22.1 |
| Every 30-60 minutes | 414 | 47.9 |
| Every 60 minutes or more | 260 | 30.1 |
| **4. Distance from laptop/tablet screen:** | | |
| Greater than a forearm length | 362 | 41.8 |
| Less than a forearm length | 503 | 58.2 |
| **5. Posture during studying using a laptop/tablet:** | | |
| Sitting | 351 | 40.6 |
| Sitting & lying down | 473 | 54.7 |
| Lying | 41 | 4.7 |
| **6. Level of the laptop/tablet screen:** | | |
| The same level of the eyes | 311 | 36 |
| Below the level of the eyes | 522 | 60.3 |
| Above the level of the eyes | 32 | 3.7 |
| **7. Source of lighting in the room:** | | |
| From the ceiling/wall | 579 | 66.9 |
| In the dark | 47 | 5.4 |
| Natural light (windows) | 143 | 16.5 |
| Table lamp | 96 | 11.1 |
| **8. Brightness of laptop/tablet screen:** | | |
| Dark | 60 | 6.9 |
| Dull | 289 | 33.4 |
| Bright | 424 | 49 |
| Very Bright | 92 | 10.6 |
| **9. Use of screen filters/anti-glare screens:** | | |
| No | 640 | 74 |
| Yes | 225 | 26 |

**Table-3: Frequency and Intensity of CVS Symptoms. (n=865)**

| | Frequency of Symptoms | | | Intensity of Symptoms | |
|---|---|---|---|---|---|
| | Never (%) | Occasionally (%) | Often/Always (%) | Moderate (%) | Intense (%) |
| Burning | 357 (41.3) | 331 (38.3) | 177 (20.5) | 400 (46.2) | 57 (6.6) |
| Itching | 342 (39.5) | 340 (39.3) | 183 (21.2) | 402 (46.5) | 80 (9.2) |
| The feeling of a foreign body | 440 (50.9) | 303 (35) | 122 (14.1) | 323 (37.3) | 64 (7.4) |
| Tearing | 356 (41.2) | 319 (36.9) | 190 (22) | 400 (46.2) | 59 (6.8) |
| Excessive blinking | 421 (48.7) | 313 (36.2) | 131 (15.1) | 316 (36.5) | 59 (6.8) |
| Eye redness | 314 (36.3) | 374 (43.2) | 177 (20.5) | 403 (46.6) | 94 (10.9) |
| Eye pain | 418 (48.3) | 294 (34) | 153 (17.7) | 324 (37.5) | 72 (8.3) |
| Heavy eyelids | 567 (65.5) | 196 (22.7) | 102 (11.8) | 212 (24.6) | 31 (3.6) |
| Dryness | 266 (30.8) | 265 (30.6) | 334 (38.6) | 370 (42.8) | 151 (17.5) |
| Blurred vision | 444 (51.3) | 257 (29.7) | 164 (19) | 292 (33.8) | 49 (5.7) |
| Double vision | 657 (76) | 144 (16.6) | 64 (7.4) | 144 (16.6) | 34 (3.9) |
| Difficulty focusing for near vision | 528 (61) | 213 (24.6) | 124 (14.3) | 251 (29) | 50 (5.8) |
| Increased sensitivity to light | 449 (51.9) | 242 (28) | 174 (20.1) | 273 (31.6) | 79 (9.1) |
| Colored halos around objects | 590 (68.2) | 173 (20) | 102 (11.8) | 202 (23.4) | 31 (3.6) |
| Feeling that sight is worsening | 473 (54.7) | 216 (25) | 176 (20.3) | 283 (32.7) | 67 (7.7) |
| Headaches | 235 (27.2) | 289 (33.4) | 341 (39.4) | 411 (47.5) | 158 (18.3) |
| Neck, shoulder, or back pain | 221 (25.5) | 276 (31.9) | 368 (42.5) | 402 (46.5) | 176 (20.3) |
| Numbness of hands/fingers | 458 (52.9) | 258 (29.8) | 149 (17.2) | 257 (29.7) | 68 (7.9) |

**Table-4: Students' Ergonomic Practices (n=865)**

| | Frequency | Mean (SD) | Percentage |
|---|---|---|---|
| **Frequent blinking & massaging of eyes** | | 2.50 | |
| Never | 244 | | 28.2 |
| Rarely | 214 | | 24.7 |
| Occasionally | 248 | | 28.7 |
| Often/Always | 60 | | 6.9 |
| Very Often | 99 | | 11.4 |
| **Taking short breaks every 20 minutes for 20 seconds and staring at objects that are at least 20 feet away (20-20-20 rule)** | | 2.41 | |
| Never | 270 | | 31.2 |
| Rarely | 225 | | 26 |
| Occasionally | 213 | | 24.6 |
| Often | 60 | | 6.9 |
| Very Often | 97 | | 11.2 |
| ***Use of anti-glare screens*** | | 1.90 | |
| Never | 509 | | 58.8 |
| Rarely | 116 | | 13.4 |
| Occasionally | 120 | | 13.9 |
| Often | 54 | | 6.2 |
| Very Often | 66 | | 7.6 |
| **Adjusting brightness level to match the surrounding lighting conditions** | | 2.95 | |
| Never | 173 | | 20 |
| Rarely | 144 | | 16.6 |
| Occasionally | 226 | | 26.1 |
| Often | 193 | | 22.3 |
| Very Often | 129 | | 14.9 |

**Table-5: Prevalence of CVS among medical students (n=865)**

| | Frequency | % |
|---|---|---|
| **Computer Vision Syndrome Diagnosis** | | |
| No (CVS-Q score <6 points) | 339 | 39.2 |
| Yes (CVS-Q score ≥6 points) | 526 | 60.8 |

**Table-6: Medical Students' Risk of CVS (n=865)**

| Table-6: Medical Students' Risk of CVS (*n*=865) | Computer Vision Syndrome | | |
|---|---|---|---|
| | CVS-*Negative* (*n*=339) | CVS-*Positive* (*n*=526) | *P*-value |
| **Sex** | | | |
| Female | 168 (49.6%) | 377 (71.7%) | <0.001* |
| Male | 171 (50.4%) | 149 (28.3%) | |
| **Year of Study** | | | |
| 1st year | 58 (17.1%) | 84 (16%) | 0.400 |
| 2nd year | 49 (14.5%) | 95 (18.1%) | |
| 3rd year | 83 (24.5%) | 117 (22.2%) | |
| 4th year | 99 (29.2%) | 137 (26%) | |
| 5th year | 50 (14.7%) | 93 (17.7%) | |
| **University** | | | |
| Imam Mohammad ibn Saud Islamic University | 60 (17.7%) | 100 (19%) | 0.618 |
| King Saud bin Abdulaziz University for Health Sciences | 98 (28.9%) | 165 (31.4%) | |
| King Saud University | 91 (26.8%) | 141 (26.8%) | |
| Princess Nourah bint Abdulrahman University | 90 (26.5%) | 120 (22.8%) | |
| **1. Time spent using laptop/tablet (n=865)** | | | |
| Less than an Hour per day | 7 (2.1%) | 15 (2.9%) | <0.001* |
| 1-2 hours per day | 28 (8.3%) | 34 (6.5%) | |
| 3-4 hours per day | 134 (39.5%) | 137 (26%) | |
| > 4 hours per day | 170 (50.1%) | 340 (64.6%) | |
| **2. Taking breaks during studying using a laptop/tablet** | | | |
| No | 32 (9.4%) | 68 (12.9%) | 0.117 |
| Yes | 307 (90.6%) | 458 (87.1%) | |
| **3. Frequency of taking breaks during studying using a laptop/tablet** | | | |
| Every 30 minutes or less | 69 (20.4%) | 122 (23.2%) | 0.020* |
| Every 30-60 minutes | 182 (53.7%) | 232 (44.1%) | |
| Every 60 minutes or more | 88 (26%) | 172 (32.7%) | |
| **4. Distance from laptop/tablet screen** | | | |
| Greater than a forearm length | 169 (49.9%) | 193 (36.7%) | <0.001* |
| Less than a forearm length | 170 (50.1%) | 333 (63.3%) | |
| **5. Posture during studying using a laptop/tablet** | | | |
| Sitting | 148 (43.7%) | 203 (38.6%) | 0.323 |
| Sitting /Lying down | 175 (51.6%) | 298 (56%) | |
| Lying | 16 (4.7%) | 25 (4.8%) | |
| **6. Level of the laptop/tablet screen** | | | |
| The same level of the eyes | 149 (44%) | 162 (30.8%) | <0.001* |
| Below the level of the eyes | 177 (52.2%) | 345 (65.6%) | |
| Above the level of the eyes | 13 (3.8%) | 19 (3.6%) | |
| **7. Source of lighting in the room** | | | |
| From the ceiling/wall | 224 (66.1%) | 355 (67.5%) | |
| In the dark | 18 (5.3%) | 29 (5.5%) | 0.952 |
| Natural light (windows) | 59 (17.4%) | 84 (16%) | |
| Table lamp | 38 (11.2%) | 58 (11%) | |

**Table-6: Medical Students' Risk of CVS (n=865)** (continued)

| | | | |
|---|---|---|---|
| **8. Brightness of laptop/tablet screen** | | | |
| Dark | 31 (9.1%) | 29 (5.5%) | 0.035* |
| Dull | 113 (33.3%) | 176 (33.5%) | |
| Bright | 169 (49.9%) | 255 (48.5%) | |
| Very Bright | 26 (7.7%) | 66 (12.5%) | |
| **9. Use screen filters/anti-glare screens** | | | |
| No | 238 (70.2%) | 402 (76.4%) | 0.042* |
| Yes | 101 (29.8%) | 124 (23.6%) | |
| **10. Worsening symptoms since the transition to virtual classrooms during the COVID-19 pandemic** | | | |
| No | 194 (57.2%) | 180 (34.2%) | <0.001* |
| Yes | 145 (42.8%) | 346 (65.8%) | |
| **Ergonomic Practices** | | | |
| Frequent blinking & massaging of eyes mean (SD) | 2.04 (1.14%) | 2.78 (1.30%) | <0.001* |
| Practicing the 20-20-20 rule, mean (SD) | 2.12 (1.24%) | 2.60 (1.28%) | <0.001* |
| Using anti-glare screens, mean (SD) | 1.66 (1.14%) | 2.06 (1.34%) | <0.001* |
| Adjusting device brightness, mean (SD) | 2.60 (1.36%) | 3.16 (1.26%) | <0.001* |

*P-value <0.05 is considered statistically significant.

**Multivariate Analysis**

As a further step, the multivariate logistic binary regression analysis was used to assess the combined and individual associations between students' characteristics with their odds of having CVS. The results in multivariate analysis findings, showcased in Table-7, showed that male students were significantly less predicted (0.498 times less) to have had CVS than females (P=0.002).

Students' years of study did not converge significantly on their odds of having CVS, but the different institutional backgrounds differed substantially concerning their odds of CVS. IMSIU students were found to be considerably more predicted to have CVS (2.35 times more predicted) compared to the students of PNU (P=0.006). In contrast, KSAU-HS students were significantly more predicted (2.34 times more) for CVS than PNU students (P=0.003). Still, KSU and PNU students may not necessarily differ in their odds of having CVS (P=0.571); note the bar graph in Figure-A.

**Table.7: Multivariate Logistic Binary Regression Analysis of the University Students' odds of CVS. (n=865)**

| | Multivariate adjusted Odds Ratio | 95% C.I.for OR | | p-value |
|---|---|---|---|---|
| | | Lower | Upper | |
| **Sex of the student= Male** | .498 | .323 | .766 | .002 |
| **Year of Study** | 1.077 | .938 | 1.237 | .291 |
| **University=P. Nourah B Abdelrahman (reference comparison group)** | | | | .004 |
| **University=Imam Mohd Bin Saudi Islamic** | 2.352 | 1.271 | 4.350 | .006 |
| **University= King Saud Bin Abdulaziz University** | 2.344 | 1.346 | 4.081 | .003 |
| **University=King Saudi University** | 1.164 | .688 | 1.969 | .571 |

Dependent Variable= Having CVS? No/Yes.

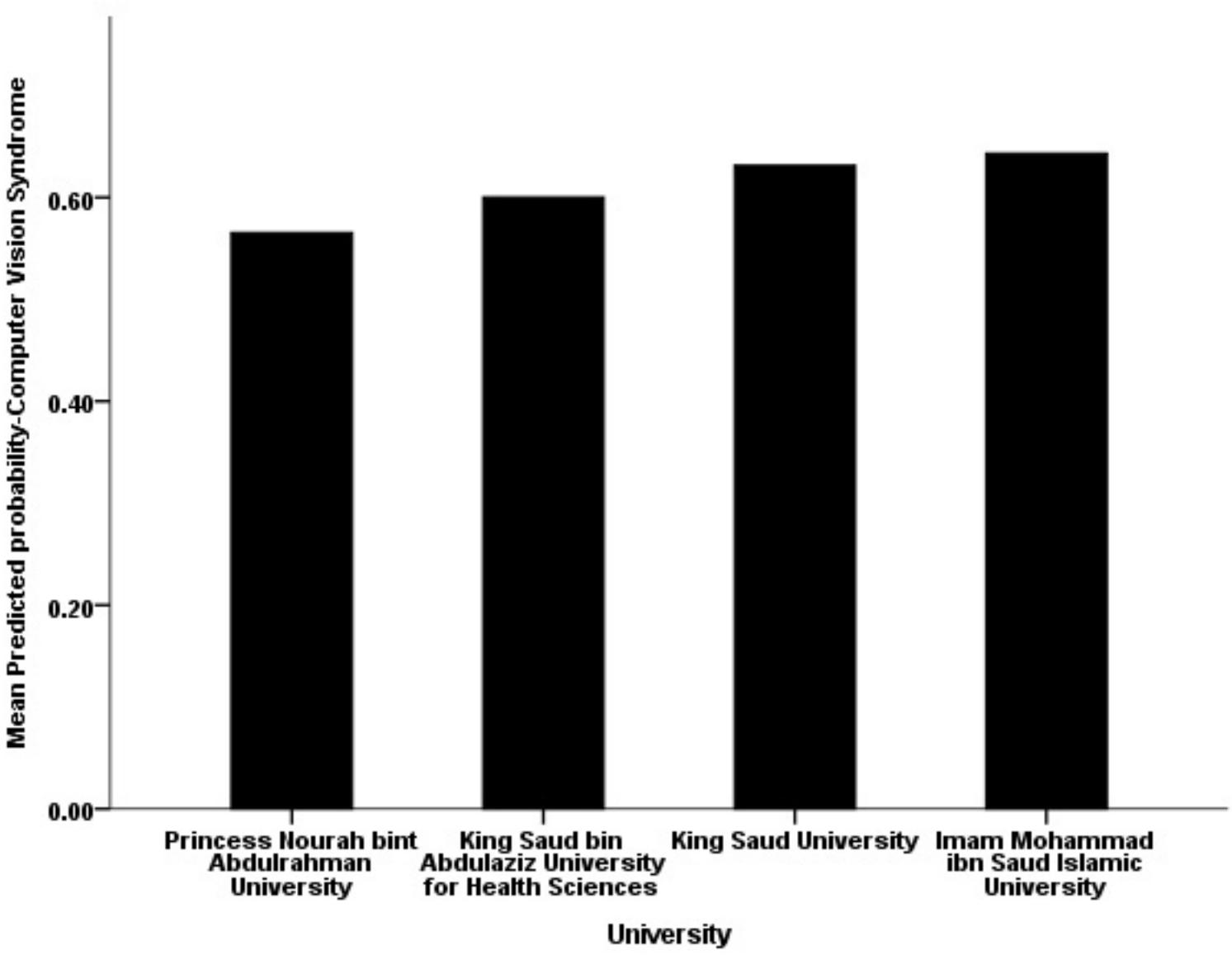


**Figure-A: The difference between different university students on their probability of having computer vision syndrome**

## Discussion

Computer Vision Syndrome (CVS) is a frequent occupational complication reported globally [10, 11, 12]. This is evident in a study conducted by Ranasinghe et al. in which the one-year prevalence of CVS among computer office workers in Sri Lanka was 67.4% [10]. In comparison, this study comprised a smaller sample of 865 medical students, of whom 60.8% (526) were considered CVS-positive, indicating slight prevalence. This is relatively similar to a study done by Alamro et al. [14], which was localized to a single university in the Riyadh region, reporting the prevalence rate of CVS to be 69.8%. However, higher prevalence rates were reported in other medical colleges in Saudi Arabia; Abdudawood et al. [4] reported a high prevalence rate of 95%, whereas Altalhi et al. [3] reported a higher prevalence of 97.3%. Other studies in Pakistan, Malaysia, and India have also reported high prevalence rates with 67.2%, 89.9%, and 78.6%, respectively [7], [8], [15].

The most frequently reported ocular symptoms were eye dryness (38.6%). In contrast, Abdudawood et al. [4] reported that excessive tearing and eye dryness were the most common ocular symptoms observed. As for extra-ocular symptoms, neck, shoulder, and back pains (42.5%), followed by headaches (39.4%), were the most frequent among respondents. This is nearly similar to Alamro et al., where the most experienced symptom was headache [14].

This current study implemented the CVS-Q scoring system [16]. Using the CVS-Q, a severity score of six points or higher (6 ≥) indicates that the respondent suffers from CVS. The resulting findings using CVS-Q yielded that 60.8% of students were considered CVS-positive. There is a disparity of rates compared to global studies, albeit this is a region-wide study. Compared to other studies, the prevalence of CVS in a Jordanian-based sample was 94.5% [17], whereas the prevalence in a Paraguayan-based sample was 82.5% [18].

The presence of sociodemographic characteristics influencing the odds of CVS was variable. University affiliation showed no association with CVS risk. However, multivariate analysis of different university affiliations differed significantly concerning students' odds of CVS. This paradoxical finding may be about individualized behaviors and personalized environments combined with variants of institutional protocols amidst the Covid-19 pandemic.

A notable finding regarding ergonomic practices is the rate of anti-glare screen use, which was significantly greater among CVS-positive students than CVS-negative students. This could be explained by how CVS-positive students would use their devices for >4 hours per day and thus leading to more exposure time regardless of utilizing protective tools. CVS-positive students were also measured significantly more for eye massaging and frequent blinking than CVS-negative students. These findings may be explained similarly to the findings mentioned above.

Screen brightness was linked to the risk of CVS. Students with bright/very bright settings risked higher for CVS than those with dimmer settings. This is a measured association validated and corroborated in literature [19]. On the contrary, a study by Wangsan et al. reported lower brightness settings associated with CVS[20].

## Conclusion

This study has revealed a slight prevalence of CVS among its participants. Therefore, future nationwide studies must assess and measure this phenomenon across a larger group to fully comprehend its magnitude and reveal its determinants. Exacerbating CVS manifestations could affect the quality of life and reduce overall productivity and performance. It is crucial to raise awareness of this overlooked condition among students and faculty to promote the healthy use of digital devices and prevent escalation to debilitating outcomes. It is also recommended to conduct ophthalmic consultations periodically.

### Limitations

The study included self-reporting of symptoms by participants without clinical examination, ophthalmic testing via instruments, or physician consultations. The presence of pre-existing ocular disorders or underlying systemic disease as risk factors was not explored. One particular university is a female-exclusive college (PNU), which may skew the results concerning gender. Thus, findings cannot be inferred from the entire study population.

### Acknowledgment

The authors would like to express their sincere appreciation and gratitude to Dr. Ghufran Abudawood for his generous assistance in forming and providing the survey questionnaire. The authors would also like to acknowledge and thank the following individuals for their helpful efforts in assisting with survey distribution: Ziyad Bokhari, Awadh Alqahtani, Sarah Maghrabi, Norah Almajli, Malath Alrowili, Ahmed Alanazi, Abdulrahman Alfantoukh, and Sarah Almutairi.

**Author Contributions:** All authors participated in the concept, Design, analysis, interpretation of data, writing, and manuscript review. They have seen and approved the final version of the manuscript.

**Institutional Review Board Statement:** The study was approved by the IMSIU Research Ethics Committee (project number 104-2020; approval date, 11 November 2020). All writing is done in accordance with the ethical principles of the Declaration of Helsinki. The survey link included a brief description of the study and a more detailed explanation on the front page. Participants were told that completion of the survey constituted consent. All participant consent and data were collected in complete confidence throughout the study.

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

### Financial Support and Funding

Nil.

### Conflicts of Interest

The authors declare no conflicts of interest.

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# The Effectiveness of Problem-Based Learning in Improving Critical Thinking and Problem-Solving Skills in Medical Students: A Systematic Review of Fifteen Years' Experience (2005-2019)

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Received: February 2023 Accepted: March 2023; Published: April 1, 2023.
Citation: Rayed Alreshidi, Fayez Saud Alreshidi The Effectiveness of Problem-Based Learning in Improving Critical Thinking and Problem-Solving Skills in Medical Students: A Systematic Review of Fifteen Years' Experience (2005-2019). World Family Medicine. March 2023; 21(3): 75-84 DOI: 10.5742/MEWFM.2023.95256077

## Abstract

Background: An ongoing challenge for medical education in the twenty-first century is determining the best method to foster problem-solving and critical thinking in learners. These higher-order aptitudes help to prepare medical doctors for practice in a rapidly evolving health system. In medical education, Problem-Based Learning (PBL) is an instructional pedagogy in which pupils are challenged to seek answers to authentic patient scenarios in small groups. PBL techniques are proposed as one method to enhance pupils' learning abilities including critical thinking and problem-solving.

Aim: This systematic review was conducted to search for evidence from the past fifteen years of literature, demonstrating the capability of PBL to improve critical thinking and problem-solving skills for medical students.

Review Question: Is there evidence to support the capability of PBL to improve problem solving and critical thinking skills in medical students?

Methods: The search process was conducted through electronic databases on publications related to the impact of PBL, particularly, on two fundamental skills; critical thinking and problem-solving for medical students. The search process was restricted to publications between January 1, 2005 and December 31, 2019. Four electronic databases were searched, namely; Medline, PubMed, EMBASE and Scopus. The Best Evidence Medical Education (BEME) guidelines were utilised to guide the way this systematic review was conducted. Quality assessment was performed through rating the evaluation methods of the included studies. This rating was through employing a five-point Likert scale (1= strongly disagree to 5= strongly agree) for each study in relation to three items; the appropriateness of study design, the implementation of the study as well as the appropriateness of data analysis. The rating for each study was then mapped to a grade from grade 1 (low) to grade 5 (high), which aligns with the BEME strength of the study findings.

Results: Searching the four aforementioned databases produced 657 publications, including 249 duplicates. Therefore, 408 publications were screened based on their titles against inclusion and exclusion criteria, leaving 86 articles to screen their abstracts. A further 9 articles were manually obtained such that a total of 95 articles were obtained for a review of their abstracts. Forty-one met the criteria for full text review. Following the full text review, twenty-nine articles were excluded. Therefore, twelve studies were included in this systematic review. The BEME strength of study findings were as follows; only two of the reviewed studies were graded as grade 5, four were graded as grade 4, and six were graded as grade 3. Of the twelve studies reviewed, only five studies provided evidence in support of the capability of PBL to improve critical

thinking and problem-solving skills among medical students. Two of these five studies were graded as grade 5 and two were graded as grade 4, while one was graded as grade 3.

Discussion: The available evidence in this systematic review provided limited support of the claim that PBL improves medical students' critical thinking and problem-solving aptitudes. Only five studies provided evidence in support of this claim, while the remaining seven studies did not. Two of these seven studies assessed only the knowledge, comprehension, and application domains, as their evaluation of problem-solving and critical thinking abilities was based on student perspectives. A further two of these seven studies, where the description provided either for case-analysis tests or modified essay questions, did not give an actual indication for measuring critical thinking and problem-solving skills. Another two of these seven studies did not describe their written tests i.e. case-analysis tests and proxy questions that are purported to measure higher-order skills, including critical thinking and problem-solving. This prevented the use of the findings from these two studies as evidence to support the specified review question. The remaining study reported that PBL students' scores in the final assessment did not improve significantly ($p>0.05$) compared to the initial assessment.

Conclusion: There is very little published evidence over the last fifteen years supporting the claim that PBL improves critical thinking and problem-solving skills in medical students. Therefore, recent practice is not based on evidence. As such, investigations are required to legitimise the claims that PBL improves critical thinking and problem-solving skills for medical students.

Key words: Problem-Based Learning, Critical Thinking and Problem-Solving Skills, Medical Students

## Background

In the past six decades, there have been significant numbers of health education institutions around the world which have adopted Problem-Based Learning (PBL) curricula as an alternative to traditional lecturing or Lecture-Based Learning (LBL) (1). Lectures still occupy an important place in the educational process through their ability to impart knowledge. One of the merits of the lectures is the ability to explain difficult concepts and introduce new topics (2). They also have an economic advantage as they can be presented to a large group of learners (2). Nevertheless, in LBL, the medical students' role is limited to receiving information from their instructors without making a mental effort in analysis, thinking and rethinking, inference, synthesis and evaluation. This process focuses on the knowledge itself without interrogation on how this knowledge can be applied in practice (3). This led to the emergence of practice-oriented and inquiry-based learning strategies that are believed to be more pertinent to medical education. These strategies were adopted by learning through a variety of innovative approaches such as PBL. PBL gives students the opportunity to place knowledge itself out of their centre of attention by emphasising the importance of learning through higher levels of thinking such as problem-solving, critical thinking and clinical reasoning, while knowledge is presumed to be acquired automatically as a secondary product (4).

Since its inception in the late 1960s at McMaster University in Canada, PBL has brought a tremendous and comprehensive change in teaching and learning strategies in medical education (2, 5, 6). PBL is a learner-centred strategy where pupils are encouraged to recognize their learning needs in a particular topic to solve a problem (6, 7). In addition, PBL can be defined as an active learning strategy which challenges pupils with genuine problems which function as a trigger for learning in which problems are the focus for synthesising what has been acquired for implementation in coming problems and situations (4, 8, 9). The ultimate purpose of using genuine problems is to encourage pupils to consider alternatives, to furnish a substantiated rationale to uphold the explanation they create and, afterward, to implement this to new situations (4, 10).

This noticeable shift from passive approaches to learning towards more active approaches encountered many different reactions across medical, educational institutions around the globe (11). Some preferred to continue with traditional instructions while implementing some principles of PBL pedagogies, while others have adopted PBL and its philosophy as a fundamental component of their curricula and as a guide for the entire educational process. PBL pedagogy, as an active learning strategy, plays a critical role in enhancing health professionals' skills such as self-directed learning, clinical reasoning, problem-solving, and critical thinking skills, as well as in preparing pupils to be lifelong learners (12, 13). The fundamental theory in implementing the principles of PBL philosophy in medical curricula is its ability to enhance the quality of education, which enhances the perception and performance of graduating doctors and thus enhances the level of healthcare provided (14-16). The fundamental presumption is that PBL pedagogies have the capability to improve pupils' knowledge, skills, and behaviour by engaging pupils through problem-solving and self-directed learning strategies (14, 17). Therefore, PBL is a small group learning strategy which utilises patient problems as a context for pupils to obtain knowledge regarding the fundamental and practical sciences.

## Purpose of the Review

The aim of this systematic review is to provide a focused insight of the literature from the beginning of 2005 to the end of 2019 regarding the efficacy of Problem-Based Learning (PBL) on two fundamental competencies which are critical thinking and problem-solving among medical students. It can be described as a focused systematic review as it targets the effectiveness of PBL in specifically enhancing these two fundamental skills, which would allay concerns related to any health education organisation that considers PBL a substantial part of its curricular renovation in graduating highly qualified doctors. Fifteen years was chosen as the time period for this review as the researcher recognised the limited available research in the area over the last five years, hence a longer period was chosen.

## Systematic Review Question

Is there evidence to support the capability of PBL to improve problem solving and critical thinking skills in medical students?

## Review Methodology

In order to answer the review question, a systematic review of the literature was executed of research published during the past fifteen years (2005-2019). The Best Evidence Medical Education (BEME) guidelines were utilised to guide the way this systematic review was conducted (18). The BEME supports the work of systematic reviews, disseminates best evidence to medical educationists and policymakers, and generates an enlightenment of best evidence among medical educators and researchers (19, 20). It was found useful for medical educators in providing theoretical guidance to guide the process of their systematic reviews (19, 20).

## Search Methods for Studies Identification

In the months of March and April of the year 2020, the search process was conducted through electronic databases on publications related to the impact of PBL, particularly, on two fundamental skills; critical thinking and problem-solving for medical students. The search process was restricted to publications between January 1, 2005 and December 31, 2019. The publications were searched for through four electronic databases, namely; Medline, PubMed, EMBASE and Scopus. Searching the four aforementioned databases produced 657 publications. Duplication of retrieved articles was noted across the aforementioned databases leaving 408 publications after identifying and eliminating unnecessarily repetitive citations. The two reviewers independently screened all of the titles, in order to exclude articles not pertinent to the systematic review. Both reviewers reached agreement on eighty-six articles that required abstract review. A further nine articles were manually [1] obtained through searching the aforementioned databases such that a total of ninety-five articles were included for a review of their abstracts. The dissertation author screened the abstracts resulting in a total of forty-one articles to be coded, which was approved by the dissertation supervisor. Following the full text review and coding process by the two researchers, twenty-nine articles were excluded. Therefore, twelve studies were included for analysis which was approved by the dissertation supervisor.

## Quality Assessment of the Reviewed Studies

After obtaining the full texts of the twelve articles, their methodological qualities were systematically evaluated by both reviewers. The BEME coding sheet was used to rate the evaluation methods of the included studies. This rating was through employing a five-point Likert scale (1= strongly disagree, 2= disagree, 3= uncertain, 4= agree, 5= strongly agree) for each study in relation to three items. These items are; the appropriateness of study design, the implementation of the study as well as the appropriateness of data analysis.

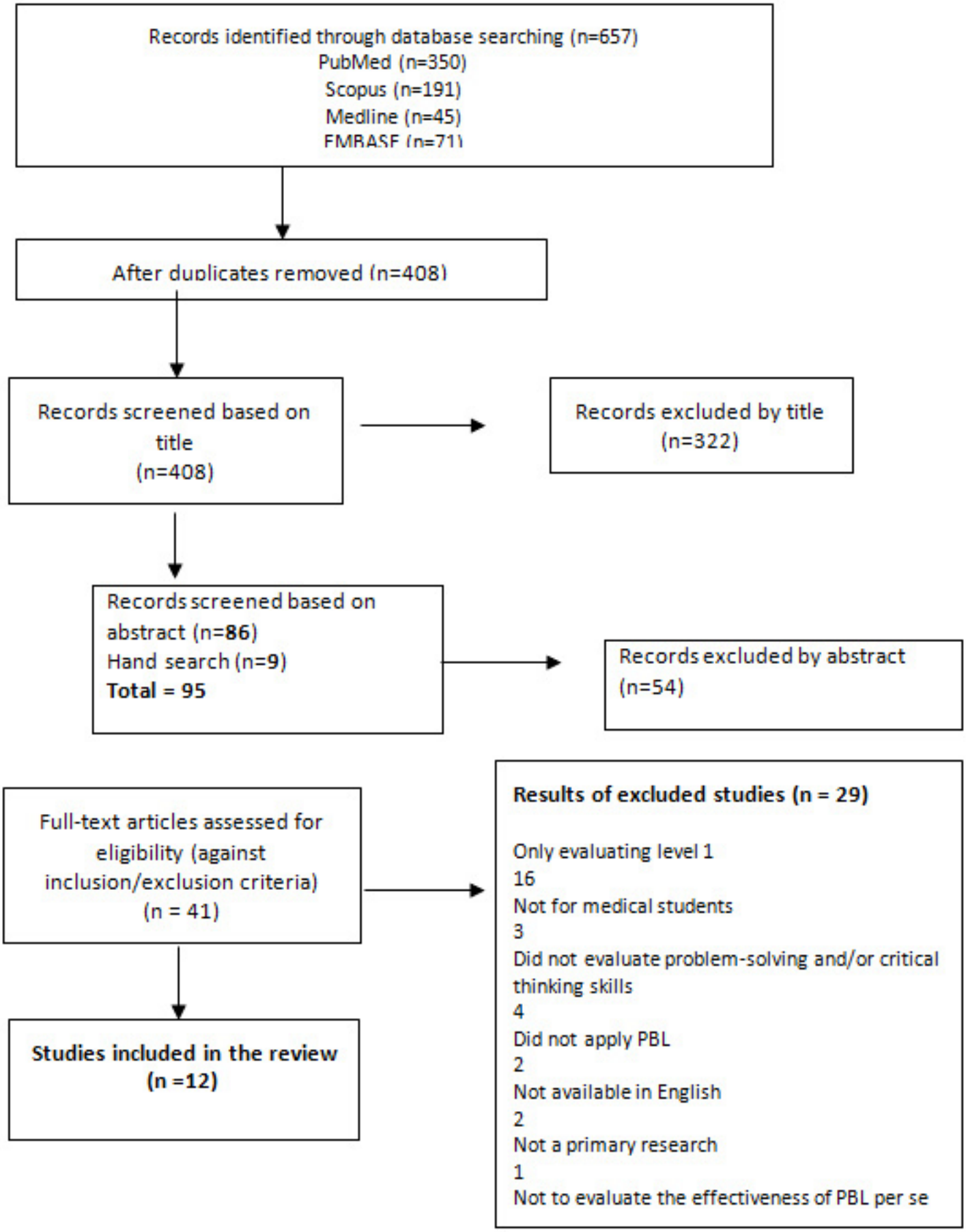
These judgments on the rating of evaluation methods for each study were then mapped to a grade from grade 1 to grade 5. This is called grading of strength of study findings which is an element in the BEME coding sheet related to quality assessment on the basis of data exhibited in the reviewed studies. As shown in (Table 1), the strength of study findings has five grades (from low to high grade findings) where grade 5 indicates that results are conclusive or unequivocal. Both the dissertation author and the supervisor of the review autonomously rated the methodological quality of the reviewed studies and after several discussions they reached an agreed quality assessment between them for the included studies.

**Table 1. The BEME Strength of the findings of the included studies (19)**

| GRADE | DETAIL |
|---|---|
| Grade 1 | No clear conclusions can be drawn. Not significant |
| Grade 2 | Results ambiguous, but there appears to be a trend |
| Grade 3 | Conclusions can probably be based on the results |
| Grade 4 | Results are clear and very likely to be true |
| Grade 5 | Results are unequivocal |

Footnote 1: Since some of electronic databases such as PubMed provide similar articles to each article appears in the search results, this feature was used to not miss any article that fulfills the inclusion criteria

**Figure 1. The search strategy and selection procedure**



## Results

**Overview of the studies included in the review**

After searching through electronic databases and applying inclusion and exclusion criteria, twelve studies were eventually included in the review. Table 2 shows the titles of the reviewed studies and their authors.

**Table 2. The Titles of the Reviewed Studies and their Authors**

| Reference | The Title of the Study |
|---|---|
| Lian & He, 2013(21) | Improved performance of students instructed in a hybrid PBL format |
| More et al., 2019(22) | Introducing Hybrid Problem-Based Learning Modules in Ayurveda Education: Results of an Exploratory Study |
| Li et al., 2013(23) | Comparison of three problem-based learning conditions (real patients, digital and paper) with lecture-based learning in a dermatology course |
| Murat et al., 2006(24) | Short-term effects of problem-based learning curriculum on students' self-directed skills development |
| Kong et al., 2009(25) | Effect of Digital Problem-Based Learning Cases on Student Learning Outcomes in Ophthalmology Courses |
| Al-Faris et al., 2008(26) | Evaluation of three instructional methods of teaching for undergraduate medical students, at King Saud University, Saudi Arabia |
| Saalu et al., 2010(27) | Quantitative evaluation of third year medical students' perception and satisfaction from problem based learning in anatomy: A pilot study of the introduction of problem based learning into the traditional didactic medical curriculum in Nigeria |
| Al-Damegh & Baig, 2005(28) | Comparison of an integrated problem-based learning curriculum with the traditional discipline-based curriculum in KSA |
| Meo, 2013(29) | Evaluating learning among undergraduate medical students in schools with traditional and problem-based curricula |
| Steadman et al., 2006(30) | Simulation-based training is superior to problem-based learning for the acquisition of critical assessment and management skills |
| Tayyeb, 2013(31) | Effectiveness of problem based learning as an instructional tool for acquisition of content knowledge and promotion of critical thinking among medical students. |
| He et al., 2018(32) | A comparison between the effectiveness of PBL and LBL on improving problem-solving abilities of medical students using questioning. |

**Study Design**

As shown in Table 3, there were four (21, 23, 25, 32) prospective randomised studies and three (27-29) cross-sectional studies. Only one (30) of the reviewed studies utilised the higher methodological quality study of a randomised controlled trials. The remaining studies were two (24, 31) quasi experimental studies, one (22) case-control study and one (26) non-randomised trial.

**Table 3. Evaluation Methods of Included Studies**

| METHODS | | NUMBER | PERCENTAGE |
|---|---|---|---|
| 1 | Prospective randomised studies | 4 | 33.33 |
| 2 | Cross-sectional studies | 3 | 25 |
| 3 | Randomised controlled studies | 1 | 8.33 |
| 4 | Quasi experimental studies | 2 | 16.7 |
| 5 | Case-control study | 1 | 8.33 |
| 6 | Non-randomised trials | 1 | 8.33 |
| Total | | 12 | 100% |

**Methodological quality of the included studies**

As discussed in the methodology section, the methodological quality of all twelve studies were systematically evaluated through applying the BEME coding sheet (19). Rating the evaluation methods of studies included in the review was through employing a five-point Likert scale (1= strongly disagree, 2= disagree, 3= uncertain, 4= agree, 5= strongly agree) for each study in relation to three items i.e. the appropriateness of study design, the implementation of the study as well as the appropriateness of data analysis (Table 4).

**Table 4. The BEME Rating of Evaluation Methods of the Included Studies**

| No | Reviewed studies | Appropriateness of study design | Implementation of study design | Appropriateness of data analysis |
|---|---|---|---|---|
| 1 | Tayyeb, 2013(31) | 5 | 5 | 4 |
| 2 | Saalu et al., 2010(27) | 4 | 3 | 3 |
| 3 | Lian & He, 2013(21) | 5 | 4 | 4 |
| 4 | More et al., 2019(22) | 4 | 4 | 4 |
| 5 | Al-Damegh & Baig, 2005(28) | 3 | 2 | 3 |
| 6 | Kong et al., 2009(25) | 3 | 3 | 4 |
| 7 | He et al., 2018(32) | 4 | 3 | 4 |
| 8 | Murat et al., 2006(24) | 5 | 5 | 4 |
| 9 | Al-Faris et al., 2008(26) | 3 | 3 | 2 |
| 10 | Meo, 2013(29) | 3 | 3 | 3 |
| 11 | Li et al., 2013(23) | 4 | 5 | 4 |
| 12 | Steadman et al., 2006(30) | 3 | 4 | 4 |

The rating for each study was then mapped to a grade from grade 1 to grade 5, which represents the strength of the study findings. As shown in (Table 5), only two (24, 31) studies were graded as grade 5. Four (21-23, 32) of the reviewed studies were graded as grade 4, and six (25-30) studies were graded as grade 3.

**Table 5. The BEME Strength of the Findings of the Reviewed Studies**

| No | Reviewed studies | Strength of the Findings (grade 1 to grade 5) |
|---|---|---|
| 1 | Tayyeb, 2013(31) | Grade 5 (Results are unequivocal) |
| 2 | Saalu et al., 2010(27) | Grade 3 (Conclusions can probably be based on the results) |
| 3 | Lian & He, 2013(21) | Grade 4 (Results are clear and very likely to be true) |
| 4 | More et al., 2019(22) | Grade 4 (Results are clear and very likely to be true) |
| 5 | Al-Damegh & Baig, 2005(28) | Grade 3 (Conclusions can probably be based on the results) |
| 6 | Kong et al., 2009(25) | Grade 3 (Conclusions can probably be based on the results) |
| 7 | He et al., 2018(32) | Grade 4 (Results are clear and very likely to be true) |
| 8 | Murat et al., 2006(24) | Grade 5 (Results are unequivocal) |
| 9 | Al-Faris et al., 2008(26) | Grade 3 (Conclusions can probably be based on the results) |
| 10 | Meo, 2013(29) | Grade 3 (Conclusions can probably be based on the results) |
| 11 | Li et al., 2013(23) | Grade 4 (Results are clear and very likely to be true) |
| 12 | Steadman et al., 2006(30) | Grade 3 (Conclusions can probably be based on the results) |

As a summary of the findings from the twelve studies reviewed in relation to the capability of PBL in improving critical thinking and problem-solving skills among medical students, only five (23, 24, 29, 31, 32) studies provided evidence. Two (24, 31) of these five studies were graded as grade 5 and two (23, 32) were graded as grade 4, while one (29) was graded as grade 3. The remaining seven studies did not provide sufficient quality evidence in support of the specified review question. In fact, one (30) of these seven studies provided evidence that PBL was not better in improving critical thinking and problem-solving skills compared to simulation-based learning. Two (21, 26) of these seven studies where the description was provided, whether for case-analysis tests or modified essay questions, did not give an actual indication for measuring higher-thinking skills. One (21) of these two studies was graded as grade 4, while the other (26) was graded as grade 3. In the study conducted by Kong et al. (25), there was no description of case-analysis tests, which prevented the findings of this study from being used as evidence for the review question. The proxy questions used in the study conducted by Al-Damegh and Baig (28) were not sufficiently clarified, which prevented their findings from being used as evidence, and the study was graded as grade 3. Written tests used in two (22, 27) studies only measured the knowledge, comprehension, and application domains, as their evaluation of problem-solving and critical thinking abilities was based on student perspectives. Findings from Steadman et al.(30) indicated that PBL students' scores in the final assessment did not improve significantly compared to the initial assessment in a type of performance test that required the student to critically assess and manage a life-threatening situation. This type of performance test requires higher-order abilities, including problem-solving and critical thinking, yet PBL failed to significantly improve the students' scores in the final assessment in this study. That is, this study (30) provided evidence that PBL was not better compared to simulation-based learning in this regard.

## Discussion

Theoretically, applying PBL techniques is purported to improve pupils' learning abilities including critical thinking and problem-solving (4), however the available evidence in this systematic review provided limited support of this theoretical basis. Only five (23, 24, 29, 31, 32) studies provided evidence in support of the capability of PBL to improve critical thinking and problem-solving skills among medical students. Two (24, 31) of these five studies were graded as grade 5 and two (23, 32) were graded as grade 4, while one (29) was graded as grade 3. The findings from the current systematic review are consistent with the findings from a systematic review in nursing education (33). In that systematic review, ten studies were reviewed to investigate the capability of PBL to develop critical thinking skills in nursing pupils. Findings of that review could not provide sufficient evidence for the evolvement of critical thinking aptitudes for nursing pupils through PBL.

The remaining seven studies did not provide evidence in support of the capability of PBL to improve critical thinking and problem-solving skills among medical students. In fact, one (30) of these seven studies provided evidence that PBL was not better in this regard compared to simulation-based learning. Two (22, 27) of these seven studies assessed only the knowledge, comprehension, and application domains, as their evaluation of problem-solving and critical thinking abilities was based on student perspectives. Two (21, 26) of these seven studies where the description provided either for case-analysis tests or modified essay questions, did not give an actual indication for measuring higher-thinking skills. Two (25, 28) of these seven studies did not describe their written tests i.e. case-analysis tests and proxy questions that are purported to measure higher-order skills. This prevented the use of the findings from these two studies as evidence to support the specified review question. The remaining study (30) of these seven studies provided evidence that PBL was not better in this regard compared to simulation-based learning. It reported that PBL students' scores in the final assessment did not improve significantly ($p>0.05$) compared to the initial assessment. This insignificant improvement was in a type of performance test on mannequins that required the student to critically assess and manage a life-threatening situation which could implicitly measure critical thinking and problem-solving skills. However, PBL failed to significantly improve the students' scores in the final assessment in this study.

Of the included studies, two studies (24, 31) compared pre and post-test scores to investigate the impact of PBL on medical students' higher-order thinking skills. In the first study, Tayyeb (31) found a statistically significant improvement ($p<0.001$) in post-test scores for PBL students in MCQs testing higher order skills, while the improvement in this aspect was insignificant ($p<0.093$) for LBL students. In the other study, Murat (24) used the PSI, STSQ, and CRS inventories to explore short-term impacts of PBL on learners' problem-solving, scientific thinking as well as conflict resolution abilities. The study consisted of three cohorts; the study group was under PBL instructions, whereas the other two control groups were under traditional lecturing. The study reported that post-test scores in the PSI, STSQ, and CRS were statistically significantly better for students in the PBL group compared to the LBL groups ($P<0.001$ in all inventories).

In addition, Li et al. (23) used written exams, OSCE stations and pupil performance throughout the course of practice to contrast the influence of three forms of PBL instructions i.e. real patients, digital as well as paper, and traditional lecturing on medical students' learning outcomes. In regard to the OSCE part, students were required to assess the patient's condition on the basis of the findings in the dermatological cases offered to them and to provide a thorough management plan. This type of clinical exam is exceedingly related to problem-solving and requires critical thinking aptitudes, and since PBL participants significantly obtained higher scores in this exam, this observation suggests a trend towards the capability of PBL to promote both skills. Moreover, findings from pupil performance throughout the course of practice as assessed by tutors demonstrates that all PBL groups statistically significantly outperformed the traditional group ($P<0.001$) in the majority of items including an item measuring problem-solving skills. Findings from this study are consistent with what Albanese and Mitchell (34) reached in their review, as they found that PBL pupils obtained higher scores than LBL pupils in clinical examinations as well as tutors' evaluations.

The three studies (23, 24, 31) discussed above, can be considered as utilizing a longitudinal, comparative methodological method. Findings from these three studies demonstrated the capability of PBL in improving medical students' problem-solving and critical thinking skills. Nevertheless, the evidence obtained from these three quality studies [(2)] (23, 24, 31) was insufficient to support the capability of PBL in improving critical thinking and problem-solving abilities among medical students. Therefore, further controlled, longitudinal studies are required as evidence to demonstrate the capability of PBL to improve these two skills. These findings from these three studies are consistent with a number of studies from different educational fields suggesting PBL as an efficient approach to foster pupils' problem-solving and critical thinking abilities (35-39).

Physicians in their daily practice ask their patients questions regarding symptoms and complaints in order to reach the accurate diagnosis. In light of this, the more effective the questioning skills, the more physicians get to a precise and timely diagnosis. Substantially, coaching medical students to become effective problem solvers through utilising aimed questions while taking patient-history, is a

**Footnote 2: As assessed by the BEME strength of study findings; two of them were graded as (grade 5), while one was graded as (grade 4).**

significant mission. This is what the study conducted by He et al.(32) relied on to explore the effectiveness of PBL compared to traditional learning in enhancing problem-solving skills for medical students through the strategic utilisation of questions. The study authors used what they called a modified 20-questions task. They found that 63% of PBL pupils solved the task using 8 questions, whereas 48% of LBL pupils solved the task using same number of questions, and that difference was significant ($p<0.05$). Therefore, this study also provided evidence in support of the review question and was graded as grade 4.

Moreover, the findings from the study conducted by Meo (29) were also in support of the specified review question. Meo (29) found that PBL students obtained statistically significantly higher scores ($P=0.001$) than LBL students in MCQs testing level 3,4,5, and 6 of Bloom's taxonomy which definitely includes critical thinking and problem-solving skills. The study also found statistically significantly higher scores ($P=0.0001$) in the OSPE part for PBL students. In the OSPE part, students were required to interpret the respiratory findings, diagnose, and make a differential diagnosis. Such type of practical exam requires higher-order skills including problem-solving and critical thinking, and since PBL students significantly outperformed LBL students in this aspect, this superiority demonstrates the beneficial influence of PBL in improving these two skills.

## Conclusion

There is very little published evidence over the last fifteen years supporting the claim that PBL improves critical thinking and problem-solving skills in medical students. Therefore, recent practice is not based on evidence. As such, investigations are required to legitimise the claims that PBL improves critical thinking and problem-solving skills for medical students. Moreover, further studies of larger samples and higher methodological quality are required to adequately illustrate the impact of PBL pedagogies on critical thinking and problem-solving progression within medical educational context, those that are indeed measuring problem-solving and critical thinking skills of medical students at the beginning and end of a PBL curriculum. Although the evidence from the current systematic review for developing critical thinking and problem-solving skills through a PBL pedagogical approach is insufficient, it does not mean it will not contribute to the development of these two skills.

**Acknowledgments**

First and foremost, praise be to God, who kindly honoured me by completing the last step for my master's degree in medical education. God has inspired me to move forward in this dissertation, despite what the whole world is going through with the Corona pandemic crisis that caused many adverse effects on the level of the individual and society.

I am deeply grateful to my parents, brothers, and sisters, for their support and constant question about my studies. I also offer my special thanks to my wife "Rayah" as her constant support was of great merit in accomplishing this dissertation. My great appreciation to my lovely kids Omar, Jayana, and Hashim, for being in my life is the greatest blessing that God has given me.

I am grateful to my supervisor, Professor Sandra Carr, for her patience, motivation, and constant guidance that has always pushed me into more effort and achievement. I much appreciate her great support for me not only through her supervision of this dissertation, but from the beginning of my studies in the Department of Health Professions Education in the past year.

My thanks and gratitude also go to the librarian, Terena Solomons, who helped me search for articles related to the topic of the dissertation using the Subject Headings.

**Author's contribution**

The author contributed to the data analysis and interpretation. He also contributed to the final draft's critical review and approval. He is also accountable for the manuscript's content and similarity score.

**Funding**

The study has not received funding from any institution.

**Conflict of interest**

The authors declare that there are no conflicts of interests.

**Data and materials availability**

All data sets collected during this study are available upon reasonable request from the corresponding author.

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# Factors Influencing Medical Students and Interns in Choosing a Career in Saudi Arabia. A Cross-Sectional Study

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Received: February 2023 Accepted: March 2023; Published: April 1, 2023.
Citation: Murad Aljiffry .Factors Influencing Medical Students and Interns in Choosing a Career in Saudi Arabia. A Cross-Sectional Study. World Family Medicine. March 2023; 21(3): 85-96 DOI: 10.5742/MEWFM.2023.95256078

## Abstract

Purpose: Medical students are exposed to various specialties during their medical school. There are different factors that play a role that affect their decision to choose a specialty. In our study, we aimed to identify the factors that affect and influence medical students and interns to choose a specialty as their career.

Methods: This is a cross-sectional survey that involved 4th, 5th, and 6th-year medical students and interns from different universities in Saudi Arabia. An online questionnaire was used to collect demographic data, information about the medical school, their preferred specialty, and what are the factors influencing their career choice. Demographics were described as numbers and percentages for categorical variables and mean and standard deviation (SD) for numerical variables. Data analysis was performed using SPSS version (26.0).

Results: A total of 1,178 participants with a mean age 23.1 were included. Among all participants, 40% of them were in their 6th year and the majority (84.1%) were from public medical schools. Among both genders, the most preferred specialty was internal medicine, followed by general surgery. The length of residency training (p=0.005), performing procedures in this specialty (p=0.006), and perceived gender bias in the specialty (<0.001) were factors significantly different between females and males in their career choice during residency. The most important factor related to the residency training that affected the decision among both genders was lifestyle during residency. However, factors related to being a consultant differed among both genders, where 54% of females stated that patients' outcome in the specialty was the extremely important factor, whereas in males, controllable lifestyle was the extremely important factor.

Conclusion: The most commonly chosen specialty was internal medicine, followed by general surgery for both genders. Different factors affected the decision among both genders. More emphasis on career planning is required during medical school to help graduates in choosing the proper specialty for them.

Key words: career choice, medical education, medical school, postgraduate training

## Introduction

The number of medical schools in Saudi Arabia has been increasing in the last decade.

During medical school, medical students rotate through different specialties with most of the time spent in the major core subjects including general surgery, internal medicine, obstetrics and gynecology, and pediatrics. Other subspecialties get less time and attention. Their personal experience during the rotation can affect their career choice. There are different factors that can affect their decision to choose a specialty as a career[1, 2]. Some of the common factors include income, having a controllable lifestyle, and the ability to have direct encounters with patients. On the other hand, others chose surgical specialties due to the surgeon's high prestige, social image and the practical ability to apply their knowledge [3].

Previous studies found that the major reasons for choosing a specialty included primary interest in the specialty [4-6], job satisfaction [4], personality type [7], academic and educational determinants [8], and cultural and social values [4, 9, 10]. Among Saudi students, lifestyle and social characteristics play an upper hand in career choice [11]. In a cross-sectional survey involving medical students and interns at AL Dammam university, the authors reported that students and interns were influenced mainly by the perceived lifestyle of a specific specialty when considering their career choice [9]. Moreover, they also found that internal medicine, family medicine, general surgery, pediatrics, and emergency medicine were the preferred specialties. In our study, we aimed to identify the factors that affect medical students and interns in their decision about career choice across all public and private medical schools in Saudi Arabia.

## Methods

### Study design

We conducted a cross-sectional study involving different universities in Saudi Arabia. The current study was conducted following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cross-sectional studies.

### Setting

The survey was administered online using SurveyMonkey (www.surveymonkey.com). The URL was sent to teaching faculties, interns and medical students in different medical schools in Saudi Arabia via email or phone.

### Survey content

The survey was divided into four sections. The first section contained questions about demographics and general information about the participant. Furthermore, it contained questions about the medical school and their level of training. The second section contained questions about their first and second specialty choices, and factors affecting their decision. The third section contained the factors that influenced or will influence their decision to choose a specialty. The fourth section explored factors that are related to being in a residency and being a consultant and how these factors affected their choice as interns and medical students. A pilot study was performed among medical students and interns to ensure the clarity of the survey.

### Statistical analysis

We analyzed the data using SPSS software for windows version 26.0. Data were presented as numbers and percentages (%) for categorical variables and mean and standard deviation (SD) for numerical variables. We used the Pearson Chi-square test to assess the relationship between categorical variables. The results were considered significant if $p < 0.05$.

## Results

### Baseline Characteristics

The included number of participants was 1,178, with 715 (61%) females. The mean age for all participants was 23.1. Two hundred and four (17.3%) of the participants had one of their parents in the medical field. However, 747(63.5%) of them had a close relative in the medical field. Most participants were single (96.2% of the females and 95.4% of the males). Most of the participants were 6th year students (39.5%), followed by 4th year students (25.3%) and interns (23.7%). A total of 927 (80.7%) belonged to medical schools from the Western Region; 969 (84.1%) were from public schools. Most participants had high GPAs, with 530 (46%) scoring 4.5-5 and 305 (26.5%) scoring 4.1-4.4. Four hundred and eighty-four (43%) hadn't decided yet about the specialty they want to pursue after medical school. 648 (57.9%) of the participants have not taken any electives in the specialty of their first choice, and 681 (62%) have not attended any workshops or lectures about medical career planning, but the majority (89.1%) were planning to take an elective of their first choice. 358 (32.4%) of the participants reported that they were influenced by a mentor during their medical school to choose a specialty, most commonly being influenced by consultants (23.1%), followed by residents (7.3%).

Factors that can help participants to choose a specialty

Eight hundred and forty-eight (80%) of the participants agreed that attending a course about medical career planning would help them to choose a specialty. Nevertheless, six hundred and eighty-two (62%) have never attended any workshop or lectures about medical career planning. Nine hundred and seven participants (77.2%) reported that taking an elective in the specialty they were considering could help them to make a decision about career choice. Furthermore, 725 (61.7%) used the summer vacation to attend an elective in the specialty, and 722 (61.4%) chose to ask residents who are in the specialty they are interested in.

There are different factors that influenced the decision of the participants. 963 (82%) of the participants chose personal interests as the most important factor that influenced or

will influence their decision. Other factors included lifestyle (62.4%), salary (41%), and job availability (40.7%), Tables 1&2., Figure 1. However, when they were asked about the single most important factor that influenced or will influence their decision, 55% chose personal interest.

**Table 1. Baseline characteristics of the included population according to gender-wise distribution**

| Variables | All | Female | Male |
|---|---|---|---|
| **Age*** | 23.15 (1.67) | 23.01 (1.59) | 23.37 (1.76) |
| **Parents education** | | | |
| Medical field | 203 (17.3%) | 109 (15.2%) | 94 (20.5%) |
| Other fields | 970 (82.7%) | 606 (84.8%) | 364 (79.5%) |
| **Relatives education** | | | |
| Medical field | 745 (63.5%) | 447 (62.5%) | 298 (65.1%) |
| Other fields | 428 (36.5%) | 268 (37.5%) | 160 (34.9%) |
| **Marital status** | | | |
| Single | 1127 (95.9%) | 689 (96.2%) | 438 (95.4%) |
| Married | 35 (3%) | 21 (2.9%) | 14 (3.1%) |
| Others | 13 (1.1%) | 6 (0.8%) | 7 (1.5%) |
| **Having children** | | | |
| Yes | 11 (0.9%) | 8 (1.1%) | 3 (0.7%) |
| No | 1163 (99.1%) | 707 (98.9%) | 456 (99.3%) |
| **Level of training** | | | |
| 4th year | 291 (25.3%) | 205 (29.2%) | 86 (19.2%) |
| 5th year | 132 (11.5%) | 76 (10.8%) | 56 (12.5%) |
| 6th year | 454 (39.5%) | 270 (38.5%) | 184 (41%) |
| Intern | 273 (23.7%) | 150 (21.4%) | 123 (27.4%) |
| **Medical school region** | | | |
| Northen Region (Northern borders, Jawf, Hail) | 10 (0.9%) | 7 (1%) | 3 (0.7%) |
| Southern region (Baha, Jizan, Asir, Najran) | 18 (1.6%) | 12 (1.7%) | 6 (1.3%) |
| Central Region (Qassim, Riyadh) | 136 (11.8%) | 45 (6.4%) | 91 (20.2%) |
| Eastern Region (Eastern province) | 58 (5%) | 42 (6%) | 16 (3.6%) |
| Western Region (Tabuk, Madinah almonawara, Makka almokaramah) | 927 (80.7%) | 593 (84.8%) | 334 (74.2%) |
| **Type of medical school** | | | |
| Public | 969 (84.1%) | 590 (84%) | 379 (84.2%) |
| Private | 183 (15.9%) | 112 (16%) | 71 (15.8%) |
| **Last year GPA** | | | |
| 4.5 - 5 | 530 (46%) | 352 (50.1%) | 178 (39.6%) |
| 4.1 - 4.4 | 305 (26.5%) | 183 (26%) | 122 (27.2%) |
| 3.6 - 4.0 | 184 (16%) | 97 (13.8%) | 87 (19.4%) |
| 3.1 - 3.5 | 56 (8%) | 44 (9.8%) | 100 (8.7%) |
| 2.6 - 3.0 | 12 (1.7%) | 12 (2.7%) | 24 (2.1%) |
| 2.1 - 2.5 | 2 (0.3%) | 3 (0.7%) | 5 (0.4%) |
| 2.0 or below | 1 (0.1%) | 3 (0.7%) | 4 (0.3%) |

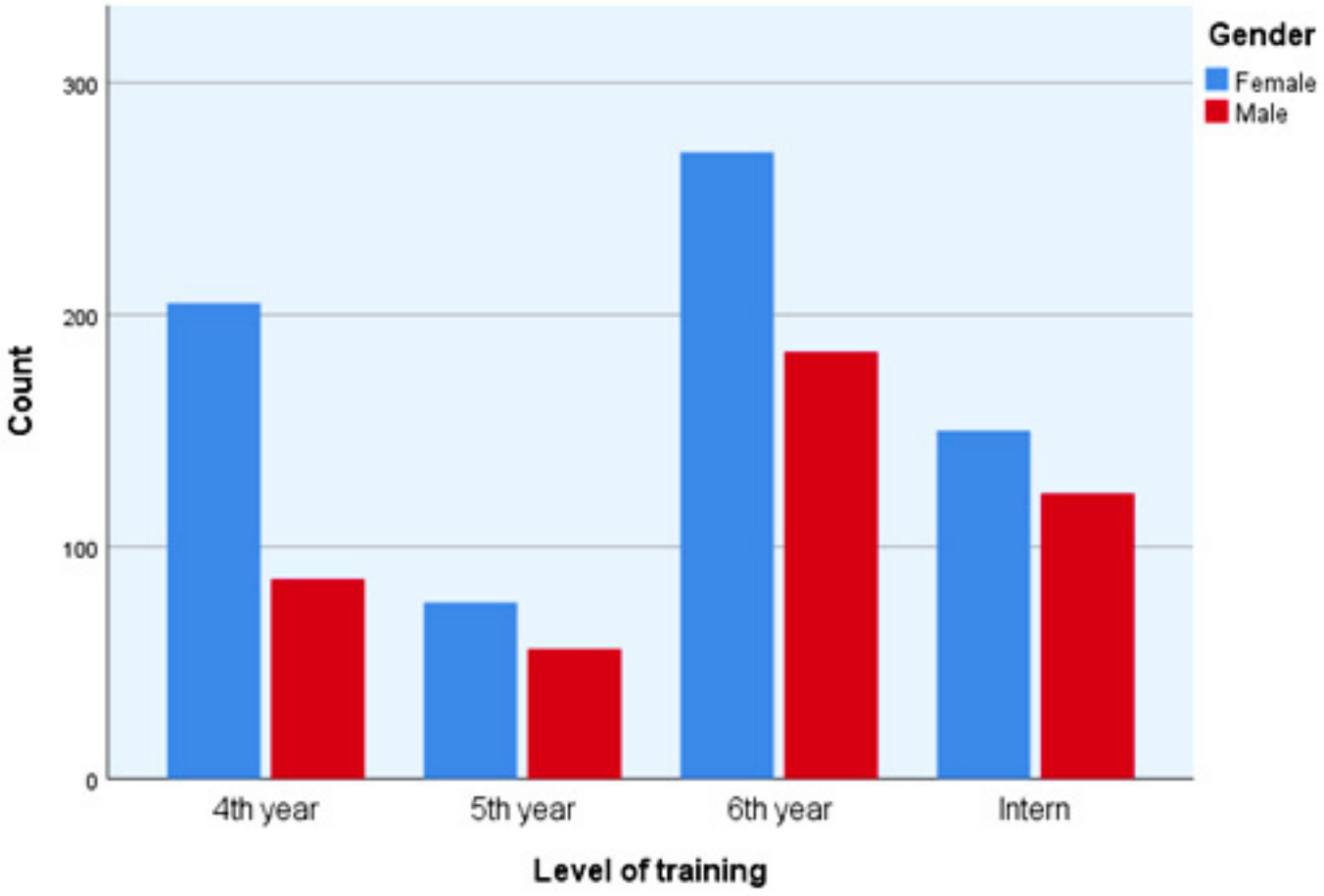
Data are presented as numbers and percentages (%) except * mean (SD)

**Table 2. Gender-wise distribution of the factors affecting carrer choice**

| Variables | Total | Female | Male |
|---|---|---|---|
| **Have you taken any electives in the specialty of your first choice?** | | | |
| Yes | 471 (42.1%) | 290 (42.3%) | 181 (41.8%) |
| No | 648 (57.9%) | 396 (57.7%) | 252 (58.2%) |
| **Who is (are) the mentor(s) who influenced your decision?** | | | |
| Resident | 86 (7.3%) | 53 (7.4%) | 33 (7.2%) |
| Consultant | 271 (23.1%) | 160 (22.3%) | 111 (24.2%) |
| Parent | 32 (2.7%) | 16 (2.2%) | 16 (3.5%) |
| Relative | 47 (4%) | 26 (3.6%) | 21 (4.6%) |
| Others | 28 (2.4%) | 20 (2.8%) | 8 (1.7%) |
| **Have you ever attended any workshops/lectures about medical career planning?** | | | |
| Yes | 418 (38%) | 290 (42.8%) | 128 (30.3%) |
| No | 681 (62%) | 387 (57.2%) | 294 (69.7%) |
| **What do you think will help you to make a decision about your career choice?** | | | |
| Incorporate lectures about career planning into the curriculum | 382 (32.5%) | 219 (30.6%) | 163 (35.5%) |
| Having a mentor to guide you | 687 (58.5%) | 431 (60.2%) | 256 (55.8%) |
| Doing elective(s) in the specialty(ies) you are considering | 907 (77.2%) | 563 (78.6%) | 344 (74.9%) |
| Asking residents about the specialty | 722 (61.4%) | 435 (60.8%) | 287 (62.5%) |
| Asking consultants about the specialty | 580 (49.4%) | 357 (49.9%) | 223 (48.6%) |
| Increase the time spent in the rotation in some of the specialties | 527 (44.9%) | 338 (47.2%) | 189 (41.2%) |
| Using the summer vacation to attend an elective in the specialty you are considering | 725 (61.7%) | 468 (65.4%) | 257 (56%) |
| Other | 35 (3%) | 24 (3.4%) | 11 (2.4%) |
| **What are the factors that influenced or will influence you to decide on the specialty you want?** | | | |
| Personal interest | 963 (82%) | 603 (84.2%) | 360 (78.4%) |
| Influence of a family member | 129 (11%) | 72 (10.1%) | 57 (12.4%) |
| Influence of a mentor or a teaching faculty | 227 (19.3%) | 137 (19.1%) | 90 (19.6%) |
| Lifestyle | 733 (62.4%) | 429 (59.9%) | 304 (66.2%) |
| Salary | 488 (41.5%) | 246 (34.4%) | 242 (52.7%) |
| Job availability | 478 (40.7%) | 271 (37.8%) | 207 (45.1%) |
| Predictability in working hours | 359 (30.6%) | 218 (30.4%) | 141 (30.7%) |
| No emergencies in the specialty | 187 (15.9%) | 110 (15.4%) | 77 (16.8%) |
| Contact with patients | 375 (31.9%) | 239 (33.4%) | 136 (29.6%) |
| Prestige | 155 (13.2%) | 69 (9.6%) | 86 (18.7%) |
| Others | 51 (4.3%) | 34 (4.7%) | 17 (3.7%) |

Data are presented as numbers and percentages (%).

**Figure 1: Level of training and gender distribution among the study population**




**Preferred first and second specialties among participants**

The most preferred first specialty among all participants was internal medicine (18.9%) followed by general surgery (13.4%). Among participants who chose general surgery, (65.3%) were females. Among all participants, one hundred and sixty-nine (15.4%) participants had not decided about their second choice of specialty. However, among participants who had decided, the most common chosen specialty as second choice was also internal medicine (14.6%), followed by surgery (11.9%), (Table 3)., Figure 2 & 3)

**Table 3. First and second specialty of choice among both genders**

| Variables | First choice | | | | Second choice | | | |
|---|---|---|---|---|---|---|---|---|
| | Female | Male | Total | P-value | Female | Male | Total | P-value |
| General Surgery | 98 (14.2%) | 52 (12%) | 150 (13.4%) | | 80 (11.9%) | 51 (12%) | 131 (11.9%) | |
| Internal Medicine | 117 (17%) | 95 (21.9%) | 212 (18.9%) | | 95 (14.1%) | 65 (15.3%) | 160 (14.6%) | |
| Obstetrics and Gynecology | 43 (6.3%) | 12 (2.8%) | 55 (4.9%) | | 38 (5.6%) | 9 (2.1%) | 47 (4.3%) | |
| Pediatrics | 78 (11.3%) | 29 (6.7%) | 107 (9.5%) | | 65 (9.7%) | 23 (5.4%) | 88 (8%) | |
| Ophthalmology | 38 (5.5%) | 24 (5.5%) | 62 (5.5%) | | 26 (3.9%) | 16 (3.8%) | 42 (3.8%) | |
| Radiology | 13 (1.9%) | 20 (4.6%) | 33 (2.9%) | | 27 (4%) | 26 (6.1%) | 53 (4.8%) | |
| Family medicine | 51 (7.4%) | 30 (6.9%) | 81 (7.2%) | | 57 (8.5%) | 53 (12.5%) | 110 (10%) | |
| Pathology | 3 (0.4%) | 4 (0.9%) | 7 (0.6%) | | 1 (0.1%) | 3 (0.7%) | 4 (0.4%) | |
| Orthopedics | 14 (2%) | 25 (5.8%) | 39 (3.5%) | <0.001 | 14 (2.1%) | 23 (5.4%) | 37 (3.4%) | <0.001 |
| Dermatology | 20 (2.9%) | 11 (2.5%) | 31 (2.8%) | | 18 (2.7%) | 6 (1.4%) | 24 (2.2%) | |
| Urology | 3 (0.4%) | 10 (2.3%) | 13 (1.2%) | | 5 (0.7%) | 4 (0.9%) | 9 (0.8%) | |
| Psychiatry | 22 (3.2%) | 13 (3%) | 35 (3.1%) | | 11 (1.6%) | 5 (1.2%) | 16 (1.5%) | |
| Plastics | 9 (1.3%) | 10 (2.3%) | 19 (1.7%) | | 4 (0.6%) | 1 (0.2%) | 5 (0.5%) | |
| Otorhinolaryngology (ENT) | 39 (5.7%) | 22 (5.1%) | 61 (5.4%) | | 35 (5.2%) | 13 (3.1%) | 48 (4.4%) | |
| Pediatric surgery | 15 (2.2%) | 6 (1.4%) | 21 (1.9%) | | 19 (2.8%) | 10 (2.4%) | 29 (2.6%) | |
| Cardiac surgery | 19 (2.8%) | 15 (3.5%) | 34 (3%) | | 24 (3.6%) | 17 (4%) | 41 (3.7%) | |
| Undecided | 59 (8.6%) | 31 (7.2%) | 90 (8%) | | 112 (16.6%) | 57 (13.4%) | 169 (15.4%) | |
| Other | 47 (6.8%) | 24 (5.5%) | 71 (6.3%) | | 42 (6.2%) | 43 (10.1%) | 85 (7.7%) | |

Data are presented as numbers and percentages (%).

The Chi-square test determined significance; if $p<0.05$, the results were considered significant.

**Figure 2: The most frequently preferred first specialty among both genders**

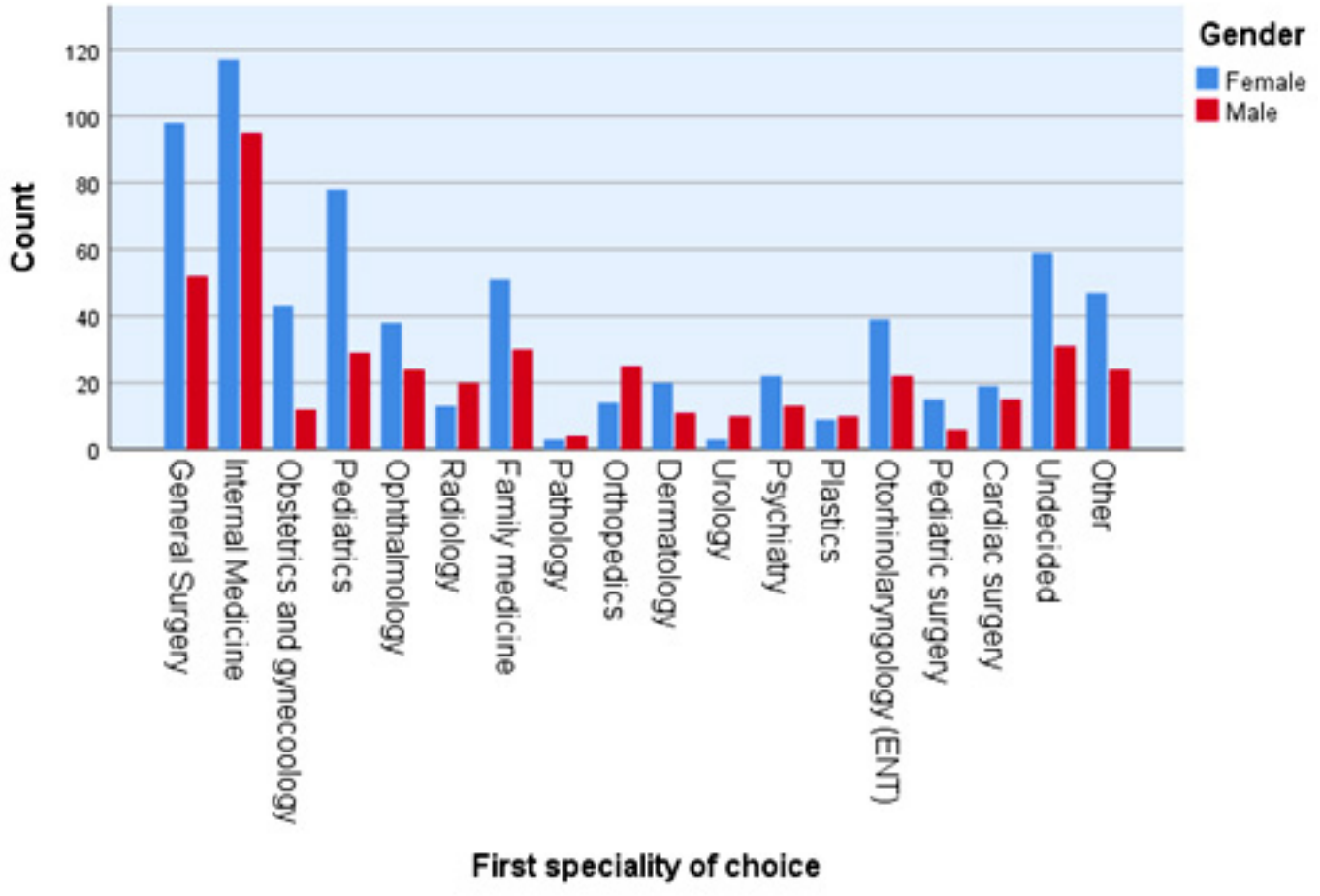
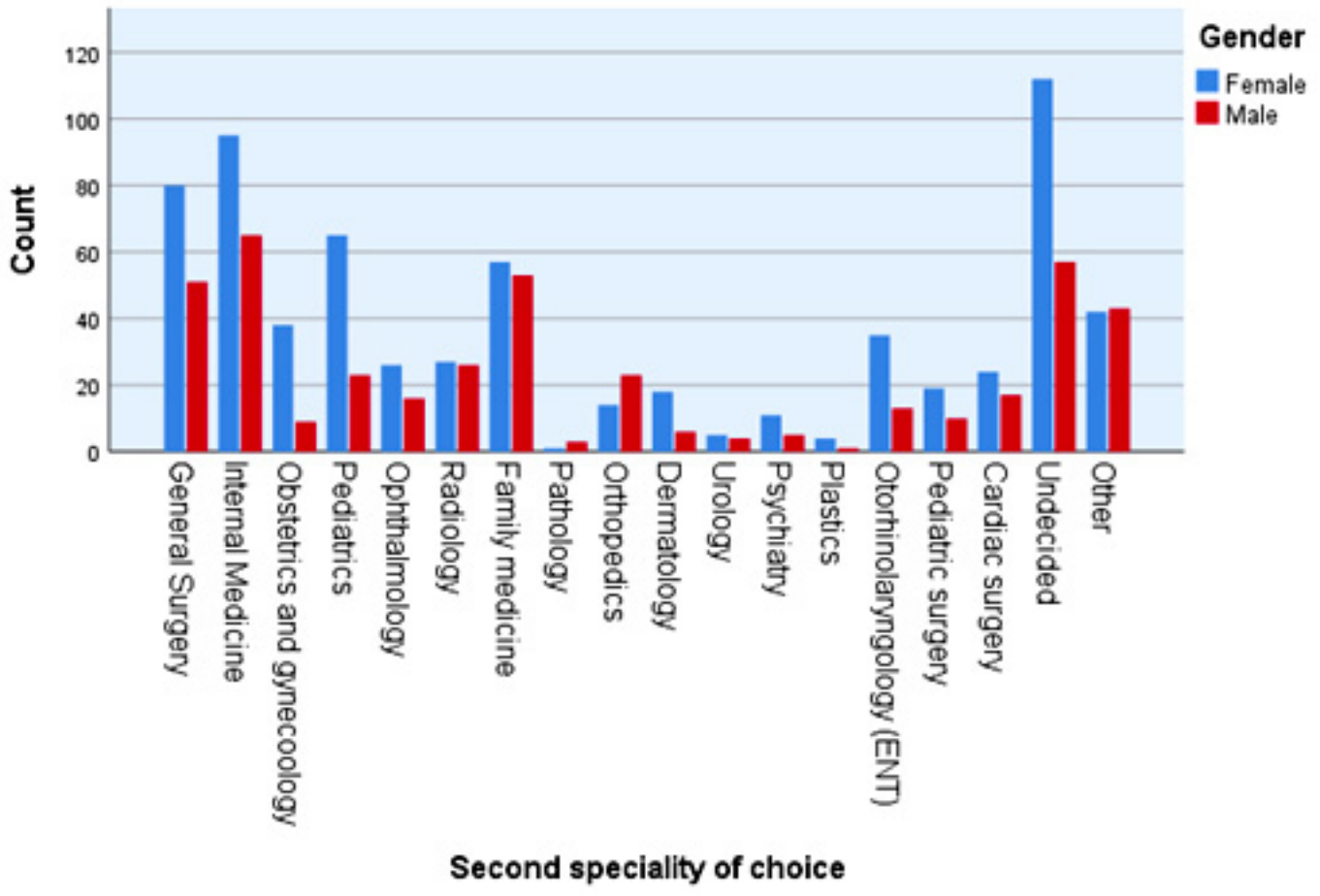



**Figure 3: The most frequently preferred second specialty among both genders**



**Factors Related to Being a Resident That Affected Their Decision to Choose a Specialty**

There were different factors related to the residency training that affected the decision of the participants. Lifestyle during residency was the single extremely important factor among both genders that affected their decision to choose a specialty. Among female participants, performing procedures in the specialty was the second extremely important factor (34.1%). However, in males, choosing a specialty allowing them to have direct contact with patients was the second extremely important factor (32.1%), (Table 4). One of the differences among both genders is the length of residency training, where 18.2% of the females found it an extremely important factor compared to males (12.8%).

**Factors Related to Being a Consultant That Affected Their Decision to Choose a Specialty**

Among both genders, the most extremely important factor related to being a consultant that affected their decision in the future was the type of patient outcomes in the specialty (50.7%). That was followed by a controllable, and predictable lifestyle (47.4%).

Next page (opposite):

**Table 4. Factors related to the residency training that affect the career choice**

(Table 4 continued on page 94)

| Variables | Level of importance | Gender | | P-value | Parents education | | P-value | Marital status | | | P-value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Female | Male | | Medical field | Other fields | | Single | Married | Others | |
| **Length of residency training** | Extremely important | 115 (18.2%) | 51 (12.8%) | | 27 (14.8%) | 139 (16.4%) | | 164 (16.6%) | 1 (3.2%) | 1 (8.3%) | |
| | Very important | 158 (25%) | 129 (32.4%) | | 54 (29.7%) | 233 (27.5%) | | 272 (27.5%) | 11 (35.5%) | 4 (33.3%) | |
| | Neutral | 244 (38.7%) | 129 (32.4%) | 0.21 | 73 (40.1%) | 299 (35.3%) | 0.546 | 352 (35.6%) | 17 (54.8%) | 4 (33.3%) | 0.21 |
| | Not so important | 81 (12.8%) | 58 (14.6%) | | 19 (10.4%) | 121 (14.3%) | | 138 (14%) | 1 (3.2%) | 2 (16.7%) | |
| | Not at all important | 33 (5.2%) | 31 (7.8%) | | 9 (4.9%) | 55 (6.5%) | | 62 (6.3%) | 1 (3.2%) | 1 (8.3%) | |
| **Working hours during residency** | Extremely important | 120 (19%) | 61 (15.3%) | | 32 (17.5%) | 149 (17.6%) | | 172 (17.4%) | 5 (16.1%) | 4 (33.3%) | |
| | Very important | 239 (37.9%) | 160 (40%) | | 69 (37.7%) | 330 (39%) | | 380 (38.4%) | 14 (45.2%) | 5 (41.7%) | |
| | Neutral | 210 (33.3%) | 123 (30.8%) | 0.58 | 62 (33.9%) | 270 (31.9%) | 0.93 | 323 (32.7%) | 10 (32.3%) | 1 (8.3%) | 0.58 |
| | Not so important | 49 (7.8%) | 40 (10%) | | 14 (7.7%) | 76 (9%) | | 86 (8.7%) | 2 (6.5%) | 2 (16.7%) | |
| | Not at all important | 12 (1.9%) | 16 (4%) | | 6 (3.3%) | 22 (2.6%) | | 28 (2.8%) | 0 (0%) | 0 (0%) | |
| **Competitiveness to get into a residency** | Extremely important | 208 (33.1%) | 119 (29.8%) | | 62 (34.1%) | 265 (31.3%) | | 310 (31.4%) | 13 (41.9%) | 4 (33.3%) | |
| | Very important | 232 (36.9%) | 132 (33.1%) | | 62 (34.1%) | 302 (35.7%) | | 352 (35.7%) | 9 (29%) | 4 (33.3%) | |
| | Neutral | 140 (22.3%) | 105 (26.3%) | 0.81 | 46 (25.3%) | 199 (23.5%) | 0.73 | 237 (24%) | 7 (22.6%) | 2 (16.7%) | 0.81 |
| | Not so important | 36 (5.7%) | 33 (8.3%) | | 9 (4.9%) | 60 (7.1%) | | 66 (6.7%) | 2 (6.5%) | 1 (8.3%) | |
| | Not at all important | 13 (2.1%) | 10 (2.5%) | | 3 (1.6%) | 20 (2.4%) | | 22 (2.2%) | 0 (0%) | 1 (8.3%) | |
| **Performing procedures in this specialty** | Extremely important | 215 (34.1%) | 106 (26.6%) | | 55 (30.4%) | 268 (31.6%) | | 316 (32%) | 4 (12.9%) | 3 (25%) | |
| | Very important | 214 (34%) | 136 (34.1%) | | 54 (29.8%) | 296 (34.9%) | | 332 (33.6%) | 14 (45.2%) | 4 (33.3%) | |
| | Neutral | 149 (23.7%) | 103 (25.8%) | 0.33 | 50 (27.6%) | 200 (23.6%) | 0.51 | 239 (24.2%) | 10 (32.3%) | 3 (25%) | 0.33 |
| | Not so important | 37 (5.9%) | 30 (7.5%) | | 15 (8.3%) | 52 (6.1%) | | 64 (6.5%) | 1 (3.2%) | 2 (16.7%) | |
| | Not at all important | 15 (2.4%) | 24 (6%) | | 7 (3.9%) | 32 (3.8%) | | 37 (3.7%) | 2 (6.5%) | 0 (0%) | |
| **Having direct contact with patients (e.g. pathology versus internal medicine)** | Extremely important | 209 (33.1%) | 128 (32.1%) | | 74 (40.7%) | 263 (31%) | | 323 (32.7%) | 11 (35.5%) | 3 (25%) | |
| | Very important | 233 (36.9%) | 133 (33.3%) | | 52 (28.6%) | 315 (37.1%) | | 352 (35.6%) | 10 (32.3%) | 6 (50%) | |
| | Neutral | 130 (20.6%) | 107 (26.8%) | 0.73 | 43 (23.6%) | 193 (22.8%) | 0.06 | 228 (23.1%) | 8 (25.8%) | 1 (8.3%) | 0.73 |
| | Not so important | 43 (6.8%) | 24 (6%) | | 11 (6%) | 56 (6.6%) | | 63 (6.4%) | 2 (6.5%) | 2 (16.7%) | |
| | Not at all important | 16 (2.5%) | 7 (1.8%) | | 2 (1.1%) | 21 (2.5%) | | 23 (2.3%) | 0 (0%) | 0 (0%) | |
| **Type of patients you are going to deal with (pediatrics vs. adults)** | Extremely important | 213 (33.8%) | 120 (30%) | | 60 (33%) | 273 (32.2%) | | 327 (33%) | 4 (12.9%) | 2 (16.7%) | |
| | Very important | 224 (35.5%) | 142 (35.5%) | | 55 (30.2%) | 312 (36.7%) | | 350 (35.4%) | 15 (48.4%) | 3 (25%) | |
| | Neutral | 158 (25%) | 104 (26%) | 0.07 | 53 (29.1%) | 208 (24.5%) | 0.402 | 248 (25.1%) | 9 (29%) | 5 (41.7%) | 0.07 |
| | Not so important | 29 (4.6%) | 20 (5%) | | 11 (6%) | 38 (4.5%) | | 44 (4.4%) | 3 (9.7%) | 2 (16.7%) | |
| | Not at all important | 7 (1.1%) | 14 (3.5%) | | 3 (1.6%) | 18 (2.1%) | | 21 (2.1%) | 0 (0%) | 0 (0%) | |
| **Lifestyle during residency** | Extremely important | 229 (36.5%) | 151 (37.8%) | | 66 (36.5%) | 314 (37.1%) | | 363 (36.8%) | 11 (35.5%) | 6 (50%) | |
| | Very important | 221 (35.2%) | 127 (31.8%) | | 65 (35.9%) | 281 (33.2%) | | 334 (33.8%) | 11 (35.5%) | 3 (25%) | |
| | Neutral | 142 (22.6%) | 89 (22.3%) | 0.97 | 37 (20.4%) | 195 (23%) | 0.92 | 222 (22.5%) | 8 (25.8%) | 2 (16.7%) | 0.97 |
| | Not so important | 30 (4.8%) | 26 (6.5%) | | 11 (6.1%) | 46 (5.4%) | | 55 (5.6%) | 1 (3.2%) | 1 (8.3%) | |
| | Not at all important | 6 (1%) | 7 (1.8%) | | 2 (1.1%) | 11 (1.3%) | | 13 (1.3%) | 0 (0%) | 0 (0%) | |
| **Perceived gender inequality in the specialty** | Extremely important | 104 (16.5%) | 39 (9.8%) | | 28 (15.3%) | 116 (13.7%) | | 139 (14.1%) | 4 (12.9%) | 1 (8.3%) | |
| | Very important | 107 (17%) | 51 (12.8%) | | 22 (12%) | 135 (15.9%) | | 151 (15.3%) | 5 (16.1%) | 2 (16.7%) | |
| | Neutral | 246 (39%) | 182 (45.5%) | 0.55 | 74 (40.4%) | 353 (41.7%) | 0.57 | 405 (41%) | 18 (58.1%) | 5 (41.7%) | 0.55 |
| | Not so important | 98 (15.6%) | 45 (11.3%) | | 26 (14.2%) | 118 (13.9%) | | 140 (14.2%) | 3 (9.7%) | 1 (8.3%) | |
| | Not at all important | 75 (11.9%) | 83 (20.8%) | | 33 (18%) | 125 (14.8%) | | 154 (15.6%) | 1 (3.2%) | 3 (25%) | |

Data are presented as numbers and percentages (%).

| Variables | Level of training | | | | P-value | Type of school | | P-value | Last year GPA | | P-value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 4th | 5th | 6th | Intern | | Public | Private | | >=3 | <3 | |
| Length of residency training | 53 (20.6%) | 16 (13.7%) | 64 (15.6%) | 32 (13%) | | 137 (15.8%) | 29 (17.8%) | | 156 (15.5%) | 9 (34.6%) | |
| | 78 (30.4%) | 37 (31.6%) | 103 (25.2%) | 69 (27.9%) | | 240 (27.6%) | 47 (28.8%) | | 281 (28%) | 6 (23.1%) | |
| | 84 (32.7%) | 40 (34.2%) | 148 (36.2%) | 101 (40.9%) | 0.05 | 304 (35%) | 69 (42.3%) | 0.03 | 366 (36.5%) | 7 (26.9%) | 0.116 |
| | 33 (12.8%) | 18 (15.4%) | 66 (16.1%) | 24 (9.7%) | | 128 (14.7%) | 13 (8%) | | 139 (13.8%) | 2 (7.7%) | |
| | 9 (3.5%) | 6 (5.1%) | 28 (6.8%) | 21 (8.5%) | | 59 (6.8%) | 5 (3.1%) | | 62 (6.2%) | 2 (7.7%) | |
| Working hours during residency | 45 (17.5%) | 17 (14.3%) | 77 (18.9%) | 41 (16.6%) | | 147 (16.9%) | 34 (20.9%) | | 175 (17.4%) | 6 (22.2%) | |
| | 98 (38.1%) | 52 (43.7%) | 146 (35.8%) | 103 (41.7%) | | 339 (39%) | 60 (36.8%) | | 388 (38.6%) | 10 (37%) | |
| | 85 (33.1%) | 40 (33.6%) | 134 (32.8%) | 75 (30.4%) | 0.88 | 281 (32.3%) | 53 (32.5%) | 0.72 | 329 (32.8%) | 5 (18.5%) | 0.24 |
| | 23 (8.9%) | 6 (5%) | 39 (9.6%) | 22 (8.9%) | | 77 (8.9%) | 13 (8%) | | 86 (8.6%) | 4 (14.8%) | |
| | 6 (2.3%) | 4 (3.4%) | 12 (2.9%) | 6 (2.4%) | | 25 (2.9%) | 3 (1.8%) | | 26 (2.6%) | 2 (7.4%) | |
| Competitiveness to get into a residency | 84 (33.1%) | 32 (26.9%) | 145 (35.4%) | 65 (26.4%) | | 282 (32.5%) | 45 (27.8%) | | 314 (31.3%) | 13 (48.1%) | |
| | 88 (34.6%) | 45 (37.8%) | 132 (32.2%) | 100 (40.7%) | | 306 (35.3%) | 59 (36.4%) | | 361 (36%) | 3 (11.1%) | |
| | 56 (22%) | 30 (25.2%) | 101 (24.6%) | 59 (24%) | 0.41 | 199 (22.9%) | 47 (29%) | 0.24 | 238 (23.8%) | 8 (29.6%) | 0.11 |
| | 21 (8.3%) | 10 (8.4%) | 21 (5.1%) | 17 (6.9%) | | 59 (6.8%) | 10 (6.2%) | | 67 (6.7%) | 2 (7.4%) | |
| | 5 (2%) | 2 (1.7%) | 11 (2.7%) | 5 (2%) | | 22 (2.5%) | 1 (0.6%) | | 22 (2.2%) | 1 (3.7%) | |
| Performing procedures in this specialty | 89 (34.8%) | 28 (23.7%) | 123 (30.1%) | 83 (33.6%) | | 275 (31.6%) | 48 (29.6%) | | 315 (31.4%) | 8 (29.6%) | |
| | 94 (36.7%) | 41 (34.7%) | 139 (34%) | 76 (30.8%) | | 298 (34.3%) | 52 (32.1%) | | 344 (34.3%) | 6 (22.2%) | |
| | 57 (22.3%) | 35 (29.7%) | 99 (24.2%) | 60 (24.3%) | 0.11 | 204 (23.5%) | 48 (29.6%) | 0.49 | 244 (24.3%) | 7 (25.9%) | <0.001 |
| | 14 (5.5%) | 10 (8.5%) | 25 (6.1%) | 18 (7.3%) | | 57 (6.6%) | 10 (6.2%) | | 67 (6.7%) | 0 (0%) | |
| | 2 (0.8%) | 4 (3.4%) | 23 (5.6%) | 10 (4%) | | 35 (4%) | 4 (2.5%) | | 33 (3.3%) | 6 (22.2%) | |
| Having direct contact with patients (e.g. pathology versus internal medicine) | 86 (33.6%) | 32 (26.9%) | 130 (31.8%) | 89 (36%) | | 283 (32.6%) | 54 (33.1%) | | 331 (33%) | 6 (22.2%) | |
| | 87 (34%) | 38 (31.9%) | 151 (36.9%) | 91 (36.8%) | | 318 (36.6%) | 50 (30.7%) | | 362 (36.1%) | 5 (18.5%) | |
| | 62 (24.2%) | 31 (26.1%) | 98 (24%) | 46 (18.6%) | 0.29 | 195 (22.4%) | 42 (25.8%) | 0.48 | 224 (22.3%) | 13 (48.1%) | 0.006 |
| | 16 (6.3%) | 14 (11.8%) | 20 (4.9%) | 17 (6.9%) | | 53 (6.1%) | 14 (8.6%) | | 66 (6.6%) | 1 (3.7%) | |
| | 5 (2%) | 4 (3.4%) | 10 (2.4%) | 4 (1.6%) | | 20 (2.3%) | 3 (1.8%) | | 21 (2.1%) | 2 (7.4%) | |
| Type of patients you are going to deal with (pediatrics vs. adults) | 98 (38.3%) | 37 (31.1%) | 130 (31.7%) | 68 (27.5%) | | 284 (32.6%) | 49 (30.1%) | | 323 (32.1%) | 10 (37%) | |
| | 80 (31.3%) | 50 (42%) | 148 (36.1%) | 89 (36%) | | 316 (36.3%) | 52 (31.9%) | | 358 (35.6%) | 9 (33.3%) | |
| | 62 (24.2%) | 28 (23.5%) | 100 (24.4%) | 72 (29.1%) | 0.26 | 209 (24%) | 53 (32.5%) | 0.14 | 256 (25.5%) | 6 (22.2%) | 0.23 |
| | 11 (4.3%) | 2 (1.7%) | 21 (5.1%) | 15 (6.1%) | | 41 (4.7%) | 8 (4.9%) | | 49 (4.9%) | 0 (0%) | |
| | 5 (2%) | 2 (1.7%) | 11 (2.7%) | 3 (1.2%) | | 20 (2.3%) | 1 (0.6%) | | 19 (1.9%) | 2 (7.4%) | |
| Lifestyle during residency | 87 (34%) | 53 (44.9%) | 156 (38.2%) | 83 (33.6%) | | 307 (35.4%) | 73 (45.1%) | | 368 (36.7%) | 12 (44.4%) | |
| | 97 (37.9%) | 33 (28%) | 132 (32.4%) | 86 (34.8%) | | 301 (34.7%) | 47 (29%) | | 341 (34%) | 6 (22.2%) | |
| | 55 (21.5%) | 27 (22.9%) | 89 (21.8%) | 61 (24.7%) | 0.09 | 201 (23.2%) | 31 (19.1%) | 0.16 | 227 (22.7%) | 5 (18.5%) | 0.33 |
| | 15 (5.9%) | 1 (0.8%) | 25 (6.1%) | 16 (6.5%) | | 47 (5.4%) | 10 (6.2%) | | 54 (5.4%) | 3 (11.1%) | |
| | 2 (0.8%) | 4 (3.4%) | 6 (1.5%) | 1 (0.4%) | | 12 (1.4%) | 1 (0.6%) | | 12 (1.2%) | 1 (3.7%) | |
| Perceived gender inequality in the specialty | 42 (16.3%) | 17 (14.3%) | 57 (14%) | 28 (11.3%) | | 121 (13.9%) | 23 (14.2%) | | 137 (13.6%) | 7 (25.9%) | |
| | 47 (18.3%) | 13 (10.9%) | 58 (14.2%) | 39 (15.8%) | | 134 (15.4%) | 24 (14.8%) | | 154 (15.3%) | 3 (11.1%) | |
| | 96 (37.4%) | 57 (47.9%) | 175 (42.9%) | 100 (40.5%) | 0.53 | 360 (41.4%) | 68 (42%) | 0.95 | 418 (41.6%) | 10 (37%) | 0.36 |
| | 37 (14.4%) | 12 (10.1%) | 57 (14%) | 38 (15.4%) | | 124 (14.3%) | 20 (12.3%) | | 142 (14.1%) | 2 (7.4%) | |
| | 35 (13.6%) | 20 (16.8%) | 61 (15%) | 42 (17%) | | 131 (15.1%) | 27 (16.7%) | | 153 (15.2%) | 5 (18.5%) | |

## Discussion

There is a steady increase in the numbers of medical students and interns across all the universities in Saudi Arabia. During the 4th, 5th, and 6th year of medical school, medical students spend their time in different rotations including surgery, internal medicine, Obstetrics and gynecology and pediatrics, with less time spent in other different specialties such as emergency medicine, pathology, anesthesia, and radiology. In this cross-sectional survey that involved medical students and interns across Saudi Arabia, we have found that among all participants, Internal medicine was the most chosen first choice specialty, followed by general surgery. We have found that there are different factors that are related to the residency training, and factors that are related to being a consultant in that specialty that affected the career choice among participants. Interestingly, the most important factor that was related to residency that affected career choice among both genders was lifestyle during residency.

These results showed similarities to what Alshahrani et al. have previously found, as internal medicine, family medicine, general surgery, pediatrics, and emergency medicine were the preferred specialties. On the other hand, unlike this study, they reported that males preferred pediatrics and emergency medicine, while females preferred internal medicine practice[9].

A recent cross-sectional study showed similar results to our study as, for medical students, the most preferred specialty was internal medicine, followed by general surgery. Moreover, males and females preferred internal medicine as their future specialty (16).

From this study and many others, it is obvious that medical students and interns lean toward the common specialties such as general surgery and internal medicine, and the minority are choosing a different less commonly wanted specialty, such as family medicine, pathology, and emergency medicine, which could lead to deficiencies in that field and unmet need in the community. In Saudi Arabia, family medicine has become exceedingly crucial and is rapidly enhancing to deal with the rise in morbidity and mortality from preventable diseases [12]

In our study, only 81 (7.2%) of the participants chose family medicine as their first choice, and 110 (10%) chose it as a second choice. Most likely the reasons for that phenomenon are that a lot of the attention during medical school is focused on a major specialty with less attention and time spent in the other specialties.

In our study, we have found that among both genders, participants considered lifestyle during residency as the most extremely important factor that is related to the residency training that affected their decision. This is similar to what has been previously found as lifestyle being the most influential factor for choosing a specialty [9]. Interestingly, we have found that the most common factor related to being a consultant that affected their career choice was type of patient outcomes, however, that differed across both genders, where males, chose controllable lifestyle (50.3%) as the extremely important factor followed by patient outcomes in the specialty (45.4%). That was different from Alsubaie et al. who found that the three main influences in choosing a specialty are specialty interest (86.5%), specialty flexibility (64.3%), and anticipated income (61.9%) [13]. Another study found that the important reasons for selecting the specialties included the presence of interesting cases, controllable lifestyle, and impact of the specialty on patient quality of life [14].

The positive impact of mentors on specialty choice was previously described in medical education [5, 15, 16]. Additionally, a clinical role model can negatively affect the students, driving them away from certain specialties [17]. In a recent study among medical students, they showed that cardiothoracic surgery is lagging behind the other specialties, where only 4.5% of that cohort chose that specialty. They suggested that a mentorship program could help with improving the knowledge about the specialty. This study is from the initial studies in Saudi Arabia that examined the career choice among both medical students and interns across Saudi Arabia in both private and public medical schools. Our study had some limitations, including the limitations associated with the cross-sectional design of the study. Furthermore, the number of participants from the other regions in Saudi Arabia was low.

## Conclusion

Career courses, and mentorship is needed to be part of the medical school curriculum to help medical students and interns to make an educated and well-informed choice about their career. In addition, more emphasis is needed on the less popular specialties among medical students in order to meet the workforce demands.

**Declarations**

Ethics approval and consent to participate
Ethical approval of the study was obtained from King Abdul-Aziz University, Faculty of Medicine, Research Ethics Committee. All study methods were ethically justifiable. On the first page of the online form, participants gave informed consent to fill out the questionnaire for research.

The authors declare no competing interests.

**Funding**
This study received no funding.

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# The Role of Ultrasound in Thyroid Assessment

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Received: February 2023 Accepted: March 2023; Published: April 1, 2023.
Citation: Yusuf Bakkar, Rana Bakkar. The Role of Ultrasound in Thyroid Assessment World Family Medicine. March 2023; 21(3): 97-106 DOI: 10.5742/MEWFM.2023.95256079

## Abstract

The recent prevalence of ultrasonography (US) has facilitated the early detection and qualitative evaluation of thyroid nodules. Furthermore, novel technical developments are extending the application range of US for other thyroid diseases.

The use of US to differentiate between thyroid carcinoma and benign nodule, between a metastatic lymph node and a reactive node, between thyroid lymphoma and chronic thyroiditis, and between destruction-induced thyrotoxicosis and Graves' disease is introduced.

Classification systems for thyroid nodule have shown high diagnostic accuracy for thyroid carcinomas except follicular carcinoma. US diagnosis of lymph node metastasis showed high specificity but low sensitivity. Patients who were suspected of thyroid lymphoma based on US findings should undergo incisional biopsy or thyroidectomy for diagnosis of the histologic type if fine needle aspiration biopsy findings suggest lymphoma. Patients should be carefully followed even if they were diagnosed as negative based on cytologic findings. Measurement of thyroid blood flow is helpful for diagnosing destruction-induced thyrotoxicosis, such as painless thyroiditis, by distinguishing the lesion from Graves' disease.

Ultrasonography is useful for diagnosing various thyroid diseases, including thyroid carcinoma. The remaining issue to be resolved is the diagnosis of follicular carcinoma. Trials using novel techniques to differentiate these lesions are expected.

Key words: ultrasound, thyroid assessment

## Introduction

The thyroid gland can be evaluated using several imaging modalities such as radionuclide imaging, ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI). Although each study has advantages and drawbacks, US is the most useful tool for detecting and diagnosing thyroid diseases, especially thyroid nodules. This is because US not only detects the nodules but also allows qualitative evaluation of these lesions. The recent prevalence and technical developments of US have resulted in its increased use for mass screening of the thyroid and carotid artery and have facilitated the incidental detection of nonpalpable thyroid nodules measuring > 3 mm. Using a combination of US and US-guided fine needle aspiration biopsy (FNAB), these nodules can be differentiated as benign or malignant [1].

Apart from the diagnosis of thyroid nodules, US is useful for the qualitative diagnosis of regional lymph nodes, which is important for determining the extension of lymph node dissection and evaluating the biologic behavior, including prognosis, of thyroid carcinoma patients. Furthermore, US can facilitate the differential diagnosis between thyroid lymphoma and chronic thyroiditis and between destruction-induced thyrotoxicosis, such as painless thyroiditis, and Graves' thyrotoxicosis. In this review, we introduce the utility of thyroid US based on data from our institution together with data from other institutions.

Since the late 1990s, several studies have been conducted to analyze the relation between specific sonographic features of thyroid nodules and malignancy [64, 65-66]. Although guidelines have been established, such as those of the Society of Radiologists in Ultrasound, the American Thyroid Association, and the European Thyroid Association [64, 67-68], they are commonly confusing and at times ignored in everyday practice, largely because of lack of familiarity with, and trust in, their validity. Common in the studies is a persistent limitation of specificity and sensitivity of specific ultrasound features in the prediction of malignancy. Some authors [69, 70] advocate a changed approach of recognition of specific patterns rather than individual ultrasound features in separation of nodules that require biopsy from those that do not. The purpose of our study was to evaluate the accuracy of such a morphologic feature-oriented approach to the identification of benign thyroid nodules.

## Diagnosis of thyroid nodules

A thyroid nodule is a discrete lesion, sonographically distinct from the surrounding thyroid parenchyma [71]. Rather than a single disease, nodules are manifestations of a gamut of thyroid diseases [72]. Although some thyroid nodules may be discovered at physical examination, many are incidental findings of other imaging studies, such as CT and MRI of the neck or chest and carotid ultrasound imaging. FNA of thyroid nodules has replaced blind surgical excision as the procedure of choice in the diagnosis of thyroid nodules. Use of FNA has led to a considerable decrease in the number of surgical excisions and to a twofold increase in the diagnosis of carcinoma [73, 74, 75]. The relative ease of FNA compared with surgery and the increased frequency and refinement of imaging studies has resulted in what some authors have referred to as an epidemic of thyroid nodules [76, 77].

In view of their ubiquity, it is not feasible to biopsy every thyroid nodule discovered with ultrasound. Reasons for limiting thyroid biopsy, which is relatively painless and safe, include the small percentage of malignant lesions, the small number of cases of thyroid cancer in which early diagnosis may actually have an influence, the economic and societal costs, the strain on radiology resources, and the patient uncertainty and anxiety incumbent on a potentially malignant diagnosis. Hence, reliable guidelines for nodules that may not require biopsy have become essential.

Not surprisingly in view of the experience of other authors [78], we concluded that no individual sonographic feature had both high sensitivity and high specificity in the detection of malignancy. Nonetheless, many of these previously described high-risk features, such as calcification, hypoechogenicity, poor definition, and hypervascularity, were found to be absent over and over again in nodules that did not require biopsy.

The persistent combination of some of these common individual ultrasound characteristics, or, more properly, their absence, led us to consider a more pattern-oriented approach, such as that advocated by Reading et al. [69] as an alternative to the analysis of individual features. Those authors described eight typical appearances of commonly encountered benign and malignant nodules, allowing them to separate more than one half of thyroid nodules into those that could be observed versus those requiring biopsy. According to their results, the following four classic patterns necessitate biopsy: 1, a hypoechoic nodule with microcalcifications; 2, coarse calcifications in a hypoechoic nodule; 3, well-marginated, ovoid, solid nodules with a thin hypoechoic halo; and 4, a solid mass with refractive shadowing from the edges, which is believed to occur as a result of fibrosis. The four classic patterns of nodules that did not require biopsy in that series were the following: 1, small (< 1 cm) colloid-filled cystic nodules; 2, a nodule with a honeycomb appearance consisting of internal cystic spaces with thin echogenic walls; 3, a large predominantly cystic nodule; and 4, diffuse multiple small hypoechoic nodules with intervening echogenic bands, which are indicative of Hashimoto's thyroiditis.

Like Reading et al. [69], we found that use of a pattern approach to thyroid nodules is highly sensitive and specific for the presence of benignity. Our patterns differed somewhat from those proposed previously, yet there are definite similarities. Analysis of our data revealed four patterns that were invariably benign at FNA biopsy. The most common overall pattern is a nodule with diffuse internal linear cysts, described as spongiform or

honeycomb, our type 1 pattern. In our cases, this finding was commonly described as a “puff pastry” pattern. This pattern was characteristic of colloid nodules or goiter. The only spongiform nodule not classically benign was a single nodule that also was intensely hypervascular. Our type 1 or spongiform nodule consequently is defined as avascular or, occasionally, isovascular in relation to the rest of the gland.

The second pattern (type 2) was a cystic nodule containing a central plug of avascular colloid, similar to the previously described small or large cyst patterns [69]. In our initial analysis of individual features, size of cyst was deemed insignificant. Important, however, was the characterization of the plug as avascular and puff pastry. All of these nodules were also colloid nodules. If the cystic portion of the lesion is subtracted visually, a type 1 spongiform nodule remains. The third pattern (type 3), or giraffe pattern, was characterized by globular areas of hyperechogenicity surrounded by linear thin areas of hypoechogenicity, similar to the two-tone blocklike coloring of a giraffe. This pattern was quite characteristic of Hashimoto’s thyroiditis. A variation of this pattern is our type 4 “white knight,” or hyperechoic, nodule, which was found commonly to be a regenerative nodule of Hashimoto’s thyroiditis.

Analysis of these patterns revealed more variability in final cytologic findings. Such nodules included both insignificant and significant lesions with such variability that prediction before biopsy was not reliable. These nodules had the four biopsy-recommendation patterns described earlier, such as isoechoic nodule with a surrounding halo or refractive edges, which came to be simplified as isoechoic nodules with or without a halo (types 7 and 8). A hypoechoic nodule with or without central microcalcification or with central macrocalcification in other series [79, 80, 81], for which biopsy was recommended, was the most worrisome pattern (type 6) in our study.

We identified other common patterns, including the type 5 “red light” pattern, or an intensely hypervascular lesion that on Doppler images glowed like a red stoplight. This pattern was commonly seen in lesions with abundant cellularity, including, commonly, follicular neoplasms and, less commonly, hyperplastic nodules and carcinoma. Other nodule types included type 9 ring-of-fire nodules with intense peripheral vascularity and nodules described as other (type 10), which did not fit any of the classic patterns. Calcification, although commonly seen in nodules requiring biopsy, was never seen as an isolated finding. The likelihood of benignity of these nodules (type 5-10) ranged from 60% (type 9, ring of fire) to 91% (type 10, other). Because of this lack of predictability, we believed that these nodules should be considered for FNA biopsy.
A prominent application of US is detection of thyroid nodules and the differential diagnosis between thyroid carcinoma, especially papillary carcinoma, and a benign nodule [2–6]. To date, several US features (e.g., microcalcifications, hypo echogenicity, irregular margins, halo signs) have been identified as indicating papillary carcinoma. In Japan, a multicenter study showed that a jagged border, irregular shape, and hypoechoic internal echo level are important characteristics for diagnosing papillary carcinoma [7].

To diagnose thyroid nodules accurately and immediately during mass US screening, a report along with scoring or categorization using a classification system is rational. Recently, classification systems for the diagnosis of thyroid nodules have been proposed.

Tae et al. [8] classified thyroid nodules into three categories based on their having one or more of four features: nodules with microcalcifications, an irregular or microlobulated margin, marked hypoechogenicity, and a shape that is taller than it is wide are classified as category 3 (malignant); nodules that show an absence of all of these features are classified as category 2 (benign); and anechogenic cystic nodules are classified as category 1 (benign). The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 87%, 87%, 48%, and 98%, respectively, by comparing their findings with cytologic results.

In 2009, Horvath et al. [9] proposed the thyroid imaging reporting and data system (TIRADS). They established six categories (TIRADS 1 to TIRADS 6) based on US patterns and estimated the incidence of malignancy for each TIRADS class: 0% for TIRADS 1 and 2;\5% for TIRADS 3; 5–10% for TIRADS 4A; 10–80% for TIRADS 4B; [80% for TIRADS 5; and 100% for TIRADS 6. They diagnosed nodules with TIRADS 4 or greater as suspected of malignancy; they compared their classification results and FNAB findings and showed that the sensitivity, specificity, PPV, and NPV were 88, 49, 49, and 88%, respectively. In both studies, follicular lesions according to FNAB findings were classified as suspicious of malignancy.

We routinely evaluate nodules according to this system to diagnose the lesions as benign or malignant [10, 11]. The classification consists of five grades from US classes (USCs) 1 to 5 as summarized in Table 1.

Typical US profiles of each class are as follows: cyst for USC1; adenomatous nodule or, if multiple, multinodular goiter for USC2; follicular neoplasm (including minimally invasive follicular carcinoma) for USC3; thyroid carcinoma (papillary carcinoma, widely invasive follicular carcinoma, medullary carcinoma, and anaplastic carcinoma) for USCs 4 and 5. Furthermore, we set intermediate classes from USC 2 to USC 5—designated USCs 2.5, 3.5, and 4.5. Nodules showing cystic change but having a partially irregular shape and/or showing strong echoes and solid nodules with an irregular shape are classified as USC 2.5 and 3.5, respectively. A solid, irregularly shaped nodule showing minor extrathyroid extension is classified as USC 4.5. Nodules classified as USC 2.5 or lower are evaluated as benign nodules; those with USC 3 are evaluated as follicular neoplasms, including minimally invasive follicular carcinoma; and those considered USC 3.5 or greater are diagnosed as, or suspected of, thyroid carcinoma.

**Table 1: US classification for thyroid nodules at Kuma Hospital**

| USC | Diagnosis |
|---|---|
| Round or oval anechoic lesion | Cyst |
| Regularly shaped nodule with cystic change (echo level of a solid lesion is similar to that of normal thyroid) | Adenomatous nodule<br>Multinodular goiter |
| Solid, regularly shaped nodule (internal echo is homogeneous or may have strong echoes internally or at the capsule) | Follicular adenoma<br>Minimally invasive follicular carcinoma |
| Solid, irregularly shaped nodule (internal echo is usually low and may have fine strong echoes internally) | Thyroid carcinoma |
| Solid, irregularly shaped nodule with extrathyroid extension | Thyroid carcinoma |

When nodules are diagnosed as carcinoma on US and FNAB, the evaluation of their location is important. When carcinoma is located in the dorsal surface of the thyroid, it may extend to the adjacent organs—recurrent laryngeal nerve, trachea, esophagus—and require resection of these organs to achieve curative surgery. US can provide information to surgeons indicating whether a carcinoma carries a risk of extending to other organs. Tomoda et al. [12] investigated the diagnostic accuracy of US regarding tracheal invasion by papillary carcinoma and showed that the sensitivity, specificity, PPV, and NPV were 91, 93, 25, and 99%, respectively. However, such findings cannot be evaluated for tumors having severe calcifications, large size, or extension inferior to the clavicle. In their series, 32 of 509 patients (6%) could not be evaluated. Other imaging studies such as CT and MRI can be useful for evaluating such tumors.

One important issue that physicians must consider is the management of small carcinomas detectable on US, most of which are papillary carcinoma measuring < 1 cm (papillary microcarcinoma, or PMC). The incidence of PMC classified into USC 3.5 or greater does not differ from that of larger carcinomas [11], indicating that it is not difficult to detect and diagnose PMC on US and US-guided FNAB. However, we must note that there has been a high incidence of microcarcinomas detected in some autopsy studies [13–15], and thyroid carcinomas (mostly < 1.5 cm) have been found in as many as 3.5% of otherwise healthy women over 30 years of age during US mass screening and FNAB [16]. These findings definitely indicate that most low-risk PMCs lacking clinically apparent nodal and/or distant metastases and massive extension to adjacent organs are not harmful to patients throughout their lives. Thus, we must carefully consider whether "early detection" of such small carcinomas and performing thyroidectomy routinely for them are truly beneficial for patients. In our institution since 1993, we have used observation alone for low-risk PMCs without immediate surgical treatment, with the result that only 6.7% of patients showed tumor enlargement after a 5-year follow up, and none of the patients showed distant metastasis or died of carcinoma during the observation [17–19]. It is suggested that routine surgical treatment for PMC forces unnecessary therapy on most PMC patients. Indeed, this is a pitfall of the technical development of imaging studies, and we propose observation without immediate surgical treatment for low-risk PMC as an alternative to initial treatment.

It is difficult to determine whether a nodule that has US features indicating a follicular tumor (USC 3 in our classification system) is follicular carcinoma or benign adenoma, which is a limitation of routine US [20, 21]. To date, several clinicopathologic features—tumor size, patient's sex, patient's age, indeterminate cytology, serum thyroglobulin level—have been reported as risk factors for follicular carcinoma [22, 23]. However, if more accurate evaluation on imaging studies becomes possible, the indications for surgery for such nodules could be narrowed.

Fukunari et al. [24] proposed a diagnostic grading system based on the findings of B-mode US and color Doppler findings, including tumor vascularity and blood flow analysis objectively indicated as the pulsatility index (PI). They reported favorable results of their examination, with the sensitivity 89% and the specificity 74%. Furthermore, real-time tissue elastography (RTE) may provide novel information for diagnosis of follicular carcinoma. Fukunari [25] reported that the sensitivity and specificity of RTE for follicular carcinoma were 83% and 98%, respectively. Also, Rogo et al. [26] demonstrated that RTE is a useful tool for diagnosing thyroid carcinoma, especially nodules with indeterminate cytology. Further studies for these new techniques by a number of institutions are desired to improve the diagnostic accuracy of follicular carcinoma on US.

## Diagnosis of lymph node metastasis

Three prominent compartments of regional lymph nodes are affected by thyroid carcinoma: the central, lateral and mediastinal compartments. US is the most useful tool for evaluating lymph node metastasis except for that in the mediastinal compartment [27, 28]. Preoperative evaluation of lymph node metastasis of thyroid carcinoma is important because it determines the extent of lymph node dissection and predicts patient outcomes. We previously showed that metastasis in the lateral compartment detectable on US (N1b) is an independent prognostic factor for

disease-free survival (DFS) and cancer-specific survival (CSS) on multivariate analysis [29, 30]. Furthermore, a study of a subset of N1b patients showed that those having five or more clinically apparent metastases, a metastasis> 3 cm, or extranodal tumor extension showed a more adverse prognosis than those having none of these features [31]. Of these three features, the former two can be preoperatively evaluated on US. Therefore, evaluation of metastasis, especially in the lateral compartment, on US is essential to determine if the surgeon should perform lateral compartment dissection (modified radical neck dissection, or MND) and to predict the clinical outcomes of patients.

To date, several US features—large size, round shape, hypoechoic structure, loss of hilar architecture, hyperechoic punctuations, microcalcifications, cystic appearance—have been proposed by various institutions [32–36]. In 1995, Antonelli et al. [37] proposed US criteria for lymph node metastasis: size larger than 1 cm; clear hypoechoic pattern or dyshomogeneous pattern, with alternating hypoechoic and hyperechoic areas; irregular cystic appearance; the presence of internal calcification; and rounded or bulging shape with an increased anteroposterior diameter. These criteria have been widely accepted, although our institution has not adopted lymph node size as a criterion.

The diagnostic accuracy of an US diagnosis of node metastasis is, however, not very high because the high specificity is offset by low sensitivity. Leboulleux et al. [38] compared various features of lymph nodes and pathologic diagnoses for 56 nodes in 19 patients and demonstrated that cystic appearance, hyperechogenic punctuations, and peripheral vascularization are useful criteria for node metastasis because their specificities are high, at 100, 100, and 82%, respectively. However, the sensitivities of the former two are low, at 11 and 46%, respectively. The sensitivity of peripheral vascularization was high at 86%, although the number of patients examined was small.

We also investigated the diagnostic accuracy of US for lateral node metastasis using a series of 3,974 patients who underwent therapeutic or prophylactic MND [31]. Although the specificity and PPV were high, at 97 and 95%, respectively, the sensitivity and NPV were low, at 30 and 43%, respectively. We have adopted FNAB for nodes suspected of metastasis along with the measurement of thyroglobulin levels in the washout of needles used for FNAB to confirm the diagnosis of metastasis [39]. It is useful to increase the specificity and PPV, but it does not improve sensitivity or NPV.

Kim et al. [40] showed that for preoperative detection of lateral node metastasis the combination of US and CT is more accurate than US alone, but the tendency toward high specificity and low sensitivity was not changed. As for metastasis to the central node, sensitivity and NPV were even worse, at only 12 and 37%, respectively [31]. This is probably because detection of lymph nodes is made difficult by the air-filled trachea and the thyroid itself.

The above findings indicate that US rather frequently overlooks lymph node metastasis in the central and lateral compartments and that there are many false-negative results in cases diagnosed as negative for node metastasis on US. These pitfalls distress surgeons trying to decide on the extent of lymph node dissection. Compartments showing clinically apparent metastasis definitely should be therapeutically dissected, but the indication for prophylactic dissection remains controversial. Dissection of the central compartment does not require wound extension and can be performed within the same surgical field as thyroidectomy. In addition, the diagnostic accuracy of central compartment metastasis on US is low and reoperation for recurrence to this compartment often causes recurrent laryngeal nerve injury and permanent hypoparathyroidism [41, 42].

In contrast, MND requires wound extension, is time-consuming and technically difficult, and increases patients' complaints, although some of these concerns can be compensated by the skill of the surgeon. Prophylactic MND is recommended for patients exhibiting a high incidence of recurrence to the nodes. The indication for prophylactic MND is affected by the incidence of nodal recurrence rates that patients and physicians can accept. Our department recommends prophylactic MND for patients having two or more of the following characteristics—male sex, > 55 years of age, tumor > 3 cm, and massive extra thyroid extension—because the 10-year lymph node DFS of those patients was < 90%; that is, lymph node recurrence rates were more than 10%, even though the patients underwent prophylactic MND [29]. Sugitani et al. [43] proposed that prophylactic MND is indicated for patients with a tumor >4 cm or metastasis to distant organs at surgery.

## Diagnosis of malignant lymphoma of the thyroid

Malignant lymphoma of the thyroid accounts for 2–5% of all thyroid malignancies and usually arises from chronic thyroiditis [44–47]. This disease can usually be diagnosed on FNAB; to confirm the histologic type, surgical examination such as open biopsy or thyroidectomy is useful [48].

Furthermore, investigations for rearrangement of the IgH gene, CD45 gating, and chromosomal abnormality are helpful for diagnosis [49]. The prognosis of thyroid lymphoma is generally favorable if treated competently [50–53], but it can suddenly enlarge, causing life-threatening asphyxia. Therefore, early detection and diagnosis are mandatory to initiate appropriate therapy during an early phase of the disease.

For early detection of thyroid lymphoma, a differential diagnosis between thyroid lymphoma and severe chronic thyroiditis is essential; and US is an extremely useful tool for this purpose. There are three US-detected patterns of thyroid lymphoma: nodular, diffuse and mixed [54]. The nodular type displays hypoechoic, homogeneous internal echoes with a well-defined border showing a broccoli-like or coastline-like growth pattern. Posterior echoes are broadly

**Table 2: Ultrasonographic classification of thyroid lymphoma**

| Ultrasonographic classification of thyroid lymphoma | | | |
|---|---|---|---|
| **Type** | **Internal echoes** | **Border** | **Posterior echoes** |
| Nodular | Hypoechoic and homogeneous nodular lesions | Broccoli-like Coastline-like | Enhanced |
| Diffuse | Internal echoes | - | Enhanced |
| Mixed | Internal echoes | - | Enhanced |

enhanced. The diffuse type also displays hypoechoic internal echoes, but the border between the lymphoma and nonlymphomatous tissue is not clear. Therefore, it is difficult to differentiate diffuse-type lymphoma and severe chronic thyroiditis, although enhanced posterior echoes are useful for diagnosing lymphoma of this type. Patchy hypoechoic lesions can be observed in the thyroid in mixed-type lymphoma. The US profile of mixed-type lymphoma often resembles multinodular goiter, but each lymphoma lesion shows enhanced posterior echoes. The US classification of these three types is summarized in Table 2. Enhanced posterior echoes are typical findings of thyroid lymphoma regardless of type, and lesions having this feature should be suspected of being a thyroid lymphoma, in which case further analyses such as FNAB are recommended.

In Kuma hospital, among 170 patients suspected of having a thyroid lymphoma based on US findings between 2000 and 2004, a total of 74 (43.5%) were diagnosed as having or suspected of having lymphoma on FNAB [53]. In all, 69 of these patients underwent incisional biopsy or thyroidectomy, and 67 were diagnosed as having lymphoma on the pathology examination. Of 96 patients who were not cytologically diagnosed as having or suspected of having lymphoma, 20 underwent a surgical procedure because lymphoma was suspected by the attending physicians. Of these 20 patients, 12 were diagnosed pathologically as having lymphoma. In total, 79 of 170 patients (46.5%) were confirmed as having lymphoma on the pathology examination.

The number of patients diagnosed as having lymphoma is increasing because only 116 patients were treated with lymphoma between 1963 and 1990 in our institution [48]. This is definitely because the resolution power of US has enabled the detection of lymphoma in an early phase. In a series between 1963 and 1990, a total of 78% of patients complained of rapid enlargement of a goiter, but only 22% of patients in a series between 2000 and 2004 showed rapid goiter enlargement [54]. US-guided FNAB is the next step for diagnosing thyroid lymphoma. In our department, the PPV for FNAB is 97.1%, indicating that cytologic examination after candidates for FNAB are selected based on US findings contributed markedly to the diagnosis of lymphoma. However, at least 12.5% of patients (12/96 patients) were misdiagnosed on FNAB, indicating that all patients suspected of lymphoma on US should be followed carefully, even though the FNAB diagnosis is negative. We encountered a patient who exhibited a serial change from chronic thyroiditis to lymphoma over an interval of at least 7 years [55].

Surgical examination is also important for establishing the final diagnosis and confirming the histologic type to facilitate any decisions on therapy, such as irradiation only or irradiation with systemic chemotherapy. In the past, incisional or core needle biopsy was performed in most patients, but at present the incidence of thyroidectomy (e.g., lobectomy, total thyroidectomy) has increased significantly. Indeed, in our series between 2000 and 2004, a total of 65% of patients underwent thyroidectomy [54]. As indicated above, the incidence of early detection of lymphoma is increasing, and most patients show a low level of malignancy. For such cases, biopsy from the surface of the thyroid only causes misdiagnosis, and thyroidectomy should be actively performed to achieve an accurate diagnosis, which might also have therapeutic value.

## Differential diagnosis between painless thyroiditis and Graves' disease

Thyrotoxicosis in patients without hyperfunctioning nodules is due to destruction-induced thyrotoxicosis and Graves' disease. Destruction-induced thyrotoxicosis may be observed in patients with painless thyroiditis, postpartum thyroiditis, and/or subacute thyroiditis [56]. It is often difficult to differentiate between painless thyroiditis and Graves' disease. There are several strategies to differentiate these diseases, among which are radioactive iodine uptake (RAIU) and the detection of anti-thyroid-stimulating hormone (TSH) receptor antibodies (TSH binding inhibitory immunoglobulin, or TBII). During the early postpartum period, destruction-induced thyrotoxicosis is more likely to occur than Graves' disease, although Amino et al. [57] showed that Graves' thyrotoxicosis may also occur 3–6 months postpartum. RAIU cannot be performed when patients are lactating; and not all clinics are equipped for this examination. TBII is, indeed, a useful marker of Graves' thyrotoxicosis because it is positive in 99–100% of patients [58, 59]. However, TBII was also positive in 6–15% of patients with painless thyroiditis, indicating that TBII is not always reliable for differentiating these two diseases [60–62].

Recently, measurement of thyroid blood flow (TBF) was reported to be another useful strategy for differentiating painless thyroiditis from Graves' disease [63]. The quantification of TBF can be expressed in a percentage

as an advanced dynamic flow/region of interest (ADF/ROI) ratio by special software. ADF is a recently developed high-resolution power Doppler mode used as a quantitative method for calculating TBF; it can present clearer information of minute blood flow than traditional power Doppler mode. TBF was significantly higher ($p < 0.0001$) in Graves' disease than in painless thyroiditis, subacute thyroiditis, or normal controls. The TBF of patients with Graves' disease was always > 4%, and all other patients had TBF < 4%, indicating that 4% is the cutoff for distinguishing destruction-induced thyrotoxicosis and Graves' disease. The TBF of patients with painless thyroiditis and those with Graves' disease were significantly correlated with the RAIU [63]. This examination is a candidate for diagnosing thyrotoxicosis as an alternative to RAIU in the future.

## Conclusions

Recent technical developments in US have facilitated the differentiation of malignant and benign nodules and metastatic and reactive lymph nodes; of whether a nodule is malignant or benign; whether lymph node is metastatic or reactive; whether a hypoechoic lesion is lymphoma or chronic thyroiditis; and whether thyrotoxicosis is due to painless thyroiditis or Graves' diseases. To establish an accurate and immediate diagnosis of thyroid nodules, the development of a classification system is rational. We established our own system in 1995 and showed favorable results. This system is simple and easy to use, indicating that it is appropriate for performing US in many patients over a short time in a screening process.

At present, thyroid nodules measuring 3 mm can be detected on US and diagnosed as malignant or benign on US-guided FNAB. However, due to the excessive resolving power of US, small and harmless thyroid carcinomas have frequently been found and a number of patients would undergo unnecessary surgical treatment if physicians recommended surgery for all such lesions. In our opinion, observation without immediate surgical treatment for low risk PMC can be a potent alternative initial treatment.

The diagnostic accuracy of US, especially the sensitivity, for lymph node metastasis is low, indicating that many metastatic nodes may remain undissected if the compartment is not dissected prophylactically. However, the incidence of such latent metastasis becoming clinically apparent is not high. In our opinion, prophylactic central node dissection should be performed to avoid severe complications at the time of possible reoperation in the future. Prophylactic MND is recommended for selected patients who have clinicopathologic features that predict a high incidence of lymph node recurrence. The indication for prophylactic MND is affected by the incidence of nodal recurrence rates that patients and physicians can accept.

Ultrasonography facilitates the selection of patients suspected of thyroid lymphoma. Early detection of thyroid lymphoma is now possible, which contributes to achieving a favorable prognosis for patients. Among patients who are suspected of having a lymphoma based on US findings, those diagnosed as having lymphoma on FNAB should immediately undergo surgical examination to confirm the histology. Thereafter, they should undergo appropriate therapy based on the pathologic findings. However, patients diagnosed as negative on FNAB should also be carefully followed because at least 13% of these patients were confirmed to have lymphoma in our series.

The biopsy of a large number of thyroid nodules can be avoided when a pattern approach to nodule characterization is used. Specific morphologic patterns are highly predictive of benignity. Specifically, a nodule that has a uniform nonhypervascular spongiform appearance, is a cystic lesion with a colloid clot, has a giraffelike pattern, or is diffusely hyperechoic can be observed rather than biopsied. If, conversely, a nodule does not correspond to one of these four patterns, according to our data biopsy should be performed regardless of the individual features or pattern of the nodule.

Routine analysis of TBF for patients with untreated thyrotoxicosis is helpful for differentially diagnosing patients with destruction-induced thyrotoxicosis from those with Graves' disease.

The remaining issue to be solved is the differential diagnosis between follicular carcinoma and benign adenoma. Trials using novel techniques are progressing at a number of institutions, and publication of their findings is expected.

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# Subclinical Hypothyroidism: significance in conception and pregnancy – a narrative review

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Received: February 2023 Accepted: March 2023; Published: April 1, 2023.
Citation: Syed Shahinul Haque, Syed Mohsin Raza. Subclinical Hypothyroidism: significance in conception and pregnancy – a narrative review. World Family Medicine. March 2023; 21(3): 107-111 DOI: 10.5742/MEWFM.2023.95256081

## Abstract

Subclinical Hypothyroidism in pregnancy and during conception has long been an area of controversy with little consensus on whether or not it should be treated. It is also an area in which the evidence base is gradually developing. This narrative review aims to summarise the research to date in this field and provide pragmatic recommendations for the Primary Care Physician when confronted with this scenario.

Key words: Subclinical Hypothyroidism, Conception, Pregnancy, Levothyroxine, Hypothyroidism.

## Introduction

It is a not an uncommon scenario in Primary Care for a patient to attend their family practitioner after having tried and failed to conceive. Initial investigations may reveal a picture consistent with Subclinical Hypothyroidism (SCH); the patient may request thyroxine – should we treat? Furthermore, a pregnant patient may have first trimester blood results which show SCH – should this be treated? What is the evidence of benefit, if any? What are the risks associated with treatment? Increasingly moreso, clinicians are opting to treat empirically (1). Anecdotally, multiple colleagues have noted successful conception shortly after starting treatment with low dose Levothyroxine (LT4). This narrative review will focus on the issue of SCH, its significance for females trying to conceive, its effects on pregnancy, and consider the question of whether or not it should be treated with LT4 in both of these scenarios.

## Physiology

There are significant changes in thyroid physiology during pregnancy (2). In general, it is accepted that there is a transient rise in free Thyroxine (FT4), stimulated by high circulating human chorionic gonadotrophin (hCG) concentration during the first trimester, followed by a decrease in the second and third trimesters, albeit within the normal range. Likewise, free triiodothyronine (T3) levels also undergo subtle and similar changes mimicking T4. Furthermore, significant modifications in the peripheral metabolism of maternal thyroid hormones occur. Therefore, both TSH and free thyroid hormone reference intervals change throughout pregnancy. Consequently, it is important to follow pregnancy trimester-specific reference ranges where available when evaluating the thyroid status of a patient.
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## Hypothyroidism

It is well established that untreated hypothyroidism in pregnancy can result in multiple adverse outcomes (3,4). Several studies have shown associations between overt thyroid dysfunction and infertility (5,6,7). Therefore it is well accepted that overt hypothyroidism, as a form of thyroid dysfunction, should be treated in women trying to conceive. In fact, the UK NICE guidelines recommend optimising thyroid function in those women in whom a deficiency has been identified, prior to any attempts at conception (8). Likewise, the negative repercussions of overt hypothyroidism on pregnancy outcomes means the recommendation to treat overt hypothyroidism in pregnancy is well established.

**Subclinical Hypothyroidism – definitions**
Numerous studies have attempted to establish normal TSH pregnancy ranges, however, owing to the variation in geography and ethnicity, such normal reference ranges are probably not valid (9,10,11). The American Thyroid Association recommends using pregnancy trimester-specific reference ranges for TSH to establish maternal thyroid status. These should be based on data from a healthy, Thyroid Peroxidase Antibody (TPO-Ab) negative, iodine-sufficient female population of local origin (12). In practice, they recognise that this may not be possible and thus, where unavailable, they recommend using an upper limit of ~ 4.0 mU/L

## Adverse outcomes of SCH on pregnancy

Most studies in this area have shown an increased risk of adverse pregnancy outcomes. These studies can be grouped into the following broad categories based upon adverse outcomes. Studies looking at:

1. Pregnancy loss
2. Adverse perinatal outcomes (i.e. premature delivery, hypertensive disorders)
3. Adverse neurocognitive outcomes in offspring

**Pregnancy loss**
This is a difficult endpoint to study since most pregnancy losses occur early in pregnancy with the patient unaware of their pregnancy status. However various studies have shown an increase in pregnancy loss with higher levels of maternal TSH. Negro et al reported a significant increase in pregnancy loss in TPOAb negative women with TSH ranges between 2.5 and 5.0mU/L compared with those with TSH less than 2.5 mU/L (13). In a Dutch prospective cohort study with 2,497 pregnant women without overt hypothyroidism, higher levels of maternal TSH increased the risk of pregnancy loss (14). Another prospective cohort study by Liu et al reported a graded increase in the risk of miscarriage as concentrations of maternal TSH increased (15). A retrospective study that tested thyroid function in samples taken at between 11 and 13 weeks of pregnancy from 202 cases that subsequently miscarried, showed higher mean TSH and lower mean T4 concentrations, compared to 3,592 normal pregnancies (16).

**Adverse perinatal outcomes**
Casey et al conducted a prospective study of more than 17,000 pregnant patients and demonstrated a higher risk of placental abruption and preterm delivery for women with SCH compared to euthyroid women. Their babies were also more likely to have respiratory distress syndrome and be admitted to the neonatal intensive care unit (17). Wilson et al, in 2012, showed an increased incidence of gestational hypertension and eclampsia (18). Several other studies comparing pregnant women with SCH and those that are euthyroid have demonstrated various adverse outcomes in the former group including gestational diabetes (19), preterm rupture of membranes (20), preterm delivery (21), intrauterine growth restriction and low birth weight (22). Although these studies are quite varied in terms of TSH cut off points, different end points used, as well as study design, overall they do show an increase in pregnancy complications with higher maternal TSH concentrations. Furthermore, these risks seem to increase in TPOAb positive women.

**Neurocognitive effect on the offspring**

There is a limited evidence base in this area and the results are inconsistent, with some studies showing a negative neurocognitive effect of SCH on offspring and other studies not confirming this. It is an area that requires further study. The inconsistent results may be a reflection of the variation in TSH cut-off points used across the various studies, the time of gestation at which interventions took place, the differing timings of TSH evaluation during pregnancy and so forth.

## Effect of SCH on conception

With regards to conception the evidence base is even more sparse. There is some research to suggest that SCH is more prevalent in infertile women: Abalovich et al demonstrated a significantly higher incidence of SCH affecting infertile women compared with controls (13.9% vs 3.9%) (23). A retrospective study by Yoshioka et al found a success rate of conception of 84.1% in infertile women with SCH (TSH >3.0 mU/L) after treatment with LT4 (24) thus suggesting that SCH may have a negative impact on fertility. Similarly, the cross-sectional designed Danish General Suburban Population Survey showed that SCH was associated with impaired fertility (25). On the other hand a cross sectional study of 704 women undergoing fertility treatment found a raised TSH in only 2.3% - this is a similar rate to the general population. Therefore the evidence base in this area is mixed and is currently not considered sufficient to conclude that SCH is associated with infertility.

## Treating SCH

This leads onto the issue of treatment of SCH: should it be treated? If so, when?

**For conception**

Is there mileage in treating SCH to improve conception rates? Although the study by Yoshioka et al, referenced above (24) found an improvement in conception rates with LT4 treatment, a significant percentage (29%) of these pregnancies ended in miscarriage. Most of the research in this area has focused on women undergoing assistive reproductive techniques and to date there have not been any randomised controlled trials examining whether LT4 treatment of SCH in infertile women improves outcomes. As such there is insufficient evidence to recommend treating SCH in women trying to conceive.

**During pregnancy**

As previously noted, treatment with LT4 is unanimously recommended in cases of overt hypothyroidism, and there are several international guidelines advocating this (10, 26). However, despite emerging evidence of adverse pregnancy and perinatal outcomes associated with SCH, there is little consensus on whether or not to treat it. The American College of Obstetricians and Gynecologists (ACOG) does not recommend treatment (26). The American Thyroid Association (ATA) guidelines (10) recommend testing for TPO Antibodies to establish the presence of Auto-immune Thyroid Disease (AITD) in women with TSH > 2.5IU/L and then treat those who are positive. The European Thyroid Association (ETA) endorses LT4 therapy regardless of TPOAb status (albeit with a weaker recommendation for TPOAb negative patients) (27). Overall it appears from interventional studies using levothyroxine that the combination of raised TSH (SCH) in the presence of AITD (TPOAb positive) is the most responsive cohort to treatment, resulting in the fewest adverse obstetric outcomes (28, 29, 30).

**Deciding not to treat SCH**

There is established consensus on treating overt hypothyroidism during pregnancy. The recommendation to treat SCH in pregnancy is more nuanced and subject to certain limitations: a reliable diagnosis of SCH, using trimester specific and population based reference ranges, is required; the presence of TPO antibodies to establish the autoimmune status of the patient should be looked for, and, any intervention should be carried out in a timely manner to maximise the positive impact on fetal development, neonatal, and obstetric outcomes. However, treatment with LT4 cannot be considered an entirely benign intervention. Excess thyroid hormones may impair fetal neurodevelopment (31), lower IQ of the offspring and reduce grey matter and cortex volume (32). An association has been shown between high maternal free LT4 levels and low birth weight in offspring (33). Furthermore, whilst LT4 treatment in women with SCH has been found to reduce the risk of pregnancy loss, it can increase the risk of other pregnancy related adverse outcomes; preterm delivery, pre-eclampsia or gestational diabetes (34).

## Conclusion

Whilst the treatment of overt hypothyroidism has long been established in pregnant women as well as women trying to conceive, the question of subclinical hypothyroidism remains one in which there is still no consensus. As yet there is insufficient evidence to recommend treating SCH in women trying to conceive. However, the ATA has issued a weak recommendation that LT4 therapy may be considered in women with SCH trying to conceive in order to reduce the risk of progression to overt hypothyroidism once pregnancy is achieved (10). Anecdotally, colleagues have seen successful conception with low dose LT4 treatment in women struggling to conceive. In light of this, in response to the initial question posed, ‘should one treat a patient diagnosed with SCH who is trying to conceive?’, a pragmatic compromise may be to offer low dose LT4 (25-50 mcg) aiming to keep the TSH below 2.5, with regular monitoring throughout pregnancy, explaining to the patient the limitations of this approach, and thus permitting the patient to make an informed choice. The discussion would include an appraisal of the intended benefits as well as the potential pitfalls of LT4 treatment. This approach may be strengthened with a positive finding of TPO antibodies.

With regards to treatment of newly discovered SCH during pregnancy, this remains an area of controversy. Further trials are required to provide a more precise understanding of how to identify women at risk of developing pregnancy complications in order to permit more targeted interventions. In practice, the ATA guideline approach, as outlined above, may be a sensible compromise.

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# Case History: A Case of primary Amelanotic Malignant Melanoma

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Received: February 2023 Accepted: March 2023; Published: April 1, 2023.
Citation: Imran Ahmad, Bilal Hasan Chaudhry. Case History: A Case of primary Amelanotic Malignant Melanoma. World Family Medicine. March 2023; 21(3): 112-116 DOI: 10.5742/MEWFM.2023.95256082

## Abstract

This case study discusses the atypical presentation of amelanotic melanoma in a 37-year-old Caucasian female patient and the challenges it poses for diagnosis and the consequent delay in treatment. 5-year survival rate is 93% for all melanomas but amelanotic melanoma survival is 88% and this is predominantly due to delayed diagnosis(1). Better patient and doctor education and readily available histopathological diagnosis confirmation can lead to earlier diagnosis and better outcome.

Key words: amelanotic malignant melanoma, case presentation

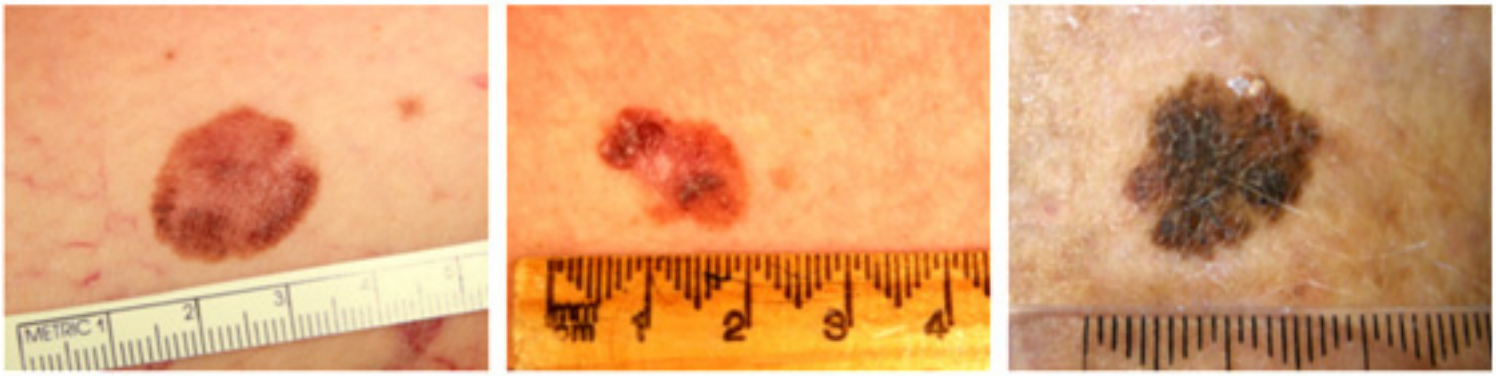

*Figure 1 Superficial spreading melanoma; most common are superficial spreading which accountfor 70% of all malignant melanomas. They are commonly found in a young age group (20-40 years old). Common sites of incidence are backs for males and legs for females. They usually present with irregular edge and irregular pigmentation.(8)*

*Figure 2 Nodular Melanoma; nodular melanomas constitute 20% of all malignant melanomas. They are commoner in older age group and appear mainly on the trunk. They present as elevated, dome shaped dark brown/black or even red/pink colour skin lesions(8).*

*Figure 3 Lentigo malignant melanoma; mainly presents on face as a dark colour freckle and gradually increase to invade surface and develops into a nodule(8).*

*Figure 4 Acral lentiginous melanoma; accounts for approximately 10% of melanomas in the western world and are commonly found on the palms of hands, soles of feet and around nails(5,8).*

## Introduction

Malignant melanoma is a cutaneous and/or extra cutaneous tumour that arises from the embryological remnants of neural crest cells/melanocytes. While melanomas are commoner in skin they can occur in eyes and internal organs(2). There has been a rapid increase in the incidence of malignant melanoma over the last few decades in all western countries. There are approximately 16,700 new diagnosed cases of malignant melanoma each year in the UK making it the fifth commonest cancer overall in the UK, accounting for 4% of all new cancer cases(3). Over the last decade, melanoma skin cancer incidence rates have increased by around a third (32%) in the UK, and is higher in males compared to females(3).

The main aetiological factors in the development of malignant melanoma are UV radiation and sun exposure along with people of higher socio-economic status and the population with Type 1&2 skin phenotype, red or blonde hair and blue eyes(4,5). Genetics also play an important role in the development of malignant melanoma and approximately 2% of patients diagnosed with malignant melanoma have a positive family history(5). A literature review on melanoma genetics by A. Nelson et al found alteration in cyclin-dependent kinase inhibitor 2A (CDKN2A) gene is the main responsible factor in the development of malignant melanoma(6). Another small study demonstrated the possible role of Human growth hormone in the pathogenesis of malignant melanoma(7).

There are four main sub types of malignant melanoma, all with distinct clinical features. Superficial spreading; Nodular; Lentigo malignant and Acral lentiginous melanomas(5).

Treatment outcome is significantly dependant on the stage of disease at time of diagnosis, the earlier the better.

## Presentation and Management

A 37-year-old Caucasian woman presented in routine family medicine clinic with a main complaint of ongoing mechanical back pain. At the end of consultation, she presented a skin lesion on her right second toe. As far as she could remember the lesion started as a small blister almost 7 months ago on the ventral surface of her right second toe. This gradually became bigger and broke the skin surface. Occasionally it wept with pinkish fluid and had a strong odour. It caused slight discomfort on walking. The lesion was not itching and there were no other systemic symptoms. She did not have other similar lesions elsewhere on the body. She was otherwise a healthy woman with no significant past medical and dermatological history. No family history of skin cancers. She lived with her husband and five children. Only surgical history was tubal sterilization after the birth of her youngest child six months ago.

At her initial consult with a General Practitioner (GP) the suspected diagnosis was superficial skin infection and she was given a one week course of Flucloxacillin. There was no improvement with antibiotics and the lesion continued to get bigger. She contacted another GP a month later about this and diagnosis was changed to fungal infection of foot. She was given topical treatment with regular dressings. She also had routine blood tests which revealed chronic mild anaemia and normal inflammatory markers and normal glucose. Thereafter there had been no change in the skin lesion which continued to stain her socks with mild discomfort on walking.

On examination she appeared well with mild restriction of her back movements. She was apyrexial with other vitals within normal range. The lesion in question was present on the plantar surface of right second toe. It was approximately 20 X 10mm in diameter, red coloured, symmetrical with regular raised borders, friable and a malodourous flat lesion with no pigmentation. The lesion appeared inflammatory and clean with no frank infection and bled easily on contact. There were no associated nail changes in any of the toes. The rest of the skin examination revealed several naevi which varied a little bit in size and shape, however all appeared benign.

History and clinical presentation of the lesion was atypical and differentials at the time were bacterial skin infection, Fungal infection of foot, Eczema, Contact dermatitis and a Pyogenic granuloma.

Due to the chronic nature of the lesion, swab was sent for culture and sensitivity before initiating further treatment. The culture result was positive for Group C-G Streptococcus (S. dysgalactiae) which are prone to causing skin abscess. According to culture and sensitivity result the patient was treated with a 2 weeks course of Penicillin.

On review at end of antibiotics the skin lesion remained the same with no improvement in signs or symptoms. As per skin cancer guidelines, a persistent skin lesion which is unresponsive to treatment with uncertain diagnosis, she was referred to suspected cancer clinic(9).

Dermatologist initially treated this lesion as pyogenic granuloma with amelanotic melanoma and an eccrine poroma on differentials list. This was treated with topical Mupirocin. Subsequently she underwent urgent biopsy of the lesion which confirmed that it is a Malignant Melanoma of 2.7mm Breslow thickness with a mitotic count of 9 and is ulcerated. She underwent amputation of right second toe with sentinel node biopsy for tumour grading and suspected metastasis. It was found that she had developed various metastasis and unfortunately she passed away soon after with carcinomatosis.

**Figure 5: Lesion as presented; (pictures were taken with the patients' consent)**

## Discussion

Amelanotic melanomas constitute only 2-8% of all melanomas(10). They are often missed due to lack of pigmentation. While criteria such as ABCDE (asymmetry, irregular borders, colour variation, diameter >6mm and evolution) are useful in diagnosis of cutaneous pigmented melanoma there is no explicit clinical appearance that is unique to the amelanotic variant(11). They are usually diagnosed at a very advanced stage when the lesion is nodular, vascular or ulcerated(12). N. Jaimes et al found in their study on 20 consecutively diagnosed amelanotic melanomas that all were erythematous, red, symmetric with regular borders and lacked clinical ABCD features commonly found in melanomas(10). Of those cases 70% exhibited a scaly appearance, which has been reported in numerous case reports of amelanotic melanoma (13–15). The report also identifies the use of dermatoscopy in correctly diagnosing these melanomas due to the presence of polymorphous vascular pattern(10). William V. Stoecker et al found that diagnostic sensitivity and specificity of amelanotic melanomas increased to 89% with use of dermatoscopy as compared to 65% without it(16). The dermatoscopic features of amelanotic melanomas include serpentine, dotted vessels throughout the lesion with central milky-red areas(17).

The case in discussion is likely Acral Lentiginous Amelanotic Malignant Melanoma due to its presence on the sole of the foot(5,18). It is a rare melanoma subtype which is mostly prevalent in dark skin population(5). Overall 5 and 10 year survival rate of acral malignant melanomas is worse than other cutaneous malignant melanomas(18,19).

Surgery is the mainstay treatment of primary cutaneous malignant melanoma (9) with margin of excision determined by the Breslow thickness(4,20). Melanomas measuring 2.01 to 4.0 mms, as in the above mentioned case, require 2-3cm margin for excision. Local recurrence of melanoma is about 5% by 2 years(9). The role of adjuvant treatment, chemotherapy and melanoma vaccines is controversial and so far show no evidence to suggest overall survival improvement in primary cutaneous malignant melanoma(4,9). Usually all patients diagnosed with malignant melanomas require specific follow up regimen on the basis of formal tumour grading(9).

## Conclusion

The incidence of malignant melanoma has increased over the last few decades. While early recognition has improved prognosis of these life-threatening skin cancers there are rare forms which pose a diagnostic challenge. This case is a clear example of delayed diagnosis primarily because of the rare anatomical position and atypical presentation with lack of pigmentation.

This case was used as a learning tool to educate other physicians and nurses of the atypical presentation. Patient and family were provided with ongoing support and care as any cancer diagnoses has profound impact on patients quality of life(21).

**Learning Points**

- Early dermatoscopy can assist diagnosis and is often easier to access in community dermatology clinics.
- Do not try laser therapy for mole removal as it can alter vascular morphology hence hindering diagnosis.

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