Taif University, Saudi Arabia

Knowledge of and practice related to foot care among diabetic patients in primary health care center at Ministry of Health, Taif, Saudi Arabia   page 6

Editorial

Chief Editor:
A. Abyad
MD, MPH, AGSF, AFCHSE
Email::
aabyad@cyberia.net.lb
Mobile: 961-3-201901

Ethics Editor and Publisher
Lesley Pocock
medi+WORLD International
AUSTRALIA
Email:
lesleypocock@mediworld.com.au
publishermwi@gmail.com

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In this second issue of the year various topics of interest to primary care are discussed.

Bakkar, et al discussed the Role of Ultrasound in Poly Cystic Ovaries Assessment. They stressed that Polycystic ovarian syndrome (PCOS) is the most common endocrine abnormality in women of reproductive age and carries with it significant health risks, including infertility, endometrial hyperplasia, diabetes, and cardiovascular disease. The workup of PCOS has evolved to include the use of pelvic ultrasonography (US). Since patients are frequently referred for radiologic imaging as a part of clinical workup, and polycystic ovaries are a common incidental finding in women undergoing US for other gynecologic complaints, radiologists should be aware of the current diagnostic criteria for PCOS, the role of imaging in workup for this abnormality, and the pertinent reporting parameters for pelvic US.

Bin Abdulrahman, et al., did a cross-sectional study was conducted among secondary and high school students in Riyadh, Saudi Arabia. The study was conducted among 901 students from different schools in the Riyadh region who were randomly included using a questionnaire distributed online. The prevalence of acne among students was 57.4 % among students. According to the Cardiff Acne Disability Index, 19.4 % of patients with acne had a high disability, 40.1 % had a moderate disability, and 40.5 % had a low disability. The index score ranged in this study from 0 (16 patients showed a score of zero with a percent of 3.1%) to 15 (16 patients showed a score of 15 with a percent of 3.1%) with a mean score of 6.15 (standard deviation=3.79). The authors concluded that this study confirmed the results of previous studies that acne causes the quality of life disabilities among school-age students. Our study showed a high prevalence of acne among students with a more significant negative impact than previous studies.

Alsumairi 1, et al., tried to assess the knowledge and practice of foot care among diabetic patients attending primary healthcare centers. They followed a cross sectional study was conducted in Taif city, among adult diabetic patients attending the primary health care centers, belonging to Ministry of health during the proposed study period from February to May 2022. A total of 385 diabetic patients were included in the study. Their age ranged between 14 and 75 years with an arithmetic mean of 40.6 and standard deviation of 13.2 years. The authors concluded that relative suboptimal level of both knowledge and practice related to foot care was observed. Educational programs including practical sessions, better through using videos regarding the best practice of foot care are highly recommended for diabetic patients.

Alhujaili, et al.,. did a cross-sectional study to assess the prevalence of SAD among the medical students at King Abdulaziz University- Rabigh branch and its associated risk factors. The study was conducted on 218 students aged between 18 and 26, which was managed by sending an online questionnaire that included participants' demographic information and The Liebowitz Social Anxiety Scale (LSAS). SAD is found to be significantly common among the participating medical students and correlated positively with multiple relevant factors, showing the effort needed for earlier detection of SAD to manage it accordingly.

Alkhalid et al., attempted to find the correlation between pseudoscience practices and depression among pseudoscience believers in Saudi Arabia. They did a cross-sectional study conducted among the Saudi population who believe in pseudoscience. Of the 409 believers, 41.8% were aged between 26 – 35 years old with females being dominant (94.5%). The most prominent practice of reading was Zodiac (81.3%). The authors concluded that there was a high prevalence of depression among pseudoscience believers. Increased depression was demonstrated more frequently by younger believers who were still single, less educated, and who were currently engaged in Zodiac reading practices. More research is needed to shed more light on the effect of pseudoscience on the mental health condition of its believers.

Alghanem et al., did a systemic review to search, analyze and identify evidence regarding the use of physical activity interventions in preventing type 2 diabetes mellitus (T2DM) in prediabetic population. This systematic review shows that most of the physical activity interventions are effective and this leaves the healthcare providers to choose one that will show to be more effective. Because of the reported effectiveness, the HIIT programs can prove to be the better choice.

Alghamdi., et al., did a descriptive cross-sectional study; conducted among healthcare professionals working at ICUs at King Fahad Hospital and Prince Meshari Hospital,. A convenient sampling technique was used to collect data using questionnaire about knowledge attitude and practice towards chest physiotherapy for Covid-19 patients which was adopted from previous validated questionnaire. This study aimed to assess the knowledge, attitude, and practice of the health-

care professionals in chest physiotherapy for COVID-19 patients. This study highlighted that majority off healthcare providers (physiotherapists, nurses or medical) are knowledgeable, they also have positive attitude and appropriate practices about COVID-19 physiotherapy management in ICUs at Al-Baha governmental hospitals.

Aljuaid, et al., did a retrospective observational cohort study of COVID-19 patients admitted in two tertiary hospitals in Saudi Arabia from May to July 2020. Patients' demographics, comorbidities and clinical manifestations were collected from the medical records. The aim of this study is to determine the obesity risk factors among hospitalized COVID-19 patients and their influence on the clinical outcomes of the disease Out of 260 patients who were included in the study, 41.6% were obese. The authors concluded that obesity is very common among hospitalized patients with Covid-19 particularly females. Obese Patients were more likely to have cardiovascular risk factors and adverse clinical outcomes.

Bin Abdulrahman, et al., did a quantitative study is a descriptive cross-sectional study conducted among medical students in different universities in Riyadh region. the main aim of this study is to assess the mental health of medical students in different levels of training to see if a certain level plays a higher role in developing mental health issues. In the current study, we collected data from 617 medical students from four universities in Riyadh region, Saudi Arabia. Among the students, 56.7 % of the participants were males, and 42.1 % were aged between 20-21 years old, and 91.6 % of them were single. According to the GHQ-12, 368 students were classified as GHQ-cases having symptoms of depression and psychiatric disorders (59.6 %). The prevalence of psychological distress among female students was significantly higher than among males (68.9 % vs. 52.6 %, P=0.000). The authors concluded that the current study confirmed the previous studies on the high prevalence of psychological distress among medical students, which was significantly higher among females, students of low income, and students with lower GPAs. Moreover, the study showed that first-level students were the most affected by psychological distress.

Helvaci, et al., tried to understand whether or not there is a relationship between smoking and diabetes mellitus (DM). Current regular smokers for the last six months and age and sex-matched non-smokers were included. Patients with current alcohol consumption (one drink a day) and patients with malignancies or inflammatory, infectious, or devastating disorders were excluded. The study included 247 smokers and 167 non-smokers. The mean age and body mass index (BMI) of smokers were 46.2 years and 26.6 kg/m2, respectively, and 70.0% of them were male. The authors concluded that smoking-induced low-grade inflammation on vascular endothelium in whole body may terminate with the endothelial dysfunction, accelerated atherosclerosis, end-organ insufficiencies, early aging, and premature death. FPG and HDL may be negative whereas triglycerides, LDL, ESR, and CRP positive acute phase reactants terminating with lower prevalence of DM but higher incidence of dyslipidemia in smokers.

Mobarki, et al., reviewed Methicillin-Resistant Staphylococcus Aureus Combination Treatment Options in Vivo and in Vitro. The authors stressed that the spread of multidrug-resistant Staphylococcus aureus continues to threaten global health. Methicillin-resistant Staphylococcus aureus (MRSA) is one of common causes of bacterial infections in hospitals and communities. Despite vancomycin being an effective treatment for MRSA, from 2006 to 2020, vancomycin-resistant MRSA increased 3.5-fold, from 5% to 7%. Bacterial genome mutations, as well as bacteria's ability to transfer genetic material with other bacteria, allowing them to obtain resistance genes from different strains, are all factors contributing to the development of vancomycin resistance in MRSA. As a result, combination therapy may be a potential treatment for MRSA infection.

We searched in PubMed and Google Scholar, and our search yielded 92 articles, out of which 74 full-text articles were reviewed and 56 were selected for this study. This literature review examines combination therapies for MRSA infections. Such as β-Lactams with vancomycin, linezolid and imipenem, daptomycin and ceftaroline. The review yielded several studies looking at the synergy between β-lactams and vancomycin. Although linezolid and rifampicin demonstrate synergy against MRSA in vivo and in vitro in various invasion diseases, more clinical research is required to prove their efficacy. Furthermore, daptomycin plus ceftaroline shows synergy for refractory staphylococcal bacteremia in vivo and in vitro. Combining ceftaroline and daptomycin has two benefits: they work synergistically together and make the innate host defense peptide cathelicidin leucine-leucine-37 (LL-37) more sensitizing. Ceftaroline plus daptomycin was recently used in MRSA biofilm infections, demonstrating a potentially promising treatment as the first combination used without side effects in humans.

Chief Editor:
A. Abyad
MD, MPH, AGSF, AFCHSE

Knowledge of and practice related to foot care among diabetic patients in primary health care center at Ministry of Health, Taif, Saudi Arabia

Nourah A. Alsumairi [1], Lama A. Alsumairi [2], Rasheed A. Alghamdi Z [3]

(1) Family Medicine Specialist, Taif region, KSA
(2) Medical student, Taif University, KSA
(3) Family Medicine Consultant, Diabetes fellow, Endocrine and Diabetes center, King Abdulaziz specialist hospital, Taif region, KSA

Corresponding author:
Dr. Nourah A. Alsumairi
Taif city, Saudi Arabia
Mobile: 0535894540
Email: dr.norahas@gmail.com

Abstract

Background: Despite the continuous efforts aimed at prevention in the studied primary health care centers, there was a notable increase in amputation rate, which has a significant negative impact on survival of diabetic patients. Sufficient awareness of diabetic patients about foot care as well as its proper practice, is essential in preventing diabetic foot problems and amputation.

Objectives: To assess the knowledge and practice of foot care among diabetic patients attending primary healthcare centers.

Patients and methods: A cross sectional study was conducted in Taif city, among adult diabetic patients attending the primary health care centers, belonging to the Ministry of Health during the proposed study period from February to May 2022. An Arabic self-administered questionnaire including four sections (sociodemographic factors, patients' knowledge about self-care of diabetic foot, patients' practices regarding self-care of diabetic foot and the barriers for not routinely checking for diabetic neuropathy at diabetic foot clinic) was utilized for data collection

Results: A total of 385 diabetic patients were included in the study. Their ages ranged between 14 and 75 years with an arithmetic mean of 40.6 and standard deviation of 13.2 years. Females represented 60.5% of them. Almost two-thirds of the participants (64.4%) were type 2 diabetic patients. Almost one quarter of diabetic patients (26.4%) expressed a good level of knowledge regarding foot care; particularly older patients (p=0.033), those living in urban areas (p=0.002), the employed (p=0.007), type 2 diabetics (p=0.029) and patients who obtained their information about foot care from internet/social media or health staff (p=0.004). Good foot care-related practice was reported among 42.1% of the diabetic patients; particularly Saudi patients (p=0.029), higher educated (p=0.016), employed (p=0.032), those with higher family income (p=0.048) and those who had their information about foot care from health staff (p<0.001).

Conclusion: A relative suboptimal level of both knowledge and practice related to foot care was observed. Educational programs including practical sessions, preferably through using videos regarding the best practice of foot care are highly recommended for diabetic patients.

Keywords: Knowledge, practice, foot, diabetic, PHC, Taif

List of abbreviations

DM	Diabetes mellitus
IDF	International Diabetes Federation
HbA1c	Glycated hemoglobin
DF	Diabetic foot
SPSS	Statistical Package for Social Sciences

Introduction

Currently, diabetes mellitus (DM) is one of the highest global health emergencies of the 21st century as stated by the International Diabetes Federation (IDF)(1). It is estimated that 415 million adults aged 20-79 exist with diabetes worldwide and this will increase to 642 million in 2040, if no efforts are taken to overcome the situation (2). The Kingdom of Saudi Arabia (KSA) has one of the world's highest prevalence rates of type 2 diabetes (1). The Arabian Gulf wealth has led to better living conditions, thereby causing an increase in urbanization, major changes in nutrition, decreased physical activity, and further dependency on migrant workers (3). In Saudi Arabia, the prevalence of DM in adults in 2016vwas 25% (4). Alsenany and Al Saif (2015) suggested that more than 44% of individuals aged 55 or older had severe to uncontrolled diabetes with long-term complications (5).

Diabetes has life altering consequences that forces individuals to add some responsibility of self-care as they are required to maintain controlled levels of glycated hemoglobin (HbA1c) (6). Up to 50% of diabetics in the US failed to control their blood sugar and developed various complications (7).

Diabetic patients have greater vulnerability to many types of complications, both short and long-term, which often lead to their early death (8). These complications are classified into two categories; macrovascular, which includes stroke, coronary and peripheral arterial disease, and microvascular, which is associated with other DM-induced long-term complications such as neuropathy, retinopathy, nephropathy, diabetic foot, and cardiovascular diseases (9).

Diabetes mellitus has specific harmful effects on the feet as ulceration of lower limbs and feet occur in about 15% of diabetic patients (10). Studies in the Arab world showed a prevalence of neuropathy ranging between 38–94% in diabetic foot (DF) cases and the prevalence of peripheral vascular disease ranged between 50–78.7% (11). Studies in Saudi Arabia about DF and its complication are numerous and indicate significant impact (12–15).

Despite the continuous efforts aimed at prevention, there has been a notable increase in amputation rate (16). Amputation has a significant negative impact on survival (17).

Sufficient awareness of diabetic patients about foot care is an essential line in preventing DF problems and amputation (18).Proper practices of foot health care are important for reducing the incidence of foot ulcers and complication (19).Studies indicate that patients` education regarding proper foot care practices could play a vital role in reducing diabetes related foot ulceration and amputations (20). Also, foot care practices reduce common foot problems such as corns and callosities and facilitate healing of foot ulcers (21). There are limited Saudi studies investigating the knowledge and practices regarding foot care among diabetic patients. A previous study done in Riyadh, Saudi Arabia in 2020 found sufficient knowledge among 65% of diabetic patients with no gender difference.22. In Asser Region, Al-Jarallah et al., 2020 found low knowledge and attitude scores. Previous training and/or attending workshop on diabetic foot care was significantly associated with higher knowledge and attitude scores (23).

This study aimed to assess the knowledge and practice of foot care among diabetic patients attending primary healthcare centers and associated socio-demographic and clinical-related factors.

Subjects and Methods

Study design, setting and time frame: A cross sectional study was done in Taif city, Saudi Arabia between February to May 2022.

Study population: The inclusion criteria were Adult diabetic patients attending the primary health care centers, belonging to the Ministry of Health in Taif during the proposed study period from February to May 2022, in addition to patients with diagnosed DMT2 or type 1 diabetes mellitus (DMT I) for more than 6 months, who had ever developed foot ulcerations, were aged over 14 years, with good mental status, and psychological status and Arabic speakers. The exclusion criteria were patients with physical disabilities, gestational diabetes, diabetic patients on insulin pump, patients who refused to sign informed consent, non-Arabic speakers, those diagnosed with DMT2 or type 1 diabetes mellitus (DMT I) for less than 6 months and those aged less than 14 years old.

Sample size
The sample size was calculated using the Cochran's formula for estimating sample size equation as follows (24):

$$N = \frac{Z_{\alpha/2}^2 \times p(1-p)}{D^2}$$

where: n=Minimum sample size, $Z_{\alpha/2}$ = the critical value of the Normal distribution at $\alpha/2$ (e.g. for a confidence level of 95%, α is 0.05 and the critical value is 1.96), P= Prevalence of sufficient knowledge about diabetic foot care: It is estimated as 65% based on a recent Saudi study carried out in Riyadh (22) D= Degree of precision. So, the calculated minimum sample size was:

1. $$n = \frac{(1.96)^2 \times 0.65 \times 0.35}{(0.05)^2} = 350$$

The sample was increased by approximately 10% to compensate for possible no or incomplete response, thus it was 385 diabetic patients.

Sampling technique: Following a simple random sampling technique, four PHCCs were randomly selected. A total of 96 diabetic patients attending these PHCCs during data collection period were selected by systematic random technique according to number of patients visiting each center daily and were invited to participate in the study by filling in the study questionnaire.

Study instrument: An Arabic self-administered questionnaire was utilized for data collection. It was done according to recommendations of the American College of Foot and Ankle Surgeons and Diabetes UK and has been previously adopted in recent studies carried out in Riyadh (25) and Makkah (26). Permission to use the questionnaire was obtained through personal communication with authors in Makkah.

The questionnaire consisted of four sections; Section 1 contained questions about sociodemographic factors and Section 2 contained questions about patients' knowledge about self-care of diabetic foot (11 items). Section 3 contained questions about patients' practices regarding self-care of diabetic foot and Section 4 contained the barriers for not routinely checking for diabetic neuropathy at a diabetic foot clinic. For each correct answer 1 point was given and for an incorrect answer, "0" was given.

The maximum score for knowledge was 11, <60% was categorized as poor level of knowledge, 60–80% was categorized as medium level of knowledge, and >80 was categorized as a good level of knowledge. The third part included 11 questions about foot-care practice. Correct practice was assigned a score of "1" while incorrect practice was assigned a score of "0". Total score was computed (ranged between 0 and 11) and its percentage was estimated. Patients who scored <60% were categorized as poor practice, 60–80% were categorized as satisfactory practice, and >80 were categorized as good practice (26).

Data collection: The researchers visited the PHC centers after getting approvals. They explained the purpose of the study to all physicians and patients chosen for the study and did not ask for their names to ensure confidentiality. Self-administered questionnaires were distributed to selected patients while waiting for physicians` appointment and collected after half an hour. The data collection was implemented during regular daytime working hours. One to two weeks was spent in each PHC center involved in the study. A trained male colleague/nurse helped in data collection from male patients.

Statistical analysis: The data were entered and analyzed by Statistical Package of Social Science SPSS, version 27. The descriptive statistics such as frequencies, and percentages were calculated to summarize nominal and ordinal data, while mean and standard deviation were adopted to describe numerical variables. Chi-squared test was used to evaluate the association between the determinants and the outcome variables. Any p-value <0.05 was considered statistically significant.

Ethical considerations: Written permission from MOH Program of Family Medicine, and from all PHCCs directors Taif Region was obtained.

Results

A total of 385 diabetic patients were included in the study. Their sociodemographic characteristics are summarized in Table 1. Their age ranged between 14 and 75 years with an arithmetic mean of 40.6 and standard deviation of 13.2 years. Females represented 60.5% of patients. More than half of them (53.2%) were married and the majority (96.9) were Saudi nationals and living in urban areas (89.6%). More than half were bachelor holders (57.3%), employed (53.5%) and having family income that ranged between 5000 and 15000 Saudi Riyals/month (59%).

Type of diabetes: As seen in Figure 1, almost two-thirds of the participants (64.4%) were type 2 diabetic patients whereas the remaining 35.6% were type 1 diabetic patients.

Source of information about diabetic foot care: The commonest reported sources of information about foot care among the participants were health staff (67%), internet/social media (46.2%) and friends/relatives (37.9%). (Figure 2).

Having risk factors for diabetic foot: History of having risk factors for diabetic foot was reported by 44.4% of patients; mainly decrease dvision/retinopathy (28.1%) and neuropathy (14.8%). (Table 2).

Knowledge of diabetic foot care: Table 3 summarizes the responses of the diabetic patients to 11 knowledge statements regarding foot care. The majority of them knew correctly that diabetic patients should take medication regularly because they are liable to get DM complications (96.9%), should look after their feet because wounds and infection may not heal quickly (93.2%) and should look after their feet because they may not feel a minor injury to their feet (91.2%). On the other hand, only 29.4% of them knew that they should be seen immediately by the physician, if they find redness/bleeding between toes and a minority of them (17.9%) knew that they should be immediately seen by the physicians if they have a corn/hard skin lesion even once.

Almost one quarter of diabetic patients (26.4%) expressed a good level of knowledge regarding foot care as illustrated in Figure 3.

Older patients were more likely to express either a medium level (41.7±12.7 years) or good level (41.2±13 years) of knowledge about foot care than relatively younger patients (37.2±14.4 years), p=0.033. Also, patients living in urban areas were more likely to have higher, medium or good knowledge about diabetic foot compared to those living in rural areas (55.3% and 27% vs. 27.8% and 22.2%, respectively), p=0.002. Employed patients were more likely to have higher, medium or good knowledge about diabetic foot compared to unemployed patients (58.3%

and 27.2% vs. 46.9% and 25.7%, respectively), p=0.007. Type 2 diabetic patients were more likely to have higher, medium or good knowledge about diabetic foot compared to type 1 diabetic patients (54.9% and 28.6% vs. 49.7% and 22.6%, respectively), p=0.029. Patients who obtained their information about foot care from internet/social media or health staff were more likely to express a good level of knowledge about foot care compared to those who obtained their information from books/journals/others (34.4% and 32.2% vs. 15.8%, respectively), p=0.004. (Table 4).

Diabetic foot care-related practice: The majority of the patients wash their feet with warm water (95.3%), trim their toenails straight across (88.3%), measure their feet size when last they bought footwear (84.4%), inspect their feet regularly (83.6%) and wash their feet regularly (81.8%). On the other hand, only 32.2% received advice when they last bought footwear. (Table 5)
.
Figure 4 shows that 42.1% of the diabetic patients expressed good foot care-related practice. Saudi patients were more likely to express good level of foot care-related practice than non-Saudi patients (43.2% vs.8.3%), p=0.029. The highest rate of good level of practice was observed among Bachelor holders (47.5%) whereas the lowest level was observed among those who are just able to read and write (23.1%), p=0.016. Employed patients were more likely to have higher good practice of foot care compared to unemployed patients (48.1% vs. 29.1%), p=0.032. Patients with the highest family income (>25000 SR/month) had the highest rate of good practice related to foot care (48.3%) while those with the lowest family income (<5000 SR/month) had the lowest rate of good practice (29.1%), p=0.048. Patients who received their information about foot care from health staff were more likely to express a good level of practice related to foot care compared to those who obtained their information from friends and relatives (60.3% vs. 24.2%), p<0.001. (Table 6).

Association between knowledge and practice of foot care: As shown in Table 7, more than half (53.9%) of patients with a good level of knowledge about diabetic foot care expressed a good level of practice in this regard, (p<0.001).

Table 1: Sociodemographic characteristics of patients (n=385)

Variable	Frequency	Percentage
Sex		
Male	152	39.5
Female	233	60.5
Age in years		
Range	14-75	
Mean±SD	40.6±13.2	
Marital status		
Single	103	26.8
Married	205	53.2
Divorced	46	11.9
Widowed	31	8.1
Nationality		
Saudi	373	96.9
Non-Saudi	12	3.1
Place of residence		
Urban	345	89.6
Rural	18	4.7
Semi-rural	22	5.7
Education		
Illiterate	18	4.7
Able to read and write	13	3.4
Primary-high school	110	28.6
Bachelor/Diploma	221	57.3
Master/PhD	23	6.0
Employment status		
Employed	206	53.5
Unemployed	179	46.5
Family income (SR/month)		
<5000	55	14.3
5000-15000	227	59.0
15001-25000	74	19.2
>25000	29	7.5

Figure 1: Distribution of the participants according to the type of diabetes
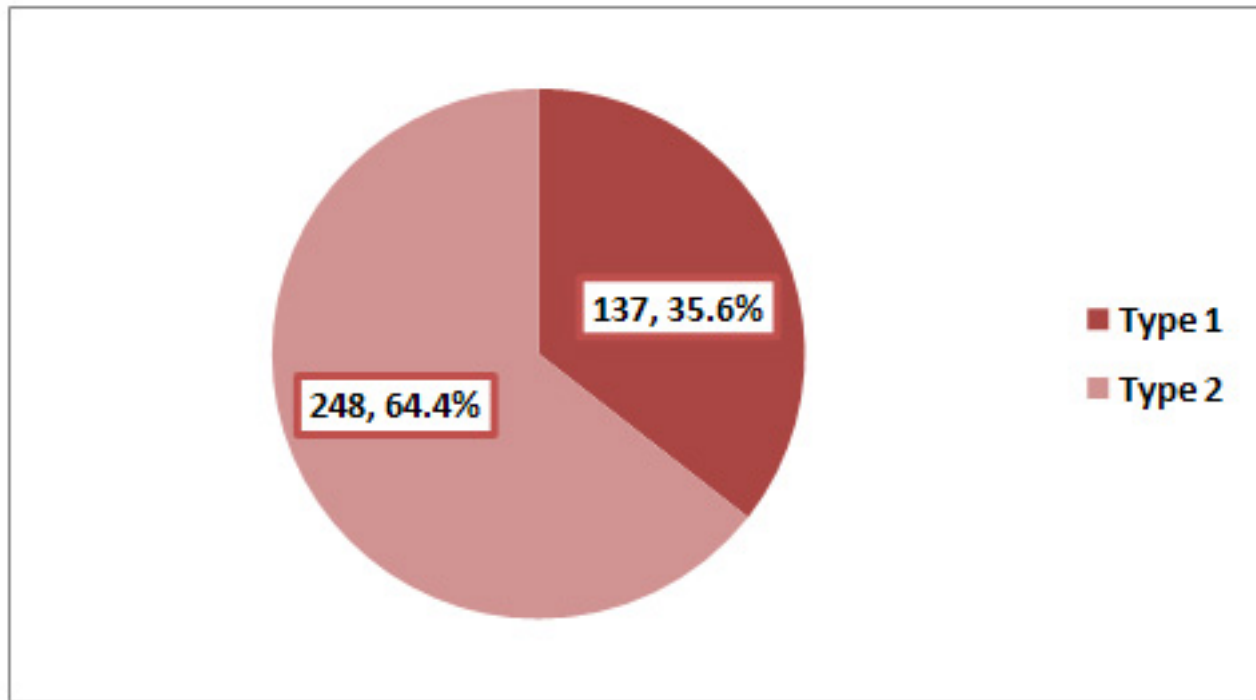
Figure 2: Source of information about diabetic foot care among the participants (Not mutually exclusive Sum exceed 100%)
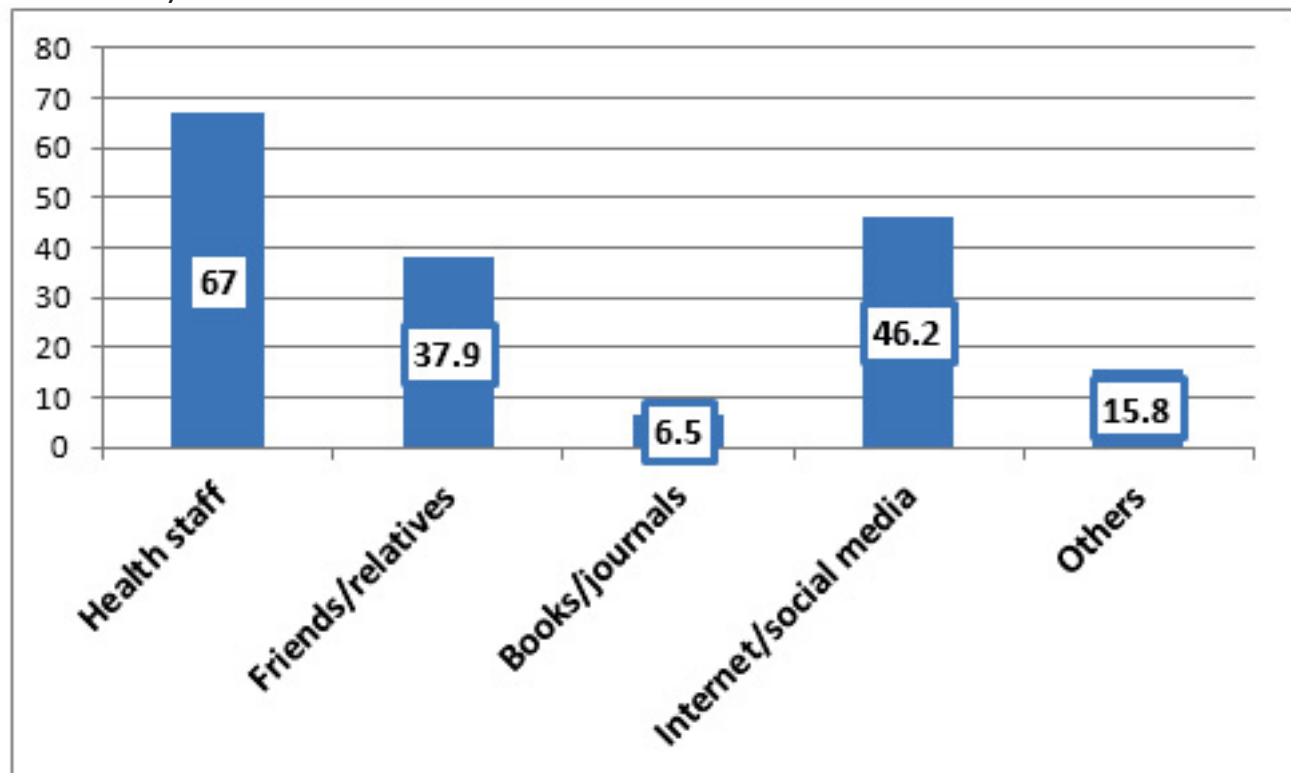
Table 2: History of risk factors for diabetic foot among the participants

	Frequency	Percentage
No	214	55.6
Yes	171*	44.4*
Neuropathy	57	14.8
Decreased vision/retinopathy	108	28.1
Angiopathy	37	9.6
Dorsal feet pulse	9	2.3

*Not mutually exclusive. Sum exceeds 100%)

Table 3: Patients` responses to diabetic foot care knowledge statements

Knowledge statements	Correct answer		
	Right response	N	%
DM patients should take medication regularly because they are liable to get DM complication	Yes	373	96.9
DM patients should look after their feet because they may not feel a minor injury to their feet	Yes	351	91.2
DM patients should look after their feet because wounds and infection may not heal quickly	Yes	359	93.2
DM patients should look after their feet because they may get a foot ulcer	Yes	346	89.9
DM patients should not smoke because smoking causes poor circulation affecting the feet	Yes	264	68.6
How often do you think you should inspect your feet?	Daily	169	43.9
If you found redness/bleeding between your toes what is the first thing you do?	To be seen immediately by physician	113	29.4
Even if you have never had a corn/ hard skin lesion, what would you do if you had one	To be seen immediately by physician	69	17.9
How often do you think your feet should be washed per day	Five times	245	63.6
What temperature of water do you think you should wash your feet in	Moderate temperature	283	73.5
How often do you think you should inspect the inside of your footwear for objects or torn lining	Once daily/every time footwear put on	322	83.6

Figure 3: Level of diabetic patients` knowledge regarding foot care

Figure 3: Level of diabetic patients` knowledge regarding foot care
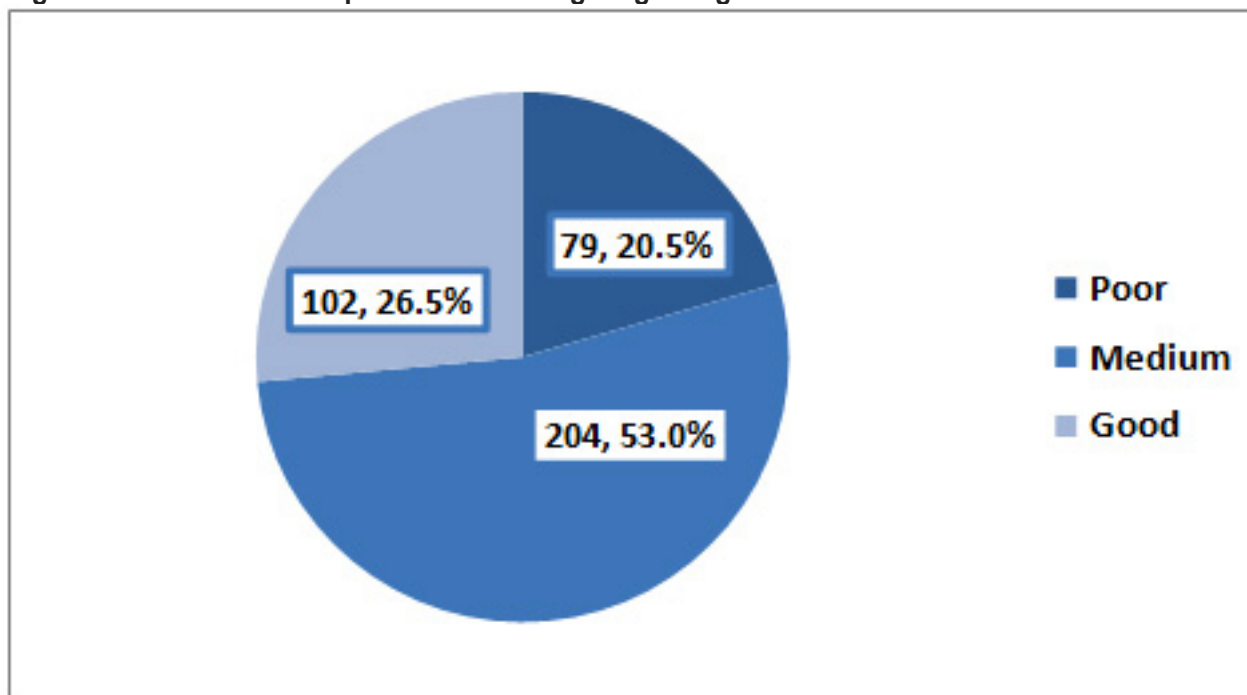
Table 4: Factors associated with knowledge of the participants about diabetic foot care

	Level of knowledge about diabetic foot care			p-value
	Poor N=79 N (%)	Medium N=204 N (%)	Good N=102 N (%)	
Sex				
Male (n=152)	29 (19.1)	85 (55.9)	38 (25.0)	
Female (n=233)	50 (21.5)	119 (51.1)	64 (27.5)	0.646*
Age in years				
Mean±SD	37.2±14.4	41.7±12.7	41.2±13	0.033‡
Marital status				
Single (n=103)	24 (23.3)	50 (48.5)	29 (28.2)	
Married (n=205)	38 (18.5)	112 (54.6)	55 (26.8)	
Divorced (n=46)	9 (19.6)	24 (52.2)	13 (28.3)	
Widowed (n=31)	8 (25.8)	18 (58.1)	5 (16.1)	0.771*
Nationality				
Saudi (n=373)	75 (20.1)	199 (53.4)	99 (26.5)	
Non-Saudi (n=12)	4 (33.3)	5 (41.7)	3 (25.0)	0.522*
Place of residence				
Urban (n=345)	61 (17.7)	191 (55.3)	93 (27.0)	
Rural (n=18)	9 (50.0)	5 (27.8)	4 (22.2)	
Semi-rural (n=22)	9 (40.9)	8 (36.4)	5 (22.7)	0.002*
Education				
Illiterate (n=18)	3 (16.7)	10 (55.6)	5 (27.8)	
Able to read and write (n=13)	5 (38.5)	6 (46.1)	2 (15.4)	
Primary-high school (n=110)	30 (27.3)	48 (43.6)	32 (29.1)	
Bachelor /Diploma (n=221)	35 (15.8)	130 (58.8)	56 (25.3)	
Master/PhD (n=23)	6 (26.1)	10 (43.5)	7 (30.4)	0.141*
Employment status				
Employed (n=206)	30 (14.6)	120 (58.3)	56 (27.2)	
Unemployed (n=179)	49 (27.4)	84 (46.9)	46 (25.7)	0.007*
Family income (SR/month)				
<5000 (n=55)	19 (34.5)	27 (49.1)	9 (16.4)	
5000-15000 (n=227)	42 (18.5)	120 (52.9)	65 (28.6)	
15001-25000 (n=74)	13 (17.6)	42 (56.7)	19 (25.7)	
>25000 (n=29)	5 (17.2)	15 (51.8)	9 (31.0)	0.156*
Type of diabetes				
Type 1 (n=137)	38 (27.7)	68 (49.7)	31 (22.6)	
Type 2 (n=248)	41 (16.5)	136 (54.9)	71 (28.6)	0.029*
Main source of information				
Health staff (n=121)	8 (6.6)	74 (61.2)	39 (32.2)	
Friends/relatives (n=33)	10 (30.3)	16 (48.5)	7 (21.2)	
Internet/social media (n=32)	7 (21.9)	14 (43.8)	11 (34.4)	
Books/journals/Others (n=19)	5 (26.3)	11 (57.9)	3 (15.8)	
Two sources (n=105)	25 (23.8)	53 (50.5)	27 (25.7)	
More than two sources (n=75)	24 (32.0)	36 (48.0)	15 (20.0)	0.004*
Having risk factors for diabetic foot				
No (n=214)	39 (18.2)	116 (54.2)	59 (27.6)	
Yes (n=171)	40 (23.4)	88 (51.5)	43 (25.1)	0.453*

*Chi-square test   ‡ANOVA test

Table 5: Patients` responses to practice of diabetic foot care statements

	Correct answer		
	Right response	N	%
Do you inspect feet regularly?	Yes	322	83.6
Do you wash feet regularly?	Yes	315	81.8
Do you wash feet with warm water?	Yes	367	95.3
Do you trim toe nails straight across?	Yes	340	88.3
Did you measure your feet size when last you bought footwear?	Yes	325	84.4
Did you receive advice when last you bought footwear?	Yes	124	32.2
Did you ever inspect inside of footwear?	Yes	255	66.2
Do you regularly walk barefoot?	No	266	69.1
Do you clean nails with sharp instrument?	No	270	70.1
Do you add irritants to water before feet cleaning?	No	245	63.6
Do you wear elasticated hosiery?	No	254	66.0

Figure 4: Level of diabetic foot care-related practice among the participants
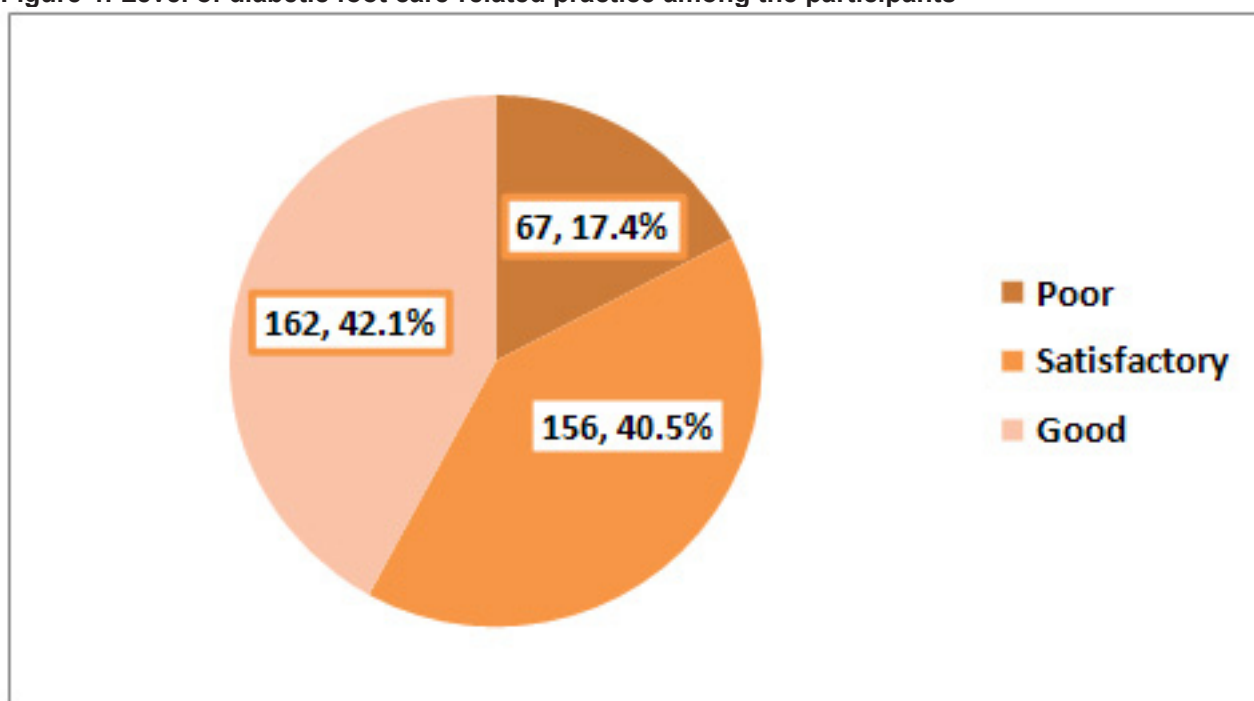
Table 6: Factors associated with diabetes foot care-related practice among the participants

	Level of practice related to diabetic foot care			p-value
	Poor N=67 N (%)	Satisfactory N=156 N (%)	Good N=162 N (%)	
Sex				
Male (n=152)	27 (17.8)	59 (38.8)	66 (43.4)	
Female (n=233)	40 (17.2)	97 (41.6)	96 (41.2)	0.858*
Age in years				
Mean±SD	42.5±13.6	40.1±13.1	40.4±13.2	0.451‡
Marital status				
Single (n=103)	9 (8.7)	46 (44.7)	48 (46.6)	
Married (n=205)	38 (18.5)	80 (39.0)	87 (42.4)	
Divorced (n=46)	11 (23.9)	17 (37.0)	18 (39.1)	
Widowed (n=31)	9 (29.0)	13 (42.0)	9 (29.0)	0.098*
Nationality				
Saudi (n=373)	64 (17.2)	148 (39.7)	161 (43.2)	
Non-Saudi (n=12)	3 (25.0)	8 (66.7)	1 (8.3)	0.029*
Place of residence				
Urban (n=345)	57 (16.5)	140 (40.6)	148 (42.9)	
Rural (n=18)	6 (33.3)	7 (38.9)	5 (27.8)	
Semi-rural (n=22)	4 (18.2)	9 (40.9)	9 (40.9)	0.443*
Education				
Illiterate (n=18)	8 (44.4)	4 (22.2)	6 (33.4)	
Able to read and write (n=13)	4 (30.8)	6 (46.2)	3 (23.1)	
Primary-high school (n=110)	19 (17.3)	52 (47.3)	39 (35.5)	
Bachelor /Diploma (n=221)	34 (15.4)	82 (37.1)	105 (47.5)	
Master/PhD (n=23)	2 (8.7)	12 (52.2)	9 (39.1)	0.016*
Employment status				
Employed (n=206)	30 (14.6)	77 (37.4)	99 (48.1)	
Unemployed (n=179)	37 (20.7)	79 (44.2)	63 (29.1)	0.032*
Family income (SR/month)				
<5000 (n=55)	16 (29.1)	23 (41.8)	16 (29.1)	
5000-15000 (n=227)	41 (18.1)	85 (37.4)	101 (44.5)	
15001-25000 (n=74)	8 (10.8)	35 (47.3)	31 (41.9)	
>25000 (n=29)	2 (6.9)	13 (44.8)	14 (48.3)	0.048*
Type of diabetes				
Type 1 (n=137)	30 (21.9)	59 (43.1)	48 (35.0)	
Type 2 (n=248)	37 (14.9)	97 (39.1)	114 (46.0)	0.070*
Main source of information				
Health staff (n=121)	6 (5.0)	42 (34.7)	73 (60.3)	
Friends/relatives (n=33)	10 (30.3)	15 (45.5)	82 (24.2)	
Internet/social media (n=32)	7 (21.9)	16 (50.0)	9 (28.1)	
Others (n=19)	8 (42.1)	6 (31.6)	5 (26.3)	
Two sources (n=105)	23 (21.9)	46 (43.8)	36 (34.3)	
More than two sources (n=75)	13 (17.4)	31 (41.3)	31 (41.3)	<0.001
Having risk factors for diabetic foot				
No (n=214)	34 (15.9)	86 (40.2)	94 (43.9)	
Yes (n=171)	33 (19.3)	70 (40.9)	68 (39.8)	0.595*

*Chi-square test   ‡ANOVA test

Table 7: Association between knowledge about diabetic foot care and its practice among the participants

Level of knowledge about diabetic foot care	Level of diabetic foot care-related practice			p-value*
	Poor N=67 N (%)	Satisfactory N=156 N (%)	Good N=162 N (%)	
Poor (n=79)	36 (45.6)	32 (40.5)	11 (13.9)	
Medium (n=204)	23 (11.3)	85 (41.7)	96 (47.1)	<0.001
Good (n=102)	8 (7.8)	39 (38.2)	55 (53.9	

* Chi-square test

Discussion

Having proper knowledge as well as sound practice concerning diabetic foot care is vital for diabetic patients in controlling the serious complications of diabetes such as the development of diabetic foot ulcers as well as amputation of the lower limbs (27,28,29).. Thus, we intended to explore both knowledge and practice related to foot care among diabetic patients attending the primary health care centers, belonging to the Ministry of Health in Taif city, Western Saudi Arabia.

In the present study, most of the patients (73.5%) could recognize that their feet should be washed daily by moderate temperature water. Lower figures (almost half) of patients were aware that they should perform proper foot hygiene in a previous study carried out in the United Kingdom (30).

In a recent Saudi study, the majority of patients (85.4%) were unaware of the suitable temperature of water used to wash their feet, and furthermore, 60.1% were unaware of how often they should inspect their feet (31).

Fortunately, the majority of patients in this study knew that they should look after their feet because they may develop foot ulcers. In disagreement with this finding, most patients in another Saudi study were unaware of the importance of looking after their feet (32). However, a low proportion of patients could recognize that if they found redness/bleeding between toes, the first action that should be done is to be seen immediately by physicians and even if they had a corn/hard skin lesion, they should be seen immediately by physician. Similar findings have been reported by others in Saudi Arabia (32) and UK (30).

In disagreement with this, most diabetic patients in the Eastern Province Saudi Arabia sought immediate medical advice when they had any feet lesions (33).

Almost two-thirds (68.6%) of diabetic patients in the current study could recognize that diabetic patients should not smoke as smoking leads to poor blood circulation, which could seriously impact their feet. The same has been observed in a recent Saudi study carried out in Tabuk (32). However, in an older study carried out in the UK, about half of diabetic patients were unaware that smoking can seriously impact the circulation of the feet (30).

In the current study, more than half of diabetic patients expressed a medium level of knowledge about diabetic foot care whereas nearly a quarter of them (26.5%) expressed a good level and 20.5% had poor level of knowledge. In Tabuk (Saudi Arabia), most of the diabetic patients had a poor level of knowledge regarding foot care with only a minority having a good level of knowledge (32).

Higher rate of poor knowledge about foot care was reported in Iran (84.8%) (34). Comparable figures of poor knowledge about foot care have been reported by others in Iran (23.3%) (29), Nigeria (30.1%) (35), Saudi Arabia (26%) (31) and South Africa (32.4%) (36). In Ethiopia (2021), good knowledge was reported among 61.3% of patients (37).

The variations in patients` knowledge regarding foot care observed in th aforementioned studies could be explained by different demographic characteristics of patients in these studies, utilizing different instruments in knowledge evaluation or application of training programs by the health care professionals in some settings (38).

In the current study, older patients, those living in urban areas, employed patients, and type 2 diabetics were more knowledgeable regarding foot care. Different findings have been observed in other similar studies. In Tabuk (Saudi Arabia), only employment status was significantly associated with knowledge about foot care (32). In Iraq (2018) (39), obese subjects, smokers, those with inadequate glycemic control, patients living in urban area, and low or high socio-economic status patients were more knowledgeable about diabetic foot care. In Ethiopia (2021), only history of retinopathy was significantly associated with good knowledge (37).

In the present study, the main sources of information about foot care among diabetic patients were health staff and internet/social media. Furthermore, patients who obtained their information about foot care from internet/social media or health staff were more knowledgeable regarding foot care. This result supports the vital role that could be played by healthcare workers in improving the diabetic patients` knowledge about foot care.

In accordance with other Saudi studies carried out in Tabuk (32), and Dammam (33), most of the diabetic patients did not regularly walk barefoot, did not add irritants to water before foot washing, did not clean nails with sharp instruments and did not wear elasticated hosiery. However

instruments and did not wear elasticated hosiery. However better practice regarding inspection and washing feet with warm water regularly have been observed in the present study compared to the before mentioned studies.

In the present study, overall, 42.1% of the diabetic patients expressed good foot care-related practice compared to none in another Saudi study carried out in Tabuk (32), 39% among diabetic patients in Ethiopia (37) and 50.4% in a study carried out in Iran (40). Furthermore, only 17.4% expressed poor foot care-related practice. Higher rates were reported in other countries such as Malaysia (61.8%) (41).

Finding an association between level of foot care knowledge and that of foot care-related practice in the present study is confirmed by others (32, 36, 39, 40).

In the present study, factors associated with better foot care-related practice among diabetic patients were Saudi nationality, higher education, employment status, having higher family income and having information about foot care from health staff. In Ethiopia (2021), female gender, age between 21 and 50 years were more likely to express good practice while singles, those living in rural areas and those with no co-morbidities were more likely to express poor practice (37). In Iran (34), place of residence, marital status, and history of hospital admission due to diabetic foot were significantly associated with foot care good practice.

In Riyadh, Saudi Arabia (2020), there was significant difference between male and female patients concerning regular self-inspection of feet and daily moisture (22). In Pakistan (2018), education of the respondents had significant association with practices regarding foot care (42).

Limitations
Limitations of the present study include being a cross-sectional which provides only association and not causality; it is also lacking some important issues such as role of family support and glycemic control. Despite those limitations, it has a public health importance in exploring this important issue in our community which is characterized by high prevalence of diabetes complications.

Conclusion

Relative suboptimal levels of both knowledge and practice related to foot care were observed among diabetic patients attending primary health care centers in Taif city, Saudi Arabia. Older patients, those living in urban areas, employed, type 2 and patients who had their information about foot care from internet/social media or health staff were more knowledgeable. Saudi patients, higher educated patients, employed, those with higher family income and those who had their information about foot care from health staff were more likely to express better practice related to foot care. Educational programs at primary healthcare centers, as well as diabetic centers and hospitals in Taif for diabetic patients, should be implemented. These programs should focus on various aspects of diabetic foot care to increase their awareness of the problem.

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Prevalence and quality of life of secondary school students with acne vulgaris in Riyadh, Saudi Arabia

Khalid A. Bin Abdulrahman[1], Mohammed Abdullah Almudawi [2], Saud Turki Alhazani [2], Fahad Shaker Alshehri [2], Khaled Abdulsalam Almodeth [2], Ali Thabet Alanazi [2].

(1) Department of medical education, College of Medicine, Imam Mohammad Ibn Saud Islamic University, Riyadh, Saudi Arabia.
(2) College of Medicine, Imam Mohammad Ibn Saud Islamic University, Riyadh, Saudi Arabia.

Correspondence:
Khalid Bin Abdulrahman, MD, ABFM, MHSc (MEd)
Professor of Family Medicine & Medical Education
College of Medicine, Imam Mohammad Ibn Saud Islamic University (IMSIU)
P.O. Box: 7544 – Othman Bin Affan Rd, Al-Nada, Riyadh 13317 – 4233, Saudi Arabia
Mobile: +966 505445384
Email: kab@imamu.edu.sa

Abstract

Background: Acne vulgaris is one of the most common dermal medical conditions that affect adolescents and young adults. The psychosocial impacts of acne appear in terms of social, vocational, and academic performance. This study aimed to determine the self-reported prevalence of acne and its repercussions on the quality of life of high and secondary school pupils in Riyadh region of Saudi Arabia.

Methodology: This cross-sectional study was conducted among secondary and high school students in Riyadh, Saudi Arabia. The study was conducted among 901 students from different schools in the Riyadh region who were randomly included using a questionnaire distributed online. The Cardiff Acne Disability Index was used to assess the quality of life of acne students. After collecting the data, MS Excel was used for data entry, cleaning, and coding. SPSS version 23 (SPSS Inc, Chicago, IL, USA) was used for data analysis.

Results: The prevalence of acne among students was 57.4 %. According to the Cardiff Acne Disability Index, 19.4 % of patients with acne had a high disability, 40.1 % had a moderate disability, and 40.5 % had a low disability. The index score in this study ranged from 0 (16 patients showed a score of zero with a percentage of 3.1%) to 15 (16 patients showed a score of 15 with a percentage of 3.1%) with a mean score of 6.15 (standard deviation=3.79).

Conclusion: This study confirmed the results of previous studies that acne causes quality of life disabilities among school-age students. Our study showed a high prevalence of acne among students with a more significant negative impact than previous studies.

Keywords: Acne vulgaris, teens, quality of life, Saudi Arabia

Background

Acne vulgaris is one of the most common dermal medical conditions that affect adolescents and young adults [1]. The causes of acne vulgaris are related to many factors that influence its etiology, associated with genetic and environmental factors [2]. According to community base studies conducted during the last decade, the prevalence of acne ranged between 49.8 % and 93.2 % of school students [3]. Furthermore, approximately 14 % of dermatologist consultations were related to acne problems [4]. Clinically, acne is known as a wide range of skin lesions, including papules, comedones, pustules, nodules, and scars [5]. Acne is a chronic multifactorial inflammatory skin disease of the pilosebaceous unit [6].

Acne vulgaris is a benign condition that can resolve spontaneously without needing treatment. However, it has a significant psychological impact on affected individuals, negatively affecting their quality of life (QoL) [7]. Many previous studies conducted to assess the psychosocial impact of acne showed great dissatisfaction with their appearance, a high level of embarrassment, a high level of self-consciousness, and lack of self-confidence among patients with acne [8,9]. High morbidity of psychological events was reported among patients with acne; minor cases can lead to mortality due to suicide [10,11]. The psychosocial impacts of acne appear in terms of social, vocational, and academic performance. Patients with acne may have a poor self-body image, high anxiety, depression, anger, frustration, low self-esteem, confidence, social isolation, and restriction of activities [12].

Acne patients also reported social dysfunction, including concerns regarding social interaction with the opposite gender, their appearance, interactions with strangers, and fair employment opportunities [13,14]. The levels of social, psychological, and emotional impairment that have been reported among acne patients may be similar to those reported in some chronic diseases, including asthma, epilepsy, diabetes, and arthritis, and do not necessarily have a positive correlation with dermatological damage and real cosmetic problems [15]. Therefore, it is crucial to evaluate the effect of acne on quality of life.

Furthermore, adolescents were more likely to be affected by the psychosocial effects of acne than older patients [16]. Many young patients with acne may suffer for years before seeking effective therapy, and most may not seek professional advice for managing acne [17]. However, effective acne treatment has been reported to improve QoL [18].

Few studies have been conducted to assess the quality of life of young patients with acne in Saudi Arabia. These studies did not show significant differences in beliefs, perceptions, and psychological impact of acne in patients from a developing society compared to more developed countries [9,19]. This study aimed to determine the self-reported prevalence of acne and its repercussions on the quality of life in high and secondary school students in Riyadh region, Saudi Arabia.

Methodology

Study design
This cross-sectional study was conducted among secondary and high school students in the Al Riyadh region of Saudi Arabia.

Study Population and Samples
The study was carried out among 901 students from different schools in the Al Riyadh region who were randomly included using a questionnaire distributed online. Inclusion criteria included high- or secondary-school students, aged between 12-19 years, of both genders, residents of Riyadh region, and who agreed to participate in the study. Those who are from outside the Al Riyadh region were excluded. Furthermore, participants who reported having no acne were excluded from the continuous questionnaire; however, they entered the study to assess the prevalence of acne.

Study questionnaire
In this study, we used a questionnaire consisting of two parts. Part one focused on the demographic factors of the participants, including age (categorized as 12-13, 14-15, 16-17, and 18-19), gender (male, female), educational level (from 7th grade to 12th grade), nationality (Saudi, Non-Saudi), family history of acne (Yes, No), duration of acne (<1 year, >=1 year) and if they take medication for acne (yes, no). Part two consisted of The Cardiff Acne Disability Index, which assessed the quality of life of students with acne. It is a simple 5-item questionnaire designed by Motley and Finlay in 1992. According to the design of the tool, the students were divided into three categories, students with low disability (0-4), moderate disability (5-9), and students with high disability (10-15) due to acne. Scores range from 0 to 15, and the higher the score, the more impaired the quality of life of the adolescent. The tool is available in different languages with full linguistic validation, and the Arabic version was used in this study [20].

The study was carried out after the agreement from the ethics committee of Imam Mohammad Ibn Saud Islamic University. All students were informed about the purpose of the study, and no personal data was collected. Data were stored on a private computer and used only for this study.

Statistical analysis:
After collecting the data, MS Excel was used for data entry, cleaning, and coding. SPSS version 23 (SPSS Inc, Chicago, IL, USA) was used for data analysis. Frequency and percent were used for categorical variables, while mean and standard deviation were used for describing continuous variables. The Chi Square test was used to determine the relationship between demographic factors and Cardiff Acne Disability Index. All statements are considered significant if the p-value equals or exceeds 0.05.

Results

In this study, we collected data from 901 students from the Al Riyadh region, Saudi Arabia. The prevalence of acne among students was 57.4 % of students (N=517) (Figure 1).

Among acne patients, 61.5 % were between 18-19 years of age, while 28.6 % were between 16-17 years of age. Furthermore, 79.5 % of the participants were women, while 20.5 % were males. Considering the level of education, the majority of participants were in 12th grade (47.7), and 93.2 % were Saudi Arabian. Furthermore, 42.6 % of participants with acne reported having a family history, and 60.3 % reported having acne for more than a year. Among the participants, 40.2 % reported having acne medications at the study time (Table 1).

According to the Cardiff Acne Disability Index, 19.4 % of acne patients had high disability levels, while 40.1 % had a moderate disability and 40.5 % had a low disability (Figure 2). The index score ranged in this study from 0 (16 patients showed a score of zero with a percentage of 3.1%) to 15 (16 patients showed a score of 15 with a percentage of 3.1%) with a mean score of 6.15 (standard deviation=3.79).

We could not find a significant correlation between any of the demographic factors and the disability of patients due to acne (Table 2). However, it was found that younger patients showed a higher disability caused by acne than older ones, where 38.5 % of those aged 12-13 years had a high disability compared with 17.6 % of those with 18-19 years. Furthermore, we found that women showed slightly higher disability scores than men, where 43.4 % of males showed low disability compared with 39.8 % of females; however, the difference is insignificant (P=0.205). Similarly to age, progress during the education stages decreases the disability caused by acne. Furthermore, non-Saudi patients showed slightly higher levels of disabilities, where 31.4 % of non-Saudi patients showed low disability compared to 41.2 % of Saudi Arabian. Having a family history of acne, duration of acne, or administration of acne medications did not have a significant effect on the disability index of patients.

Figure 1: The prevalence of acne among school age students

42.60%

57.40%

■ Patients with acne   ■ No acne
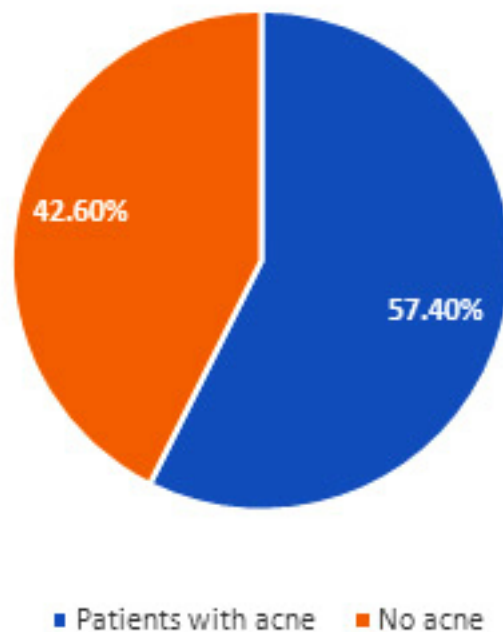
Table 1: Demographic factors of patients with acne (N=517)

		Count	Column N %
Age	12-13	26	5.0%
	14-15	25	4.8%
	16-17	148	28.6%
	18-19	318	61.5%
Gender	Male	106	20.5%
	Female	411	79.5%
Educational level	7th grade	21	4.1%
	8th grade	8	1.5%
	9th grade	16	3.1%
	10th grade	26	5.0%
	11th grade	34	6.6%
	12th grade	412	79.7%
Nationality	Saudi	482	93.2%
	Non-Saudi	35	6.8%
Family history of acne	Yes	220	42.6%
	No	297	57.4%
Duration of acne	≤1 year	205	39.7%
	>1 year	312	60.3%
The current administration of acne medication	Yes	208	40.2%
	No	309	59.8%

Figure 2: The disability because of acne according to The Cardiff Acne Disability Index
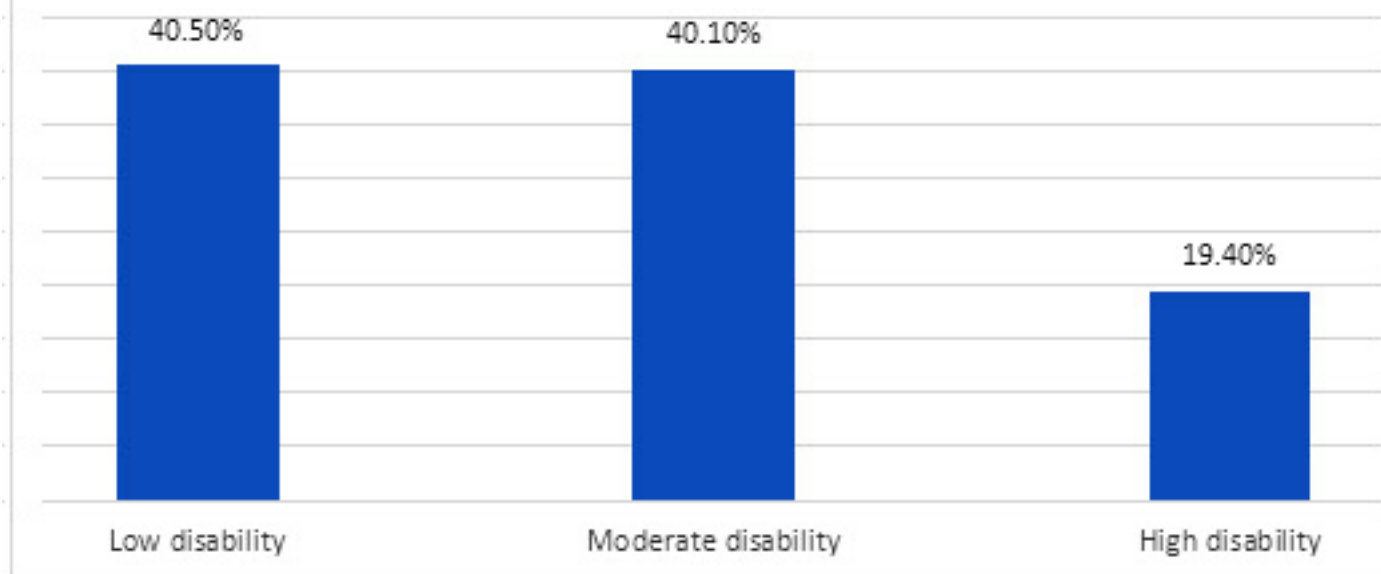
Table 2: The relationship between QoL among acne patients with demographic factors

		QoL						
		Low disability		Moderate disability		High disability		
		N	N %	N	N %	N	N %	
Age	12-13	7	26.9%	9	34.6%	10	38.5%	0.118
	14-15	8	33.3%	13	54.2%	3	12.5%	
	16-17	64	43.2%	53	35.8%	31	20.9%	
	18-19	130	40.9%	132	41.5%	56	17.6%	
Gender	Male	46	43.4%	35	33.0%	25	23.6%	0.205
	Female	163	39.8%	172	42.0%	75	18.3%	
Educational level	7th grade	7	33.3%	7	33.3%	7	33.3%	0.427
	8th grade	3	37.5%	3	37.5%	2	25.0%	
	9th grade	6	37.5%	8	50.0%	2	12.5%	
	10th grade	8	32.0%	13	52.0%	4	16.0%	
	11th grade	14	41.2%	9	26.5%	11	32.4%	
	12th grade	171	41.5%	167	40.5%	74	18.0%	
Nationality	Saudi	198	41.2%	191	39.7%	92	19.1%	0.524
	Non-Saudi	11	31.4%	16	45.7%	8	22.9%	
Family history of acne	Yes	88	40.0%	87	39.5%	45	20.5%	0.524
	No	121	40.9%	120	40.5%	55	18.6%	
Duration of acne	≤1 year	82	40.0%	80	39.0%	43	21.0%	0.752
	>1 year	127	40.8%	127	40.8%	57	18.3%	
The current administration of acne medication	Yes	89	42.8%	82	39.4%	37	17.8%	0.623
	No	120	39.0%	125	40.6%	63	20.5%	

Discussion

Acne is considered one of the most prevalent chronic skin disorders, primarily caused by inflammation that causes increasing sebum production in the pilosebaceous unit [2–4]. In this study, our objective was to assess the prevalence of acne, as well as the effects of acne on quality of life in the age group of 12-19 years. According to the students' self-reporting, the prevalence of acne in our study is 57.4 %, higher than reported in a previous study conducted among teenage females in Makkah, with a prevalence of 45.7 % [21]. Furthermore, a previous study conducted among students of both genders in Australia showed that the overall prevalence of acne was 36.1 % [22]. Moreover, another study conducted in the northern region of Saudi Arabia showed that the prevalence of acne among students was 53.5 % [23].

Furthermore, in a previous study conducted in Turkey, the authors found that the prevalence of acne among high school students was 23.1 % [24]. Again, our prevalence of acne was lower than the previous study conducted in the Riyadh region, where acne vulgaris among adolescents was 68.2 %, and the mean age of onset was 15.5 years [25]. In addition, other reports showed a higher prevalence of acne among school-aged students, between 70.0 % and 90 % [12,26,27]. On the other hand, our results follow a previous study conducted in Greece, with a prevalence of 59.2 % [28].

In our study, we found that women represented a higher percentage of acne patients, with 79.5% of female patients. This is different to the results of other studies, which showed that the prevalence of acne is more frequent among boys than girls [17,29,30]. The difference in the results considering the higher female percentage of acne patients could be due to our study depending on a self-reported questionnaire distributed online. Thus, the distribution of women/men could not be associated with the actual distribution among patients. Furthermore, in our study, almost two-thirds of students with acne (60.3%) of both genders reported more than one year of acne duration. A study in Japan showed that 23.4 % of adolescents with acne reported acne for 1-2 years, and 29.5 % reported more than two years [31].

Skin disease, including acne vulgaris, is associated with many consequences that may significantly affect patients' quality of life. The effect of acne on quality of life has been investigated for the past 30 years. In this study, we relied on the Arabic version of the CADI questionnaire. In our study, the Arabic version of the tool showed Cronbach's alpha of 0.82, which is similar to Cronbach's alpha of other tool translations [29]. This finding indicates that the Arabic version of the CADI questionnaire

is reliable for measuring acne-causing disabilities among the Arabic-speaking population. Furthermore, the questionnaire consists of 5 questions that are easy to administer, could be used among young participants aged 12-19 years, and could be used as a practical tool in routine clinical practice. In our study, the mean Cardiff acne disability index was 6.15 (3.79), which is significantly higher than other previous studies, including the study by Peric J et al., who reported a mean score of 2.9 [29], a previous study conducted in 2012 in Serbia which showed a CADI score of 3.6 [32] and another study conducted in Scotland which reported a score of 1.9 [26].

Another study by Alfalogy et al. in Makkah, Saudi Arabia, showed that the mean CADI was 4 ± 2.3 [21]. A survey by Bajawia S et al. among adolescent students in the Jazan region, Saudi Arabia, showed mean and median scores are 5.4 and 5.0, respectively, for women and males [3]. Furthermore, in our study, 19.4 % of patients with acne had a high disability, 40.1 % had a moderate disability, and 40.5 % had a low disability. In a previous study, the authors reported that 56.7 % of the participants had a mild disability due to acne, 30 % had a moderate disability, and 13.3 % had a severe disability [21]. Moreover, another study showed that 17.2 % of participants had high disability scores [3]. This indicates that acne had a significant effect on their well-being. In another study conducted in Malaysia, the authors reported that 1.8 % of the participants scored 13 on the CADI tool, which meant severe impairment [33].

Furthermore, other studies showed that 20 % of students with acne had moderate to severe effects of acne in terms of affecting their quality of life [26,32]. These results indicated that teenagers are mildly affected by acne in their lives. However, our results showed a higher prevalence of students who reported high disabilities.

Limitations
This study has some limitations, including the requirement of using a self-reported questionnaire, which could lead to personal bias. Some students may not be able to determine their conditions, which can lead to an increase in the prevalence of acne in this study. Furthermore, most participants were older, which may be due to the use of online means, which are easier to use by older adolescents than younger ones. Additionally, the study relies on some information from previous months, which may lead to some recall bias.

Conclusion

In conclusion, this study confirmed the results of previous studies that acne causes quality of life disabilities among school-age students. Our study showed a high prevalence of acne among students with a more significant negative impact than previous studies.

Authors' Contributions:
All authors participated in the concept and design, analysis and interpretation of the data, drafting and revising of the article, and have seen and approved the final version of th manuscript.

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All data supporting the study findings are contained in this manuscript.

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The authors declare that they have no conflict of interest.

Ethical considerations
The institutional review board approved the study at Imam Mohammad Ibn Saud Islamic University (project number 244-2022; approval date, 08 May 2022). All writing is done in accordance with the ethical principles of the Declaration of Helsinki. A brief description of the study was included with the survey link, with a full explanation on the front page. Participants were told that consent was given by filling out the survey. Throughout the study, the consent of all participants and the data were collected in complete confidence.

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What a lower prevalence of diabetes mellitus but higher incidence of dyslipidemia in smokers

Mehmet Rami Helvaci[1], Ali Rıza Ozer[2], Ayse Ceylan[2], Merve Zengin[3],
Abdulrazak Abyad[4], Lesley Pocock[5]

(1) Specialist of Internal Medicine, MD, Turkey
(2) Manager of Writing and Statistics, Turkey
(3) Ministry of Health of Turkey, MD, Turkey
(4) Middle-East Academy for Medicine of Aging, MD, Lebanon
(5) Medi-WORLD International, Australia

Corresponding author:
Mehmet Rami Helvaci, MD
07400, ALANYA, Turkey
Phone: 00-90-506-4708759
Email: mramihelvaci@hotmail.com

Abstract

Background: We tried to understand whether or not there is a relationship between smoking and diabetes mellitus (DM).

Methods: Current regular smokers for the last six months and age and sex-matched non-smokers were included. Patients with current alcohol consumption (one drink a day) and patients with malignancies or inflammatory, infectious, or devastating disorders were excluded.

Results: The study included 247 smokers and 167 non-smokers. The mean age and body mass index (BMI) of smokers were 46.2 years and 26.6 kg/m2, respectively, and 70.0% of them were male. Although the mean weight, BMI, systolic and diastolic blood pressures, and hematocrit values were similar in both groups, fasting plasma glucose (FPG) and DM were lower in the smokers (102.3 versus 111.6 mg/dL, p=0.007 and 8.9% versus 14.3%, p<0.05, respectively). Similarly, high density lipoproteins (HDL) were lower in the smokers, again (40.9 versus 44.0 mg/dL, p<0.05). On the other hand, triglycerides (163.1 versus 151.3 mg/dL, p<0.05) and low density lipoproteins (LDL) (123.8 versus 117.5 mg/dL, p<0.05) were higher in the smokers. Parallel to triglycerides and LDL, erythrocyte sedimentation rate (ESR) (10.6 versus 9.3 mm/h, p<0.05) and C-reactive protein (CRP) (2.3 versus 2.0 mg/L, p<0.05) were also higher in them.

Conclusion: Smoking-induced low-grade inflammation on vascular endothelium in whole body may terminate with the endothelial dysfunction, accelerated atherosclerosis, end-organ insufficiencies, early aging, and premature death. FPG and HDL may be negative whereas triglycerides, LDL, ESR, and CRP positive acute phase reactants terminating with lower prevalence of DM but higher incidence of dyslipidemia in smokers.

Key words: Smoking, fasting plasma glucose, diabetes mellitus, high density lipoproteins, triglycerides, low density lipoproteins, dyslipidemia

Introduction

The monolayer of endothelial cells that forms the inner lining of arteries, veins, capillaries, and lymphatics is called as the endothelium. Probably, the whole endothelium all over the body may act as a separate organ that may be the largest organ in the body. It may contract vasculature of the peripheral organs while relaxing the internal ones during cold, anxiety, and depression-like stresses of the body. Because we measure the systolic and diastolic blood pressures (BP) of the arms and legs, they may not show the actual BP of the brain, heart, lung, liver, and kidney-like internal organs. The endothelium may be the main organ in the control of blood fluidity, platelets aggregation, and vascular tone all over the body. It may also be the main organ in the immunology, inflammation, angiogenesis, and endocrinology. The endothelium may control vascular tone and blood flow by releasing nitric oxide, reactive oxygen species, and metabolites of arachidonic acid into the circulation. It may also be important for synthesizing of vasoactive hormones such as angiotensin II. An endothelial dysfunction-induced accelerated atherosclerosis all over the body may be the main cause of end-organ insufficiencies, aging, and death. Such a dysfunction may also be important in the development of cancers by preventing clearance of malignant cells by the natural killers in terminal points of the circulation. Similarly, physical inactivity, animal-rich diet, excess weight, higher BP and glucose levels, chronic inflammations, prolonged infections, cancers, smoking, and alcohol may be accelerating factors of the chronic endothelial inflammation and dysfunction terminating with the accelerated atherosclerosis-induced end-organ insufficiencies (1, 2). The much higher BP of the afferent vasculature may be the major accelerating factor by inducing recurrent injuries on the vascular endothelium. Probably, whole afferent vasculature including capillaries are mainly involved in the process. Thus the term of venosclerosis is not as famous as atherosclerosis in the medical literature. Due to the chronic endothelial damage, inflammation, edema, fibrosis, and dysfunction, vascular walls thicken, their lumens narrow, and they lose their elastic natures, those eventually reduce blood flow to the terminal organs, and increase systolic and decrease diastolic BP further. Some of the irreversible consequences of the systemic inflammatory process are obesity, hypertension (HT), diabetes mellitus (DM), cirrhosis, peripheric artery disease, chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD), chronic renal disease (CRD), mesenteric ischemia, osteoporosis, stroke, dementia, other end-organ insufficiencies, early aging, and premature death (3). Although early withdrawal of the accelerating factors may delay terminal consequences, endothelial changes can not be reversed, completely after development of the irreversible end-points due to their fibrotic natures. The accelerating factors and irreversible consequences are researched under the titles of the metabolic syndrome, aging syndrome, and accelerated endothelial damage syndrome in the literature, extensively (4, 5). As some of the well-known components of the syndrome, there may be a significant relationship between smoking and DM, clinically.

Material and Methods

The study was performed in the Internal Medicine Polyclinic of the Dumlupinar University between August 2005 and March 2007. Current regular smokers at least for the last six months were studied. Patients with current alcohol consumption (one drink a day) and patients with inflammatory, infectious, or devastating disorders including eating disorders, malignancies, acute or chronic renal failure, cirrhosis, COPD, hyper- or hypothyroidism, or heart failure were excluded. A routine check up procedure including hemogram, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), fasting plasma glucose (FPG), triglycerides, low density lipoproteins (LDL), high density lipoproteins (HDL), albumin, creatinine, thyroid function tests, hepatic function tests, markers of hepatitis A, B, C, and human immunodeficiency viruses, a urinalysis, a posterior-anterior chest x-ray graphy, and an electrocardiogram was performed. An additional Doppler echocardiogram and/or abdominal ultrasonography were performed just in required cases. Body mass index (BMI) of each individual was calculated by measurements of the Same Physician instead of verbal expressions. Weight in kilograms is divided by height in meters squared (6). Office BP were checked after a 5-minute of rest in seated position with mercury sphygmomanometer. Cases with an overnight FPG level of 126 mg/dL or greater on two occasions or already using antidiabetic medications were defined as diabetics. An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG level between 100 and 125 mg/dL, and diagnosis of cases with a two-hour plasma glucose level of 200 mg/dL or higher is DM (6). Eventually, all smokers were collected into the first, and age and sex-matched non-smokers were collected into the second groups. The mean weight, BMI, systolic and diastolic BP, triglycerides, LDL, HDL, FPG, ESR, CRP, and hematocrit values and prevalence of DM were detected in each group, and compared in between. Mann-Whitney U test, Independent-Samples T test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 247 smokers (74 females and 173 males) and 167 (55 females and 112 males) non-smokers. The mean age and BMI of smokers were 46.2 years and 26.6 kg/m2, respectively, and 70.0% of them were male. Although the mean weight, BMI, systolic and diastolic BP, and hematocrit values were similar in both groups, FPG and DM were lower in the smokers (102.3 versus 111.6 mg/dL, p=0.007 and 8.9% versus 14.3%, p<0.05, respectively). Similarly, HDL were lower in the smokers, again (40.9 versus 44.0 mg/dL, p<0.05). On the other hand, triglycerides (163.1 versus 151.3 mg/dL, p<0.05) and LDL (123.8 versus 117.5 mg/dL, p<0.05) were higher in the smokers. Parallel to triglycerides and LDL, ESR (10.6 versus 9.3 mm/h, p<0.05) and CRP (2.3 versus 2.0 mg/L, p<0.05) were higher in the smokers, again (Table 1).

Table 1: Comparison of smokers and non-smokers

Variables	Smokers	p-value	Non-smokers
Number	247		167
Female ratio	*29.9%*	Ns*	32.9%
Mean age (year)	46.2 ± 13.4 (19-76)	Ns	44.8 ± 15.7 (13-77)
Weight (kg)	76.1 ± 13.8 (44-118)	Ns	74.7 ± 13.0 (45-122)
BMI† (kg/m²)	26.6 ± 4.4 (16.2-39.4)	Ns	26.5 ± 4.5 (16.6-41.1)
Systolic BP‡ (mmHg)	127.5 ± 23.7 (80-200)	Ns	130.0 ± 22.6 (80-200)
Diastolic BP (mmHg)	88.0 ± 12.4 (60-130)	Ns	88.5 ± 11.9 (60-130)
Hematocrit (%)	41.9 ± 4.6 (28-60)	Ns	41.0 ± 3.7 (31-49)
FPG§ (mg/dL)	*102.3 ± 25.5 (70-309)*	*0.007*	111.6 ± 37.6 (74-327)
DM ‖	*8.9%*	*<0.05*	14.3%
*HDL** (mg/dL)*	*40.9 ± 9.6 (26-70)*	*<0.05*	44.0 ± 9.4 (24-70)
Triglycerides (mg/dL)	163.1 ± 101.4 (40-585)	*<0.05*	*151.3 ± 86.2 (20-410)*
*LDL*** (mg/dL)*	123.8 ± 34.3 (10-282)	*<0.05*	*117.5 ± 29.0 (43-185)*
*ESR**** (mm/h)*	10.6 ± 10.2 (1-51)	*<0.05*	*9.3 ± 8.0 (1-35)*
*CRP***** (mg/L)*	2.3 ± 2.6 (0-13)	*<0.05*	*2.0 ± 2.5 (0-12)*

*Nonsignificant (p>0.05)   †Body mass index   ‡Blood pressures   §Fasting plasma glucose   ‖Diabetes mellitus
**High density lipoproteins   ***Low density lipoproteins   ****Erythrocyte sedimentation rate   *****C-reactive protein

Discussion

Obesity may be one of the irreversible end-points of the metabolic syndrome. Although some transient successes can be achieved, nonpharmaceutical approaches provide limited benefit to reverse the obesity, permanently. Due to the excess weight-induced chronic low-grade inflammation on the vascular endothelium all over the body, the risk of death from all causes including cardiovascular diseases and cancers increases parallel to the range of excess weight in all age groups (7). The chronic low-grade inflammation may even cause genetic changes of the endothelial cells, and the systemic atherosclerosis may prevent clearance of malignant cells, effectively. Similarly, the effects of excess weight on the BP were shown in the literature, extensively (8). For example, prevalences of sustained normotension (NT) were higher in the underweight than the normal weight (80.3% versus 64.0%, p<0.05) and overweight groups (80.3% versus 31.5%, p<0.001) (8), and 52.8% of patients with HT had obesity against 14.5% of patients with the sustained NT (p<0.001) (9). So the major underlying cause of the metabolic syndrome appears as weight gain that may be the main cause of insulin resistance, hyperlipoproteinemias, impaired fasting glucose, impaired glucose tolerance, and white coat hypertension (WCH) (10). Interestingly, weight gain before the development of an obvious overweight or obesity may even cause development of several components of the metabolic syndrome. For example, WCH alone may be a strong indicator of weight gain even before development of excess weight (8, 9). On the other hand, prevention of the weight gain with physical activity even in the absence of a prominent weight loss usually results with resolution of many parameters of the syndrome (11). According to our experiences, excess weight may actually be a result of physical inactivity instead of an excessive eating habit. In

another words, there is a problem with burning of calories instead of getting them. Therefore prevention of weight gain cannot be achieved by diet, alone (12). On the other hand, limitation of excess weight as excessive fat tissue around the abdomen under the heading of abdominal obesity may be meaningless. Instead it should be defined as overweight or obesity via the BMI. Because adipocytes function as an endocrine organ, and they release leptin, tumour necrosis factor (TNF)-alpha, plasminogen activator inhibitor-1, and adiponectin-like cytokines into the plasma (13). Eventual hyperactivities of sympathetic nervous system and renin-angiotensin-aldosterone system are probably associated with insulin resistance, elevated BP, and chronic endothelial inflammation and dysfunction. Similarly, the Adult Treatment Panel (ATP) III reported that although some people classified just as overweight with larger muscular masses, most of them also have excess fat tissue predisposing to the irreversible end-points of the metabolic syndrome (6).

Smoking may be the second common cause of systemic vasculitis in the world. It is one of the major risk factors for the atherosclerotic end-organ insufficiencies (14). Its atherosclerotic effect is the most obvious in Buerger's disease. Buerger's disease is an obliterative vasculitis characterized by inflammatory changes in the small and medium-sized arteries and veins, and it has never been reported in the absence of smoking in the medical literature. Beside the obvious atherosclerotic effects of smoking, some studies reported that smoking in human being and nicotine administration in animals are associated with the lower values of BMI (15). Some evidence revealed increased energy expenditure during smoking, both at rest and doing light physical activity (16). Nicotine supplied by patch after smoking cessation decreased caloric intake in a dose-related manner (17). According to an animal study,

nicotine may lengthen inter-meal time, and decrease amount of meal eaten (18). Similarly, the BMI seems to be the highest in the former, the lowest in the current, and medium in never smokers (19). Smoking may be associated with a post cessation weight gain, but the risk is the highest during the first year, and decreases with the following years (20). As the opposite findings to the above studies, the mean weight and BMI were similar both in the smokers and non-smokers, here (p>0.05 for both). Similarly, prevalence of smoking was similar in the normal weight (35.9%), overweight (32.9%), and obesity groups (33.7%, p>0.05 between all) in the other study (21). On the other hand, although the CHD was detected with similar prevalence in both genders, prevalence of smoking and COPD were higher in males against the higher BMI, LDL, triglycerides, WCH, HT, and DM in females (22). Beside that the prevalence of myocardial infarctions is increased three-fold in men and six-fold in women who smoked at least 20 cigarettes per day (23). In another words, smoking may be more dangerous for women about the atherosclerotic end-points probably due to the higher BMI and its consequences in them. Similar to the present study, smoking is consistently higher in men in the literature (14). Several toxic substances found in the cigarette smoke get into the circulation, and cause a vascular endothelial inflammation in all organ systems of the body. For example, smoking is usually reported together with depression, irritable bowel syndrome (IBS), chronic gastritis, hemorrhoids, and urolithiasis in the literature (24-26). There may be several underlying mechanisms to explain these associations in the smokers (24). First of all, smoking may have some antidepressant properties with several side effects. Secondly, smoking-induced vascular endothelial inflammation may disturb epithelial functions for absorption and excretion in the gastrointestinal and genitourinary tracts. These functional problems may terminate with urolithiasis and components of the IBS including loose stool, diarrhea, and constipation. Thirdly, diarrheal losses-induced urinary changes may even cause urolithiasis (25, 26). Fourthly, smoking-induced sympathetic nervous system activation may cause motility problems in the gastrointestinal and genitourinary tracts terminating with the IBS and urolithiasis. Eventually, immunosuppression secondary to smoking-induced vascular endothelial inflammation may even terminate with the gastrointestinal and genitourinary tract infections causing loose stool, diarrhea, and urolithiasis, because some types of bacteria can provoke urinary supersaturation, and modify the environment to form crystal deposits in the urine. Actually, 10% of urinary stones are struvite stones which are built by magnesium ammonium phosphate produced during infections with the bacteria producing urease. Parallel to the results above, urolithiasis was detected in 17.9% of cases with the IBS and 11.6% of cases without in the other study (p<0.01) (25).

Alcohol may be the third common cause of systemic vasculitis in the world. Alcohol is addictive to humans, and can result in alcohol use disorder (AUD), dependence, and withdrawal. Alcohol is the only drug that mostly damage the other individuals. It is causally associated with more than 200 different pathologies (27). Eventually, people

hospitalized with AUD have an average life expectancy of 47-53 years in men and 50-58 years in women, and die 24-28 years earlier than the others (28). People with AUD have three-fold higher mortality in men and four-fold in women (29). Similar to the smoking, alcohol may be more dangerous for women about the atherosclerotic end-points probably due to their lower body mass induced lower capacity to metabolize alcohol and higher mass of fat in their body. A very substantial part of the Danish excess mortality and lower life expectancy compared to Sweden can be attributed to higher mortality related with the alcohol and smoking (28). Alcohol is one of the main causes of cancers all over the body (27). It may even cause unconsciousness and sudden death if taken in high amounts. Hepatic alcohol dehydrogenase is the main enzyme to metabolize alcohol that requires the cofactor, nicotinamide adenine dinucleotide (NAD). Normally, NAD is used to metabolize fats in the liver but alcohol competes with these fats for the use of NAD. Eventually, prolonged exposure of alcohol causes fatty liver. Ethanol is the only alcohol that is found in alcoholic beverages. Ethanol crosses biological membranes and blood-brain barrier by means of the passive diffusion, easily. Alcohol works particularly by increasing effects of the gamma aminobutyric acid that is the major inhibitory neurotransmitter in the brain. Alcohol induces happiness and euphoria, decreased anxiety, increased sociability, sedation, generalized depression of central nervous system, and impairment of cognitive, memory, motor, and sensory functions. It may even cause fetal disorders in pregnancy since ethanol is classified as a teratogen. Regular alcohol consumption leads to cell death in the liver, scarring, cirrhosis, and hepatocellular carcinoma. Heavy alcohol consumption may even terminate with permanent brain damage. Alcohol is a major contributing factor of elevated triglycerides, and triglycerides behave as sensitive acute phase reactants (APR) in the plasma (10). Although the regular alcohol consumers were excluded, plasma triglycerides were higher in the smokers in the present study (163.1 versus 151.3 mg/dL, p<0.05), indicating the inflammatory effects of smoking in the body.

The acute phase response occurs in case of infection, infarction, foreign body, autoimmune disorder, allergy, neoplasm, trauma, and burn-like inflammatory conditions of the body. Certain mediators known as APR are increased or decreased during the response (30, 31). These markers are commonly used in the clinical practice as the indicators of acute and chronic inflammations of the body. The terms of acute phase proteins and APR are usually used synonymously, although some APR are polypeptides rather than proteins. Positive and negative APR are those whose concentrations increase or decrease during the acute phase response, respectively. The response is predominantly mediated by the pro-inflammatory cytokines including TNF, interleukin-1, and interleukin-6 secreted by neutrophils and macrophages into the circulation. The liver and other organs respond to the cytokines by producing many positive APR. ESR, CRP, fibrinogen, ferritin, procalcitonin, hepcidin, haptoglobin, ceruloplasmin, complement proteins, and serum amyloid A are some of the well-known positive APR. CRP is a

useful indicator of the acute phase response, clinically. It is responsible for activation of the complement pathway. CRP reaches up to the maximum concentration within two days, and decreases with the resolution of the inflammation with a half-life of 6-8 hours, rapidly. It correlates with ESR, but not simultaneously since ESR is largely dependent upon elevation of fibrinogen with a half-life of one week, approximately. Thus ESR remains higher for a longer period of time despite the removal of the inflammatory stimulus. Similarly, white blood cells and platelet counts may also behave as some other positive APR in the body (32). On the other hand, productions of the negative APR are suppressed, simultaneously. Albumin, transferrin, retinol-binding protein, antithrombin, transcortin, alpha-fetoprotein, and hemoglobin are some of the well-known negative APR in the body. Suppressions of such negative APR are also used as the indicators of the acute phase response in the body. Suppressions of such negative APR may actually be secondary to the protection of amino acids and polypeptides required for the production of positive APR, sufficiently. As also observed in the smokers in the present study, production of HDL may also be suppressed in the liver during the acute phase response (33). Similarly, triglycerides, DM, and CHD were all higher in patients with plasma HDL values of lower than 40 mg/dL, significantly (33). So HDL may actually behave as negative whereas triglycerides positive APR in the plasma. Similarly, the highest CHD of the group with HDL values of lower than 40 mg/dL can also be explained by the same hypothesis in the other study (10). Additionally, plasma triglycerides increased whereas HDL decreased during infections (34). On the other hand, a 10 mg/dL increase of plasma LDL values was associated with a 3% lower risk of hemorrhagic stroke (35). Similarly, the highest prevalence of HT and DM parallel to the elevated values of LDL and HDL, and the highest prevalence of COPD, CHD, and CRD in contrast to the lowest values of LDL and HDL may show initially positive but eventually negative behaviors of LDL and HDL as the APR (36). Probably, HDL turns to the negative direction much earlier than LDL in the plasma. Interestingly, the most desired values were between 80 and 100 mg/dL for LDL, between 40 and 46 mg/dL for HDL, and lower than 60 mg/dL for triglycerides in the plasma (10). Parallel to ESR and CRP, plasma triglycerides and LDL may behave as positive whereas FPG and HDL negative APR in smokers in the present study. In another words, lower HDL values should alert clinicians for researching of any acute phase response in the body (37, 38).

Cholesterol, triglycerides, and phospholipids are the major lipids of the body. They do not circulate in the plasma, freely instead they are bound to proteins, and transported as lipoproteins. There are five main classes of lipoproteins in the plasma. Chylomicrons carry exogenous triglycerides to the liver via the thorasic duct. Very low density lipoproteins (VLDL) are produced in the liver, and carry endogenous triglycerides to the organs. VLDL are converted into the intermediate density lipoproteins (IDL) by removal of 90% of triglycerides by lipases in the capillaries of adipocytes and muscle tissues. Then the IDL are degraded into LDL

by removal of more triglycerides. So VLDL are the main source of LDL in the plasma, and LDL deliver cholesterol from the liver to organs. Although the liver removes majority of LDL from the circulation, a small amount is uptaken by scavenger receptors of the macrophages migrating into the arterial walls, and become the foam cells of atherosclerotic plaques. HDL remove fats and cholesterol from cells including the arterial wall atheroma, and carry the cholesterol back to the adrenals, ovaries, and testes-like steroidogenic organs and liver for excretion, re-utilization, or disposal. All of the carrier lipoproteins are under dynamic control, and are readily affected by diet, drug, chronic inflammation, prolonged infection, cancer, tissue damage, smoking, alcohol, and excess weight. Thus lipid analysis should be performed during a steady state. But the metabolic syndrome alone is a low grade inflammatory process, thus the metabolic syndrome may even cause abnormal levels of lipoproteins in the plasma. For instance, HDL may normally show various anti-oxidative, anti-inflammatory, and anti-atherogenic properties including reverse cholesterol transport (39). However, HDL may become 'dysfunctional' in pathologic conditions which means that relative compositions of lipids and proteins, as well as the enzymatic activities of HDL are altered (39). For example, properties of HDL are compromised in patients with DM by means of the oxidative modification, glycation, and/or transformation of HDL proteomes into the proinflammatory proteins. Additionally, the drugs increasing HDL values such as niacin, fibrates, and cholesteryl ester transfer protein inhibitors can not reduce all cause mortality, CHD mortality, myocardial infarction, and stroke (40). In another words, HDL may just be some indicators instead of being the main actors of the health. Similarly, BMI, DM, and CHD were the lowest between the HDL values of 40 and 46 mg/dL, and the prevalence of DM was only 3.1% between these values against 22.2% outside these limits (41). Similar to the present study, HDL and FPG values were also suppressed in the sickle cell diseases (SCD), probably due to the severe inflammatory nature of the diseases (42). Smoking may reduce HDL and FPG by means of the systemic inflammatory effects on the vascular endothelium all over the body. On the other hand, triglycerides alone may be one of the most sensitive APR indicating the metabolic syndrome (43). Although ATP II determined the normal plasma triglycerides as lower than 200 mg/dL in 1994 (44), World Health Organisation in 1999 (45) and ATP III in 2001 reduced the normal limits as lower than 150 mg/dL (6). Although these cutpoints, there are still suspicions about the safest values of triglycerides in the plasma (43). Beside that triglycerides are the only lipids which were not suppressed with the pathological weight losses (46). For example, plasma triglycerides increased in contrast to the suppressed body weight and BMI in the SCD (46). Similarly, prevalences of excess weight, DM, HT, and smoking were all higher in the hypertriglyceridemia group (200 mg/dL and higher) in the other study (47). Interestingly, the greatest number of deteriorations in the metabolic parameters was observed with the triglycerides values of 60 mg/dL and higher (43).

The body's homeostatic mechanism keeps blood glucose levels within a narrow range with two groups of mutually antagonistic hormones. Glucagon, cortisol, and catecholamines are the catabolic hormones increasing the blood glucose, whereas insulin is the anabolic hormone decreasing the blood glucose levels. Glucagon is secreted from the alpha cells, while insulin is secreted from the beta cells of pancreatic islets which are the bundles of endocrine tissues. They regulate the blood glucose levels through a negative feedback mechanism together. When the blood glucose levels are too high, insulin tells muscles to take up excess glucose for storage. When the blood glucose levels are too low, glucagon informs the tissues to produce more glucose. Catecholamines prepare the muscles and respiratory system for a 'fight to fight' response. Cortisol prepares the body for the various stresses. A blood glucose level of four grams, or about a teaspoon, is critical for the normal function of millions of cells in the body (48). The four grams of glucose circulates in the blood stream of a person with the body weight of 70 kg. This amount is kept constant with a sophisticated control mechanism in the body. The constant blood glucose levels are maintained via the hepatic and muscular glycogen stores during fasting since glucose is stored in the skeletal muscles and hepatocytes in the form of glycogen. There are approximately 100 and 400 grams of glycogen stored in the skeletal muscles and liver, respectively (48). The brain consumes about 60% of the blood glucose during fasting. FPG, which is measured after a fasting period of 8 hours, is the most commonly used indication of overall glucose homeostasis. Infections, inflammations, surgical operations, depressions, alcohol, and smoking-like stresses may affect the blood glucose homeostasis. For instance, smoking was negatively associated with FPG and DM in Chinese men with the normal weight, but not in men with excess weight or in women (49). Similarly, smokers have a lower likelihood of newly-diagnosed DM in Chinese men with a lower BMI in the other study (50). Parallel to the above studies, FPG and DM were also lower in the smokers, here (102.3 versus 111.6 mg/dL, p=0.007 and 8.9% versus 14.3%, p<0.05, respectively). Although majority of the smokers were male again (70.0%), the mean BMI of the smokers was higher (26.6 kg/m2) in contrast to the above studies.

As a conclusion, smoking-induced low-grade inflammation on the vascular endothelium all over the body may terminate with the endothelial dysfunction, accelerated atherosclerosis, end-organ insufficiencies, early aging, and premature death. FPG and HDL may be negative whereas triglycerides, LDL, ESR, and CRP positive acute phase reactants terminating with lower prevalence of DM but higher incidence of dyslipidemia in the smokers.

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Prevalence of Psychological distress among medical students in different levels of training and other associated factors in Riyadh

Khalid A. Bin Abdulrahman [1,] Abdulrahman Omar Ahmed Alomar[2],
Rayan Ahmed Nasser Alghamdi[2], Ahmed Farhan Ayfan Alanazi[2], Hamoud Meshal
Hamoud Almutairi[2], Faisal Abdulaziz Hamdan Altoom[2], Hussam Saeed Alzahrani[2]

(1) Department of medical education, College of Medicine, Imam Mohammad Ibn SaudIslamic University, Riyadh, Saudi Arabia.
(2) College of Medicine, Imam Mohammad Ibn Saud Islamic University, Riyadh, Saudi Arabia.

Corresponding author:
Khalid A. Bin Abdulrahman
Professor of Family Medicine & Medical Education,
Professor Chair, Dr. AlKholi Chair for Developing Medical Education in Saudi Arabia,
Imam Mohammad Ibn Saud Islamic University (IMSIU)
P.O Box: 7544 - Othman Bin Affan Rd. Al-Nada, Riyadh 13317- 4233
Mobile: +966505445384
Email: kab@imamu.edu.sa

Abstract

Background: Medical school is commonly perceived as a demanding environment that can negatively affect a student's academic performance, physical fitness, and mental well-being. According to a study, 23 percent of undergraduate clinical college students in the United States had clinical depression, and 57 percent were under mental stress. Our main aim of this study is to assess the mental health of medical students in different levels of training to see if a certain level plays a higher role in developing mental health issues.

Methodology: This quantitative study is a descriptive cross-sectional study conducted among medical students in different universities in Riyadh region. The study depended on a self-reported questionnaire that included validated GHQ-12 for the Arab population that was used for assessing psychological distress.

Results: In the current study, we collected data from 617 medical students from four universities in Riyadh region, Saudi Arabia. Among the students, 56.7 % of the participants were males, and 42.1 % were aged between 20-21 years old, and 91.6 % of them were single. According to the GHQ-12, 368 students were classified as GHQ- cases having symptoms of depression and psychiatric disorders (59.6 %). The prevalence of psychological distress among female students was significantly higher than among males (68.9 % vs. 52.6 %, P=0.000). Furthermore, we found that the prevalence of distress was the lowest among students who reported higher than 30000 SR monthly income (P=0.015). Concerning educational level, the results of the current study did not show any significant difference in the prevalence of distress among students of different levels (P=0.096); however, students of the first level showed the highest level of distress (72.2 %).

Conclusion: The current study confirmed the previous studies on the high prevalence of psychological distress among medical students, which was significantly higher among females, students of low income, and students with lower GPAs. Moreover, the study showed that first-level students were the most affected by psychological distress.

Keywords: Mental health, psychological distress, medical students, medical education, Saudi Arabia

Introduction

Medical school is commonly perceived as a demanding environment that can negatively affect a student's academic performance, physical fitness, and mental well-being. According to a study, 23 percent of undergraduate clinical college students in the United States had clinical depression, and 57 percent were under mental stress [1].

Burnout, social isolation, cynicism, and medical doctor impairment are only some of the intense emotional repercussions of intellectual illness. If intellectual fitness problems remain neglected or untreated, they will persist into adulthood. Furthermore, in psychologically and emotionally afflicted clinical college students, harmful coping mechanisms, which include substance misuse, alcohol usage, smoking, and self-and other damage, can be noted [2].

The atmosphere in many clinical colleges creates all-pervasive stressful conditions condition. Students are subjected to an authoritarian, restrictive environment that promotes competitiveness over collaboration among college students [3]. Stressful environments permeate not just the undergraduate schooling period but all through internship, the postgraduate observation period, and even later within the physician's working life [4]. According to well accepted studies, college students' intellectual fitness deteriorates as their education proceeds. As college students progress in their studies, they're much more likely to be subject to burnout [5]. Another observation discovered a better outcome of burnout toward the start of the healing cycle. Except for the last 12 months of observation, carried out at King Saud University in Saudi Arabia, it was observed that the extent of strain dropped as the 12 months of observation progressed. Some strain can assist in gaining knowledge in the clinical faculty. "Favorable strain" is defined as strain that promotes gaining knowledge, whereas "destructive strain" is described as strain that inhibits gaining knowledge.

On this subject, some studies have been undertaken in several situations. These intellectual morbidities are widespread, consistent with an intensive evaluation of the levels of depression, anxiety, and misery amongst clinical college students in North America [4].

We set out to discover the level of intellectual fitness issues and some of their relationships within this cohort because, to our knowledge, there is no published study analyzing intellectual fitness at exceptional levels among Saudi Arabian clinical college students.

Methodology

Study design and sample selection: This is a quantitative study scoped to a descriptive cross-sectional study. Descriptive cross-sectional studies describe the prevalence of one or more health outcomes in a given group. This kind of research is the most effective for determining the prevalence and studying the relationships between numerous exposures and outcomes [7]. This study has been conducted before on a middle eastern sample [3].

Our sample demographic is Saudi Arabia's medical students, specifically in the capital city of Riyadh. The sampling is random, and these institutions were picked based on the number of students enrolled, academic excellence, and popularity among Saudi Arabian universities in Riyadh. The universities chosen were King Saud University, Alfaisal University, Al-imam Muhammad Ibn Saud Islamic University, and King Saud bin Abdulaziz University for Health Sciences, focusing primarily on medical students in different levels of training. After obtaining the IRB, the universities' administration was responsible for distributing the survey through email.

Materials/instruments: Psychological distress was measured on a validated GHQ-12 for the Arab population. The GHQ-12 is a quick, basic, and easy-to-complete assessment, and its use as a screening tool in research contexts is widely established. The instrument consisted of 12 questions, six positively phrased and six negatively worded. On a four-point scale, each item is graded (less than usual, no more than usual, rather more than usual, or much more than usual). The scale asks if the responder has lately encountered a particular symptom or behavior. The answers were coded as 0-3 points, in which higher scores indicate an increase in distress, which leads to a decrease in quality of life. To assess the prevalence of psychological distress, the answers were coded as 0,0,1,1, where participants scoring a mean of more than four are considered "psychiatric cases" [8,9].

Procedure: Between April 2022 and May 2022, it was distributed via a Google forms survey. The medical students were asked to complete the self-rated GHQ-12 questionnaire and a brief questionnaire comprising demographic information such as the university they are attending, their age, gender, GPA, and training level. All participants assured confidentiality and provided consent via the form.

Analysis: The demographic data and GHQ-12 scores were presented using descriptive statistics. Frequency and percent were used to describe categorical variables such as age, gender, marital status, and university level. In contrast, mean and standard deviation were used to describe continuous variables as GHQ-12 results. Statistical tests, such as linear or logistical regression, were utilized depending on the variables to help predict psychological distress. The student's t-test and one-way variance analysis were used for comparison.

Results

In the current study, we were able to collect data from 617 medical students gathered from four universities in Riyadh region, Saudi Arabia, where 27.9 % of the students were from Imam Mohammad Ibn Saud Islamic university, 25.1 % were at King Saud bin Abdulaziz for Health Science University, 24.8 % were at King Saud University, and 22.2 % were at AL Faisal University. Moreover, 56.7 % of the participants were males, 42.1 % were aged between 20 and 21, and 91.6 % were single. Furthermore, 27.4 % of the participants were at the 2nd level, 21.4 % were at the 3rd level, and 15.7 % were at the 1st level. Considering current GPA, 45.9 % of the students reported having a GPA of 4.5 points or more (out of 5), while 30.0 % reported having GPA between 4-4.5 points. Moreover, 38.6 % of the participants reported having a household income of more than 30000 SR (Saudi Riyal), while 12.8 % reported less than 10000 SR (Table 1).

Table 1: Demographic factors of the participants (N=617).

		Count	Column N %
Gender	Male	350	56.7%
	Female	267	43.3%
Age	18-19	86	13.9%
	20-21	260	42.1%
	22-23	177	28.7%
	24 or older	94	15.2%
Marital status	Never married	565	91.6%
	Married	33	5.3%
	Divorced	10	1.6%
	Widowed	9	1.5%
Current educational level	1st year	97	15.7%
	2nd year	169	27.4%
	3rd year	132	21.4%
	4th year	71	11.5%
	5th year	74	12.0%
	Intern	74	12.0%
University	King Saud University	153	24.8%
	Alfaisal university	137	22.2%
	Imam Mohammad Ibn Saud Islamic University	172	27.9%
	King Saud bin Abdulaziz for Health Sciences University	155	25.1%
Current GPA (Grade Point Average) out of 5	Below 2.50	18	2.9%
	2.50 - <3.00	30	4.9%
	3.00 - <4.00	101	16.4%
	4.00 - <4.50	185	30.0%
	4.50 or above	283	45.9%
Household Income	<10000 SR	79	12.8%
	10000 - <20000 SR	148	24.0%
	20000 - <30000 SR	152	24.6%
	>30000 SR	238	38.6%

Among the participants, only 163 students had reported that they had completed any clinical psychiatry rotations before (26.4 %), while 454 students reported never completing any clinical psychiatry rotations before (73.6 %) (Figure 1).

According to the GHQ-12, 368 students were classified as GHQ- cases having symptoms of depression and psychiatric disorders (59.6 %).

Figure 1: Have you completed any clinical psychiatry rotations before?
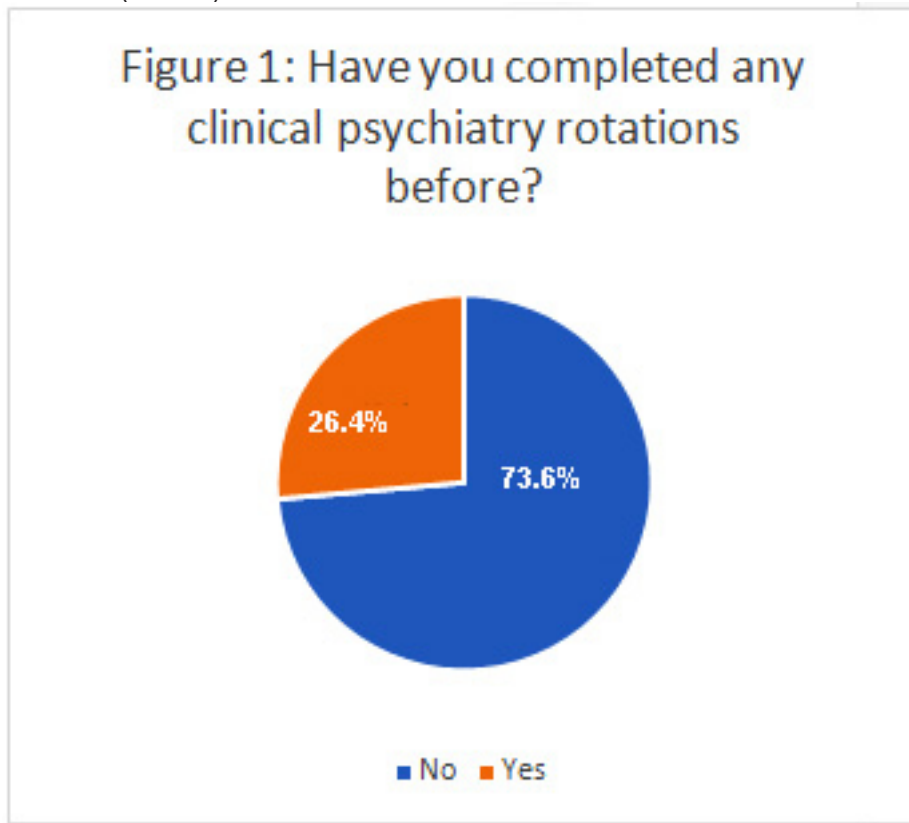
Table 2 shows a significant difference between male and female students in the prevalence of psychological distress (GSQ case), where the prevalence of psychological distress among female students was significantly higher than among males (68.9 % vs. 52.6 %, P=0.000). Moreover, no significant difference was found between students of different ages (P=0.414); however, younger students (18-19 years old) showed the highest prevalence of distress (67.4 %), which reduced to 57.3 % of students aged between 20-21 years and 58.8 % in students aged 22-23 years old and slightly increased to 60.6 % of students older than 24 years old. Furthermore, marital status was found to have no significant impact on the prevalence of distress among students (P=0.119); however, married students showed the highest prevalence (78.8 %). Moreover, it was found that the prevalence of distress was the lowest among students at Imam Mohammad Ibn Saud Islamic University (50.6 %) and the highest among students of AL Faisal university (65.7 %). Furthermore, we found that the prevalence of distress was lowest among students who reported higher than 30000 SR monthly income (P=0.015). Moreover, the prevalence of distress was found to decrease with the increase in GPA of the students ranging between 77.8 % in students with a GPA of below 2.5 to 52.7 % in students who had a GPA of more than 4.5 (P=0.003) (Table 2).

Concerning educational level, the results of the current study did not show any significant difference in the prevalence of distress among students of different levels (P=0.096); however, students of the first level showed the highest level of distress (72.2 %). Completing clinical psychiatry rotations did not affect the prevalence of distress among students (59.5 % vs. 59.7 %, p=0.968) (Table 3). According to Table 4, the prevalence of distress in all students of each level is significantly lower than in level one except for level five. No significant difference in the prevalence of distress was noticed between students of levels two and interns.

Table 2: The relation between demographic factors of the students and the prevalence of psychological distress

| | | GHQ Cases (GHQ ≥ 4) | | | | |
| | | No | | Yes | | P-value |
		Count	Row N %	Count	Row N %	
Gender	Male	166	47.4%	184	52.6%	0.000*
	Female	83	31.1%	184	68.9%	
Age	18-19	28	32.6%	58	67.4%	0.414
	20-21	111	42.7%	149	57.3%	
	22-23	73	41.2%	104	58.8%	
	24 or older	37	39.4%	57	60.6%	
Marital status	Never married	234	41.4%	331	58.6%	0.119
	Married	7	21.2%	26	78.8%	
	Divorced	5	50.0%	5	50.0%	
	Widowed	3	33.3%	6	66.7%	
University	King Saud University	59	38.6%	94	61.4%	0.033*
	AL Faisal university	47	34.3%	90	65.7%	
	Imam Mohammad Ibn Saud Islamic University	85	49.4%	87	50.6%	
	King Saud bin Abdulaziz for Health Sciences University	58	37.4%	97	62.6%	
Household Income	<10000 SR	31	39.2%	48	60.8%	0.015*
	10000 - <20000 SR	55	37.2%	93	62.8%	
	20000 - <30000 SR	49	32.2%	103	67.8%	
	>30000 SR	114	47.9%	124	52.1%	
Current GPA (Grade Point Average) out of 5	Below 2.50	4	22.2%	14	77.8%	0.003*
	2.50 - <3.00	7	23.3%	23	76.7%	
	3.00 - <4.00	31	30.7%	70	69.3%	
	4.00 - <4.50	73	39.5%	112	60.5%	
	4.50 or above	134	47.3%	149	52.7%	

Table 3: The relation between educational level and prevalence of psychological distress

| | | GHQ cases (GHQ ≥ 4) | | | | |
| | | No | | Yes | | P-value |
		Count	Row N %	Count	Row N %	
Current educational level?	1st year	27	27.8%	70	72.2%	0.096
	2nd year	71	42.0%	98	58.0%	
	3rd year	58	43.9%	74	56.1%	
	4th year	33	46.5%	38	53.5%	
	5th year	27	36.5%	47	63.5%	
	Intern	33	44.6%	41	55.4%	
Have you completed any clinical psychiatry rotations before?	No	183	40.3%	271	59.7%	0.968
	Yes	66	40.5%	97	59.5%	

Table 4: Difference between psychological distress between students of different years

	1st year	2nd year	3rd year	4th year	6th year	Intern
1st year	Reference					
2nd year	0.532 [0.31: 0.91], P= 0.022*	Reference				
3rd year	0.492 [0.28: 0.86], P=0.013*	0.924 [0.58: 1.46], P=0.737	Reference			
4th year	0.444 [0.23: 0.84], P=0.014*	0.834 [0.47: 1.45], P=0.524	0.903 [0.51: 1.61], P=0.728	Reference		
5th year	0.67 [0.35: 1.28], P=0.229	1.261 [0.72: 2.22], P=0.419	1.36 [0.76: 2.44], P=0.297	1.512 [0.77: 2.93], P=0.223	Reference	
Intern	0.479 [0.25: 0.91], P=0.024*	0.900 [0.52: 1.56], P=0.708	0.974 [0.55: 1.73], P=0.928	1.07 [0.56: 2.07], P=0.819	0.714 [0.37: 1.37], P=0.316	Reference

Discussion

The general population has always considered medicine a popular tertiary education choice. Moreover, due to excess applicants, only those with excellent academic achievement are successfully accepted to medical schools. Therefore, medical programs are even more competitive and pose a highly stressful environment for accepted students [10]. If this stress is ignored, it will cause further tensions in the students' life [11]. In the current study, we aimed to assess the mental health of medical students at different levels of training to see if a certain level plays a higher role in developing mental health issues.

In the current study, the prevalence of psychiatric distress among medical students of different levels and universities was 59.6 %. This is higher than reported in a survey by Ahmad N et al., who reported a prevalence of psychiatric distress among medical students in Malaysia and India of 33.0 % [9]. Moreover, the study of Yusoff M. et al. among Malaysian medical students reported a prevalence of psychiatric distress of 50 % [12]. Furthermore, another study conducted among Iranian medical students reported that nearly half scored above the threshold on the GHQ-12 [3]. In addition, another study conducted by Aktekin et al. reported a prevalence of psychological distress of 48 % in second-year Turkish medical students [13].

In comparison, a survey by Sreeramareddy C et al. reported a prevalence of 21 % among Nepalese medical students [14]. Some other studies reported a higher prevalence of psychiatric distress, including the study of El Gabry D et al., which reported that 64% of Egyptian medical students reached the threshold as cases on the GHQ-12 [15], and the study of Chau S et al., which reported that 87 % of medical students in Hong Kong were positive on the GHQ-12 [16]. In addition, another study conducted among final-year medical students at a Sri Lankan university reported that 62.9 % had psychological distress [17]. In Saudi Arabia, a previous study conducted by Alghamdi T et al. among undergraduate medical students at Majmaah university showed that more than half of the students reported psychological distress [18]. Compared with the prevalence of psychological distress among non-medical students reported in different studies, the results showed that medical students had a higher level of psychological distress [17,19,20].

In the current study, we found that the prevalence of psychological distress was significantly higher among female medical students than males. This is similar to the results of Jafari et al., which showed that psychological disturbance was more frequent in females than males [3], as well as studies of Dyrbye LN et al. [21], Sherina MS et al. [1], and Assadi SM et al. [22] which reported higher mental health problems among females. Moreover, this result is similar to previous studies indicating that women usually show higher levels of psychological distress than men in the general population [23]. Furthermore, another study revealed that since female students feel less social support, they might suffer from a decreased sense of coherence, a vital explanatory variable for psychological distress among medical students in general and in female students in particular [24].

Moreover, the current study showed a higher incidence of psychological distress among students with lower household incomes and those with lower GPA scores. This is in disagreement with the results of a previous study, which showed that the prevalence of psychological distress was significantly higher among students with higher GPAs [9]. Those with low GPAs were under enormous pressure to improve their academic scores, which increased the stressors and their risk of developing psychological distress and other psychological disorders. Furthermore, the current study revealed no significant difference between students of different levels in the prevalence of psychological distress except for first-level students who reported the highest level of distress. This is in disagreement with the study of Akdemir M et al., which showed that the GHQ-12 score of medical students increased significantly at all cut-off points after the first year [25]. Baldassin S et al. also reported that students in the internship period showed the highest psychological distress compared to students in the basic and intermediate periods [26]. On the other hand, other studies reported similar results, including a survey by Jafari et al., which showed that students at the basic science level were more psychologically distressed than interns and students of clinical clerkship [3]. The study of Aktekin M et al., showed that the global mental health, depression, and anxiety in medical students became worse during the first year of medical education [13], the study of Dahlin M et al. showed first year- Swedish students indicated experiencing the highest degree of pressure [27], and Dyrbye L et al., showed that the level of depressive symptoms varies by year of training, with the highest during the second year [21]. Transferring from high school to medical students and the new life and competency in the medical college put the new students under pressure which may be associated with a higher prevalence of distress rather than older students who may be adapted to the life of the college. Moreover, our findings may be related to heavy workloads and intense curricula, complications adjusting to the college's different environments, and poor campus conditions [26].

In conclusion, the current study confirmed previous studies in the high prevalence of psychological distress among medical students, which was significantly higher among females, students of low income, and students with lower GPAs. Moreover, the study showed that first-level students were the most affected by psychological distress. Providing greater attention to that concern is vital to reduce this prevalence and help students be less stressed, which will positively impact their quality of life. More investigations should be conducted to assess if the curriculum affects this prevalence. Preparing campaigns at the start of the year to meet the new students and prepare them for college life could reduce the impact on them.

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Knowledge, attitude, and practice of healthcare providers towards chest physiotherapy for COVID-19 patients at Al Baha, Saudi Arabia

Wael Alghamdi [1], Osman Babiker Osman [2], AbdAllah Ibrahim Mudawi [3], Waled AM Ahmed [1]

(1) Nursing Department, Faculty of Applied Medical Sciences, Al Baha University, Al-Baha, Saudi Arabia.
(2) Public Health Department, Faculty of Applied Medical Sciences, Al Baha University, Al-Baha, Saudi Arabia.
(3) Dental Health Department, Faculty of Applied Medical Sciences, Al Baha University, Al-Baha, Saudi Arabia.

Corresponding author:
Wael Alghamdi,
Nursing Department, Faculty of Applied Medical Sciences,
Al Baha University,
Al-Baha, Saudi Arabia
Email: waelalghamdi@bu.edu.sa

Abstract

Background: The knowledge, attitude, and practice of health professionals in Covid-19 medical centers are considered as the cornerstone for improvement of Covid-19 patients. This study aimed to assess the knowledge, attitude, and practice of the healthcare professionals in chest physiotherapy for COVID-19 patients.

Methods: This is a descriptive cross-sectional study; it was conducted among healthcare professionals working at ICUs at King Fahad Hospital and Prince Meshari Hospital, in Al-Baha Region, Saudi Arabia. A convenient sampling technique was used to collect data using a questionnaire about knowledge attitude and practice toward chest physiotherapy for COVID-19 patients which was adopted from a previously validated questionnaire. A specific coding for knowledge, attitude and practice was used to calculate the overall scores. Data was analyzed using SPSS software.

Results: Among 34 of healthcare providers working at King Fahad Hospital (44.1%) and Prince Meshari Hospital (55.9%), it was shown that 82.4% of healthcare providers have adequate knowledge, 91.2% have positive attitude and 70.6% have appropriate practice towards COVID-19 physiotherapy in ICUs.

A significant relationship was reported between marital status of healthcare providers and adequate knowledge (p=0.39), where singles and divorced participants have 100% adequate knowledge compared to married workers. It was also reported that knowledge significantly enhances levels of attitude and practice of healthcare providers by 0.609 and 0.61 respectively. Furthermore, their attitude affects positively the level of practice by 0.572.

Conclusions: This study highlighted that majority of healthcare providers (physiotherapists, nurses or medical) are knowledgeable; they also have positive attitude and appropriate practices about COVID-19 physiotherapy management in ICUs at Al-Baha governmental hospitals.

Keywords: knowledge, attitude, practice, healthcare professionals, COVID-19, physiotherapy.

Introduction

All levels of the health care system were affected by the ongoing pandemic of coronavirus disease 2019 (COVID-19) which is caused by the SARS CoV-2 virus. This highly infectious respiratory disease has yet infected more than 199 million people worldwide and has already resulted in 4.2 million deaths [1].

A significant number of patients with COVID-19 admitted to rehabilitation have spent time in the intensive care unit (ICU) and have symptoms common to other ICU patients, including dyspnea, anxiety, depression, prolonged pain, impaired physical function and poor quality of life [2, 3]. Although the lung is the primary target of coronavirus infection, clinical signs of central (i.e., dizziness, headache, and/or impaired consciousness) and/or peripheral nervous system (i.e., taste and/or smell impairment) involvement have been reported, especially in patients requiring mechanical ventilation [4].

The rehabilitation system, including patient care, education and research is strongly affected and physiotherapeutic practice is currently changing during the COVID-19 pandemic. Even though clinical studies on post-acute CO-VID-19 rehabilitation are still ongoing, several reports and guidelines provide recommendations for physiotherapeutic rehabilitation based on previous SARS/MERS experience as well as being based on recent data and patient case studies [5-9]. Recommended physiotherapy for post-acute COVID-19 syndrome can be conducted at home or in outpatient settings [5, 10, 11].

Based on the above-described functional problems, pulmonary rehabilitation (PR) is essential following the acute phase. So, a comprehensive multimodalities and interdisciplinary pulmonary rehabilitation is needed, triaged according to the level of the impairment caused by the infection, the activity restrictions, and the patients' disorders.

However, little is known regarding to what extent these goals of pulmonary rehabilitation can be achieved in post-COVID-19 patients, particularly in comparison to patients with pulmonary diseases usually referred to pulmonary rehabilitation. The first experiences with pulmonary rehabilitation in post-COVID-19 patients indicated that improvements were significant according to physical performance and subjective health status, regardless of previous ventilation [12].

Accordingly, the knowledge, attitude, and practice of the health professionals in COVID-19 centers are considered as the corner stone of improvement of COVID-19 patients especially those cases that were complicated by the necessity of retransfer to an acute clinic due to a renewed deterioration. So, this study aimed to assess the knowledge, attitude, and practice of the healthcare professionals in chest physiotherapy for COVID-19 patients.

Methods and Materials

Design: This is a Descriptive cross-sectional study; it was conducted among healthcare professionals working at ICUs.

Study population: This study was conducted on all healthcare professionals working at ICUs in King Fahad Hospital and Prince Meshari Hospital, in Al-Baha Region, Saudi Arabia.

Inclusion Criteria:
1. Healthcare professionals who work directly with CO-VID-19 diagnosed patients.
2. Those who can read English
3. Those who agreed to participate

Exclusion Criteria:
1. Refused to fill out the questionnaire
Sampling and sample size: A Convenient sampling technique was used; it included healthcare professionals in the hospital who agreed to participate.

Data collection: Direct questions were asked to participants concerning their Knowledge attitude and practice towards chest physiotherapy for COVID-19 patients.

Instruments:
Demographic questionnaire, knowledge of physiotherapy care questionnaire, attitude of physiotherapy care questionnaire, practice of physiotherapy care questionnaire; they were all adopted from one questionnaire used by Alfadil TA.

Measurements of KAP among healthcare workers:
The measurement of the KAP among healthcare workers were calculated as follows: For knowledge (14 items), the response gives 1 point for the correct, and zero point for incorrect or I don't know answers. The total of 7 points or more was considered as adequate knowledge about CO-VID-19 physiotherapy. For the attitude (twelve items), the response gives two points for each positive response, one point for neutral, and zero points for negative answers; a total of 12 points or more is considered as a positive attitude towards COVID-19 physiotherapy. For practice (fifteen items), the response gives three points for "always," two points for "sometimes," one point for "rarely," and zero points for "never." A total of 30 points or more was considered as an appropriate practice.

Data analysis plan:
Data was analyzed using descriptive statistics like frequency and percentage for demographic data and for details of knowledge attitude and practice of health professionals towards chest physiotherapy for COVID-19 patients. Inferential statistics like correlation and associations were established using an appropriate statistical test such as Chi square, Pearson correlation coefficient and regression. Secondary outcomes were drawn according to the data extraction.

Ethical consideration:
Formal permission was obtained from Al-Baha Health Affairs, IBR:1442-21.

Results

Results and summary:
Table 1 shows the demographic characteristics of 34 healthcare providers working at King Fahad Hospital (44.1%) and Prince Meshari Hospital (55.9%). Male participants represent 41.1% and female participants represent 58.9%. The age of included healthcare providers was distributed between two groups: 20-<30 years by 47.1% and 30-<40 years by 52.9%. Most participants were nurses (64.8%), medical (17.6%) or physiotherapists (17.6%); more than half of them (55.9%) have worked less than 5 years, and 20.6% have worked between 5 to 10 years. Table 1 also shows the average level of participants' knowledge (72.7% ±24.5), attitude (87.5% ±16.9), and practice (73.5% ±22.5).

As shown in Figure 1 t82.4% of healthcare providers have adequate knowledge, 91.2% have a positive attitude and 70.6% have appropriate practice towards Covid-19 physiotherapy in ICUs.

Table 2 shows the participants' responses to the knowledge questions regarding physiotherapy management of Covid-19 Patients in the ICUs. The true responses were among the majority of them. The correct answers for all questions ranged between 44.1% for (Physiotherapy interventions have a negative impact on the quality of life of COVID-19 patients managed in the ICUs) to 91.2 for (Physiotherapy service is provided to COVID-19 patients in ICU during the recovery from critical illness) and (Mobilization technique can improve functional status of COVID-19 patients in ICU).

Table 3 shows the participants' responses to the attitude questions regarding physiotherapy management of COVID-19 Patients in the ICUs. The positive responses were among the majority of them. The positive responses towards the questions ranged between 55.9% for (referral between medical staff and physiotherapist regarding COVID-19 patients in ICU is rarely practiced) to 88.2% for (It is important to have teamwork between healthcare professionals in ICU to improve patient care).

Table 4 shows the participants' responses to the practice questions regarding physiotherapy management of COVID-19 Patients in the ICUs. The appropriate responses came from the majority of participants. The correct practices towards the questions ranged between 44.1% for (Positive Expiratory Pressure (PEP) Bottle) to 85.3% for (Positioning - Supine, side-lying, prone, sitting, etc.).

Table 5 indicates the relationships between demographic variables of healthcare providers working at ICUs and their knowledge, attitude, and practices towards COVID-19 physiotherapy management. It was reported that the significant relationship was reported between marital status of healthcare providers and adequate knowledge (p=0.39), where singles and divorced participants have 100 % adequate knowledge compared to married workers.

In Table 6, it was reported that the correlation between knowledge and attitude and practice of healthcare providers is fair and positive since increase in knowledge level increases attitude by 0.609 and increases practice by 0.61, significantly. Furthermore, the attitude of healthcare providers affects positively their practice by 0.572 significantly. Further information about the data and conditions for access are available from the corresponding author.

Table 1: Demographic characteristics of participants (n=34)

Variables	Frequency	Percentage	Mean	SD
Gender				
Male	14	41.1%	-	-
Female	20	58.9%	-	-
Age				
20-<30 years	16	47.1%	-	-
30-<40 years	18	52.9%	-	-
Marital Status				
Single	13	38.3%	-	-
Married	18	52.9%	-	-
Divorced	3	8.8%	-	-
Profession				
Nursing	22	64.8%	-	-
Medicine	6	17.6%	-	-
Physiotherapy	6	17.6%	-	-
Years of experience				
1- < 5 years	19	55.9%	-	-
5- < 10 years	7	20.6%	-	-
10- < 15 years	6	17.6%	-	-
15- < 20 years	2	5.9%	-	-
Hospital				
King Fahad Hospital	15	44.1%	-	-
Prince Mashari Hospital	19	55.9%	-	-
Knowledge, attitude, and practice scores				
Knowledge	-	-	72.7%	24.5
Attitude	-	-	87.5%	16.9
Practice	-	-	73.5%	22.5

Table 2: The participants' responses to the knowledge questions regarding physiotherapy

Questions	True	False	I don't know
1. Physiotherapy is an integral part of the management of COVID-19 patients in ICUs.	79.4	14.7	5.9
2. Physiotherapy service is provided to COVID-19 patients in ICU during the recovery from critical illness.	91.2	2.9	5.9
3. Physiotherapy services can be provided to COVID-19 patients in different settings such as CCU, ward and HDU.	82.4	5.9	11.8
4. The lack of early physiotherapy care involvement in COVID-19 patients admitted to ICU is associated with increased pulmonary and functional complications.	73.5	14.7	11.8
5. The most common physiotherapy techniques used among COVID-19 patients in the ICU are limb exercises and breathing exercises.	88.2	5.9	5.9
6. Incontinence care such as Catheter, is part of physiotherapy care for COVID-19 patients	50.0	38.2	11.8
7. Early Physiotherapy management prevents delay in weaning from mechanical ventilation for COVID-19 patients.	61.8	8.8	29.4
8. Manual hyperinflation (MH) is one of the physiotherapy interventions for COVID-19 patients	55.9	20.6	23.5
9. Chest physiotherapy can improve the respiratory function of COVID-19 patients admitted to ICU.	88.2	11.8	0
10. Mobilization technique can improve functional status of COVID-19 patients in ICU	91.2	2.9	5.9
11. It is important to provide diet therapy services for COVID-19 patients.	79.4	5.9	14.7
12. Percussion, vibrations and suction are physiotherapy techniques for COVID-19 patients in ICU.	76.5	14.7	8.8
13. Physiotherapy management reduces the length of stay (LOS) of COVID-19 patients in the ICU.	67.6	23.5	8.8
14. Physiotherapy interventions have a negative impact on the quality of life of COVID-19 patients managed in the ICU.	44.1	50.0	5.9

Table 3: The participants' responses to the attitude questions regarding physiotherapy management of COVID-19 Patients in the ICU (n=34)

Question	Agree	Neutral	Disagree
1. It is necessary to have physiotherapy care services for COVID-19 patients in the ICU.	85.3	11.8	2.9
2. Your participation in management of COVID-19 patients in ICU is essential and must be considered.	85.3	8.8	5.9
3. In any hospital there is urgent need to apply physiotherapy that deals with pulmonary complications of COVID-19 patients in the ICU.	76.5	20.6	2.9
4. From your experience in ICU, workers have an important role in management of COVID-19 patients.	79.4	17.6	2.9
5. It is important to have teamwork between all Healthcare Professionals in ICU to improve patient care.	88.2	11.8	0
6. Healthcare Professionals must be a part of routine medical staff rounds in ICU providing care to COVID-19 patients.	85.3	14.7	0
7. The physiotherapist should attend the physiotherapy care for COVID-19 patients in ICU.	79.4	17.6	2.9
8. Healthcare Professionals should always participate in case discussion regarding COVID-19 patient progress in ICU.	88.2	11.8	0
9. Healthcare Professionals should be involved in decisions regarding patient weaning from mechanical ventilation for COVID-19 patients in ICU.	85.3	14.7	0
10. Physiotherapy care for COVID-19 patients managed in the ICU is effective.	82.4	11.8	5.9
11. The referral between medical staff and physiotherapist regarding COVID-19 patients in ICU is rarely practiced.	55.9	29.4	14.7
12. Healthcare Professionals should be involved with other medical staff in discharge decisions regarding COVID-19 patients.	88.2	5.9	5.9

Table 3: Factors associated with the risk of eating disorders among adolescents.

Question	Agree	Neutral	Disagree
1. It is necessary to have physiotherapy care services for COVID-19 patients in the ICU.	85.3	11.8	2.9
2. Your participation in management of COVID-19 patients in ICU is essential and must be considered.	85.3	8.8	5.9
3. In any hospital there is urgent need to apply physiotherapy that deals with pulmonary complications of COVID-19 patients in the ICU.	76.5	20.6	2.9
4. From your experience in ICU, workers have an important role in management of COVID-19 patients.	79.4	17.6	2.9
5. It is important to have teamwork between all Healthcare Professionals in ICU to improve patient care.	88.2	11.8	0
6. Healthcare Professionals must be a part of routine medical staff rounds in ICU providing care to COVID-19 patients.	85.3	14.7	0
7. The physiotherapist should attend the physiotherapy care for COVID-19 patients in ICU.	79.4	17.6	2.9
8. Healthcare Professionals should always participate in case discussion regarding COVID-19 patient progress in ICU.	88.2	11.8	0
9. Healthcare Professionals should be involved in decisions regarding patient weaning from mechanical ventilation for COVID-19 patients in ICU.	85.3	14.7	0
10. Physiotherapy care for COVID-19 patients managed in the ICU is effective.	82.4	11.8	5.9
11. The referral between medical staff and physiotherapist regarding COVID-19 patients in ICU is rarely practiced.	55.9	29.4	14.7
12. Healthcare Professionals should be involved with other medical staff in discharge decisions regarding COVID-19 patients.	88.2	5.9	5.9

Table 4: The participants' responses to the practice questions regarding physiotherapy management of COVID-19 Patients in the ICU (n=34)

Questions	Always	Sometimes	Rarely	Never
1. Manual airway clearance techniques	73.5	8.8	11.8	5.9
2. Positioning (Supine, side-lying, prone, sitting, etc.)	85.3	11.8	0	2.9
3. Chest manipulation and suctioning	76.5	8.8	2.9	11.8
4. Chest percussion	70.6	23.5	2.9	2.9
5. Vibration	64.7	17.6	11.8	5.9
6. Postural drainage	52.9	14.7	20.6	11.8
7. Limbs exercises	73.5	17.6	5.9	2.9
8. Manual hyperinflation	47.1	29.4	5.9	17.6
9. Breathing exercises	70.6	26.5	0	2.9
10. Non-invasive continuous positive airway pressure (CPAP)	47.1	32.4	2.9	17.6
11. Assisted coughing	61.8	23.5	11.8	2.9
12. Nebulization	61.8	20.6	2.9	14.7
13. Spirometer exercises	50.0	38.2	8.8	2.9
14. Positive Expiratory Pressure (PEP) Bottle	44.1	29.4	11.8	14.7
15. Chest support	55.9	23.5	5.9	14.7

Table 5: Relationships between the demographics and characteristics of the participants and adequate knowledge, positive attitude, and appropriate practices (n=34)

Variables	Adequate knowledge		Positive attitude		Appropriate practices	
	N (%)	p-value	N (%)	p-value	N (%)	p-value
Gender						
Male	11(78.6%)	0.672	12 (85.7%)	0.555	9 (64.3%)	0.7
Female	17 (85.0%)		19 (95.0%)		15 (75.0%)	
Marital Status						
Single	13(100.0%)	0.039*	13 (100.0%)	0.232	11(84.6%)	0.109
Married	12(66.7%)		15 (83.3%)		10(55.6%)	
Divorced	3(100.0%)		3(100.0%)		3(100.0%)	
Profession						
Nursing	20(90.9%)	0.066	21(95.5%)	0.062	17(77.3%)	0.084
Medicine	5(83.3%)		6(100.0%)		5(83.3%)	
Physiotherapy	3(50.0%)		4(66.7%)		2(33.3%)	
Age						
20-<30 years	14(87.5%)	0.66	15(93.8%)	0.61	10(62.5%)	0.33
30-<40 years	14(77.8%)		16(88.9%)		14 977.8%)	
Years of experience						
1- < 5 years	16(84.2%)	0.67	17(89.5%)	0.77	12(63.2%)	0.54
5- < 10 years	6(85.7%)		6(85.7%)		6(85.7%)	
10- < 15 years	5(83.3%)		6(100.0%)		4(66.7%)	
15- < 20 years	1(50.0%)		2(100.0%)		2(100.0%)	

(*): significant

Table 6: The Pearson correlations between overall knowledge, positive attitude, and appropriate practices of the participants

	Knowledge	Attitude	Practice
Knowledge		r =0.609 p =0.000*	r =0.610 p =0.000*
Attitude			r =.572 p =0.000*
Practice			

(*): significant

Discussion

This descriptive study was conducted among 34 healthcare providers, who were working at King Fahad Hospital (44.1%) and Prince Meshari Hospital (55.9%). They are working in nursing (64.8%), medicine (17.6%) or physiotherapy (17.6%).

The following are reported as the average level of participants' knowledge (72.7% ±24.5), attitude (87.5% ±16.9), and practice (73.5% ±22.5). The findings of this study showed that 82.4% of healthcare providers have adequate knowledge, 91.2% have positive attitude and 70.6% have appropriate practice towards COVID-19 physiotherapy in ICUs. These findings showed that most healthcare providers at Al-Baha hospitals (72.7%) are knowledgeable about physiotherapy for (COVID-19) patients, which is in line with previous reports from different countries such as a study by Ali AA, et al. [13], about awareness of COVID-19 among the physiotherapists in Pakistan where the majority (96.3%) of them were aware of Covid-19, and other reports by Pedersini et al and [14] Salman et al [15] which showed that the physiotherapists were aware of preventive strategies [14, 15]. On the other hand, a study conducted by Guan et al and Pegado et al indicated that physiotherapists need more knowledge regarding infectious diseases prevention [16, 17].

It was reported that singles and divorced participants have significantly more knowledge compared to married workers. These study findings were found in agreement to the study findings of research conducted in KSA by Omar A. AL Mohammed, et al 2020, where they reported that single HCWs were more likely than married to have adequate knowledge, positive attitude, and follow appropriate practices most of the time [18]. On the other hand, the majority (88.6%) of Physiotherapists of Sindh, Pakistan found married participants showed sound knowledge (93.6%) of COVID-19 [13].

It was also reported that knowledge of participants significantly enhances the level of attitude and practice of healthcare providers by 0.609 and 0.61 respectively. These relationships are similar to the study conducted by Charles Ezema, 2021, across 53 countries to assess participants physiotherapists' demographics, knowledge of COVID-19, attitude, practices, and standard precaution adherence during the pandemic. They reported that all participants had good knowledge of COVID-19 pathology and a positive attitude towards safe clinical practices. They also reported that the percentage score of participants' knowledge regarding COVID-19 pathology, and prevention, their attitude, and adherence to standard precautions averaged 77.73±10.11, 89.70±9.26, 77.44±7.04, and 61.59±16.63, respectively and this level of Knowledge about COVID-19 pathology was found to be statistically significant across all studied demographic variables (p<0.001) [19].

Furthermore, their attitude affects positively the level of practice by 0.572. these findings are in the same line with the study findings that conducted in Ethiopia by Gedamnesh Bitew,et al, 2021, where they reported that the mean attitude score for the participants was (19.9 ± 5.9.) and (64%) of the participants had a good/favorable attitude toward COVID-19 prevention and control and the mean score of practice for the HCP was 3.5 with (SD = 1.5). The study also showed that 55% of participants had good practice toward COVID-19 prevention and prevention mechanisms [20].

There are several limitations associated with our study; the approach for data gathering, was conducted while the incidence rate of the pandemic had dropped which makes it difficult to assess healthcare providers practice of a larger sample size. The method utilized for another limitation is the lack of generalizability of study findings since it was conducted at Al-Baha region solely. Another limitation was the limited number of physiotherapists at the ICU in Al-Baha hospitals; however, nurses could help to overcome this shortage. Nonetheless, this study has several strengths; this study is the first descriptive study for physiotherapy management in Al-Baha region, Saudi Arabia, and it was conducted in the two main hospitals in Al-Baha region (King Fahad Hospital and Prince Meshari Hospital).

Conclusion

This study highlighted that the majority of healthcare providers (physiotherapists, nurses, or medical) are knowledgeable about Covid-19 physiotherapy management. They also have a positive attitude and appropriate practices towards physiotherapy management for COVID-19 cases at Al-Baha governmental hospitals.

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Obesity is a risk factor for COVID-19 infection in Saudi Arabia

Mohammed Aljuaid [1], **Salman Rawaf** [2], **Farrah K. Alnajjar** [3], **Mashael K. Alshaik** [4], **Yasmeen Saleh** [5], **Hadil AK Al Otair** [6]

(1) Department of Health Administration, College of Business Administration, King Saud University, Riyadh, Saudi Arabia
(2) WHO Collaborating Centre for Public Health Education and Training, Department of Primary and Public Health, Faculty of Medicine, School of Public Health, Imperial College of London, London, United Kingdom
(3) Rabigh General Hospital, Ministry of Health, Jeddah, Saudi Arabia;
(4) Pharmacy Services Department, King Saud University Medical City (KSUMC), Riyadh, Saudi Arabia
(5) College of Medicine, University of Sharjah, Sharjah, United Arab Emirates;
(6) Department of Medicine. King Saud University Medical City (KSUMC), King Saud University, Riyadh, Saudi Arabia

Corresponding Author:
Dr. Hadil AK Al Otair
Department of Medicine (38)
King Saud University Medical City (KSUMC)King Saud University
PO Box 2825 Riyadh 11461, Saudi Arabia.
Mobile: +966 56 627 8975
Email: hadil.alotair@live.com

Abstract

Background: Obesity is a global health hazard that has recently been linked to adverse clinical outcomes of COVID-19 infection.

Objective: The aim of this study is to determine the obesity risk factors among hospitalized COVID-19 patients and their influence on the clinical outcomes of the disease

Methods: This is a retrospective observational cohort study of COVID-19 patients admitted to one tertiary hospital in Saudi Arabia from May to July 2020. Patients' demographics, comorbidities and clinical manifestations were collected from the medical records. The clinical outcomes were compared between patients with different categories of body mass index (BMI).

Results: Out of 260 patients who were included in the study, 41.6% were obese. Compared to those patients with normal and overweight BMI, obese patients with COVID-19 were more likely to have hypertension, ischemic heart disease, chronic lung disease and heart failure. Pneumonia (81.1%), ARDS (80.8%), mechanical ventilation (80%), acute kidney injury (74.2%) and heart failure (86.7%) were more prevalent in patients who were either overweight or obese. More than 50% of the patients admitted to the intensive care unit were either overweight or obese, representing nearly 55% of the mortalities. On an average, the BMI of females (32.2 ± 8.3 kg/m²), was significantly higher than males (28.3 ± 5.1 kg/m²), (P<0.01) and with higher BMI, the chance of having hypertension increases by threefold (P<0.01).

Conclusion: Obesity is very common among hospitalized patients with COVID-19, particularly females. Obese patients were more likely to have cardiovascular risk factors and adverse clinical outcomes.

Keywords: COVID-19, Obesity, BMI, Risk factors, Outcome

Introduction

After more than two years since Corona Virus Disease 19 (COVID-19) was declared a global pandemic, nearly 450 million people (as of March 9, 2022) have been infected with the disease worldwide, and more than 16 million people have lost their lives. In Saudi Arabia, almost 749,000 were affected with more than 9,000 mortalities (1,2). Multiple risk factors have been linked with high morbidity and mortality of COVID-19 worldwide (3,4,5,6).

Numerous reports have highlighted many adverse clinical outcomes in obese patients who develop COVID-19 (3). This could be in part related to the pro-coagulant and pro-inflammatory state associated with obesity, resulting in the amplification of oxidative stress, and impairment of the innate and adaptive immune response to infections. Likewise, comorbidities associated with obesity including other metabolic, cardiovascular, pulmonary, and renal diseases can further aggravate the clinical outcomes of COVID-19 (7,8).

In Saudi Arabia, the latest World Health Survey conducted in 2019, reported that 20% of Saudis were obese, with a higher prevalence in Saudi females (21%) than Saudi males (19%) (4). Studies published in the Middle East and North African (MENA) region, especially in Saudi Arabia, are still scarce considering the high prevalence of obesity in the region.

Thus, the aim of this study is to describe the clinical characteristics of patients with COVID-19 infection admitted to hospitals in Saudi Arabia and identify the obesity risk factors and their impact on the clinical outcomes of the disease by employing the Body Mass Index (BMI) to classify them. The results of this study may help to prioritize patients infected with COVID-19 according to their medical needs with respect to obesity, within the available resources.

Materials and Methods

This is a retrospective observational case-control study from the medical records of patients infected with COVID-19 who were admitted to a tertiary hospital in Riyadh, Saudi Arabia from May to July 2020. Adult patients with confirmed COVID-19 infection by real-time reverse transcription-polymerase chain reaction (RT-PCR) test using the nasopharyngeal swab and between 18–80 years of age were included in the study, while cancer patients, pregnant or lactating women were excluded.

Demographic profile of the patient in addition to Body Mass Index (BMI), comorbidities and clinical manifestations were collected from patients' electronic medical records. The clinical outcomes recorded were the Hospital Length of Stay (LOS), pneumonia, Acute Respiratory Distress Syndrome (ARDS), mechanical ventilation, shock, Acute Kidney Injury (AKI), Acute heart failure (AHF) and death. AKI is defined as an abrupt reduction in kidney function characterized by an elevation in serum creatinine level within 48 hours, with reduction in urine output thus needing dialysis, or a combination of these factors. Meanwhile, AHF is defined as a rapid onset of new or worsening signs and symptoms of heart failure.

Ethical Considerations

The study was approved by the King Saud University (KSU) Institutional Review Board (IRB), (Ref. No. 20/0497/IRB). This study was conducted in accordance with the Declaration of Helsinki. KSU IRB did not require patient consent to review his or her medical record as anonymity in collecting the data was maintained with confidentiality.

Statistical Analyses

All statistical analyses were performed using the Statistical Package for the Social Sciences software, version 22.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as the means ± standard deviations (SDs) and compared using t-test and one-way ANOVA to test the difference between continuous normal variables and three age groups. The categorical data were presented in numbers and percentages (%) and the Chi-square test for dependencies were carried out to determine whether there are significant dependencies between categorical variables and levels of BMI. Multiple regression analysis was used to determine the significant relationships and to arrive at a mathematical model for estimating the BMI based on the independent risk factors. All the statistical tests were considered statistically significant at 5% level of significance.

Results

A total of 304 patients with confirmed COVID-19 were admitted to King Khalid University Hospital in Riyadh, Saudi Arabia between May and July 2020. Forty-four patients were excluded from the study due to incomplete or missing data. The medical records of the remaining 260 patients were retrospectively reviewed. Patients were categorized into three BMI classes; Normal (BMI-19 to 25 kg/m2), Overweight (BMI-25 to 30kg/m2) and Obese (30 to 35 kg/m2 and above). The baseline data is summarized in Table 1. About 20.7% of the patients were in the normal BMI group, 37.7% were overweight and 41.6% were obese. The average mean of the patients' age was 53.9 ±15.2 years, and the majority of the patients were males (68.5%). To test the significant differences in BMI, the ages of subjects were categorized into three different age-groups; <45 years, 45-64 years and ≥65 years. However, there was no significant difference in BMI among the three age groups (p=0.187). For females, the mean of BMI was (32.2 ± 8.3 kg/m²), which was significantly higher than the BMI for males (28.3 ± 5.1 kg/m²), (P<0.01). Obese patients with COVID-19 infection were more likely to have hypertension, ischemic heart disease, chronic lung disease and heart failure compared to those patients within the normal weight or overweight groups. However, this did not reach statistical significance. Meanwhile, the most common initial clinical symptoms on admission of the patients to the hospital were shortness of breath (78.6%, P<0.05), fever (74.2%, P<0.05), and cough (67.2%). The laboratory results showed that prothrombin time (PT) and Activated partial thromboplastin time (APTT) were higher among COVID-19 patients categorized by normal BMI (P<0.001 and P=0.057 respectively).

The baseline data is summarized in Table 1.

Table 1: Baseline characteristics of COVID-19 patients categorized by BMI classes

Variable	Total (n = 260)	Normal (n =54)	Overweight (n = 98)	Obese (n = 108)	P value
Age (year)	53.9± 15.2	51.2 ± 17.7	54.8 ± 14.1	54.5 ± 14.8	0.187
<45 yrs		20(37.0)	28(28.6)	30(27.8)	
45 – 64 yrs		22(40.7)	44(44.9)	52(48.1)	0.761
65 or more yrs		12(22.3)	26(26.5)	26(24.1)	
Sex (%)					
Male	178 (68.5)	40 (74.1)	79 (80.6)	59 (54.6)	0.000*
Female	82(31.5)	14(25.9)	19(19.4)	49(45.4)	
Nationality (%)					
Saudi	114 (43.8)	20 (37.0)	34 (34.7)	60 (55.6)	0.006*
Non- Saudi	146 (56.2)	34 (63)	64 (65.3)	40 (44.4)	
Civil Status, Married (%)	152 (58.5)	29 (53.7)	63 (64.3)	60 (55.6)	0.326
Blood Pressure					
SBP (mmHg)	125.5 ± 20.7	126.2 ± 22.7	126.1 ± 20.3	124.6 ± 20.1	0.872
DBP (mmHg)	71.3 ± 12.5	69.2 ± 12.3	72.8 ± 11.3	70.9 ± 13.5	0.984
Smoking History (%)					
Smoker	20 (7.7)	4 (7.4)	10 (10.2)	6 (5.6)	0.415
Non-smoker	240 (92.3)	50 (92.6)	88 (89.8)	102 (94.4)	
Comorbidities ((%)					
HTN	119 (45.8)	20 (37.0)	41 (41.8)	58 (53.7)	0.082
DM	116 (44.6)	27 (50.0)	41 (41.8)	48 (44.4)	0.625
IHD	29 (11.2)	6 (11.1)	9 (9.2)	14 (13.0)	0.691
CKD	25 (9.6)	8 (14.8)	9 (9.2)	8 (7.4)	0.316
CLD	20 (7.7)	5 (9.3)	4 (4.1)	11 (10.2)	0.231
HF	23 (8.8)	4 (7.4)	8 (8.2)	11 (10.2)	0.804
CVA	18 (6.9)	6 (11.1)	5 (5.1)	7 (6.5)	0.367
Clinical Symptoms (%)					
Cough	174 (67.2)	34 (63.0)	68 (70.1)	72 (66.7)	0.662
Fever	192 (74.4)	33 (62.3)	79 (81.4)	80 (74.1)	0.036*
SOB	202 (78.6)	36 (67.9)	85 (86.7)	81 (76.4)	0.021*
Sputum	39 (15.0)	6 (11.1)	16 (16.3)	17 (15.7)	0.663
Hemoptysis	3 (1.2)	0 (0)	3 (3.1)	0 (0)	0.081
Sore Throat	25 (9.6)	4 (7.4)	11 (11.2)	10 (9.3)	0.737
Neurological symptoms	25 (9.6)	7 (13.0)	9 (9.2)	9 (8.3)	0.631
Diarrhea	51 (19.7)	9 (16.7)	18 (18.4)	24 (22.4)	0.629
Nausea and vomiting	53 (20.4)	10 (18.5)	18 (18.4)	25 (23.1)	0.647
Abdominal Pain	20 (7.7)	5 (9.3)	5 (5.1)	10 (9.3)	0.476
Laboratory results					
HbA1c (mmol/L)	8.2 ± 8.3	7.7 ± 2.2	7.4± 2.0	8.8 ± 10.9	0.625
D-dimer (mcg/L)	2.1 ± 3.6	3.6 ± 5.3	2.6± 4.9	1.5 ± 1.8	0.426
HDL(mmol/L)	0.98 ± 0.48	0.9 ± 0.4	1.0± 0.5	1.0 ± 0.5	0.141
LDL(mmol/L)	1.94 ± 0.99	1.9 ± 1.1	2.2± 0.9	1.8 ± 1.0	0.872
PT (seconds)	15.3 ± 4.3	17.5 ± 6.9	14.7± 2.1	15.1 ± 4.4	0.001*
APTT (seconds)	40.6 ± 8.3	44.1 ± 10.2	39.6± 6.0	40.3 ± 8.9	0.057
Ferritin (mcg/L)	1110.3±1567.6	1275.7±1849.9	1113.4±1033.1	1068.1±1747.5	0.059
LDH (U/L)	434.1 ± 177.7	418.3 ± 147.2	492 ± 166	407.3 ± 186.1	0.579

Data are presented as mean ± standard deviation or number (%);* Statistically significant; SBP- systolic blood pressure; DBP- diastolic blood pressure; HTN- hypertension; DM, diabetes mellitus; IHD-ischemic heart disease; CKD-chronic kidney disease; CLD-chronic lung disease; HF-heart failure, CVA-cerebrovascular accident; SOB-shortness of breath; HbA1c-glycated haemoglobin ; HDL-high density lipoprotein; LDL-low density lipoprotein; PT-prothrombin time; aPTT- activated partial thromboplastin time ; LDH-lactate dehydrogenase

Initial treatment given upon admission in the hospital were cephalosporin antibiotics (89.2%), azithromycin (62.3%), and steroids (61.8%). Regarding the outcome of the patients with COVID-19 infection, pneumonia (81.1%), ARDS (80.8%), mechanical ventilation (80%), shock (57.9%), acute kidney injury (74.2%) and heart failure (86.7%) were more prevailing in patients who were either overweight or obese. Furthermore, more than 50% of the patients admitted to ICU were either overweight or obese and their mean LOS of 22.9 ± 18.1days and 16.1 ± 13.6 days respectively, and nearly 30% of obese patients in the study have died (Table 2).

A multiple linear regression model was used to evaluate the association between risk factors of COVID-19 patients and BMI. Several demographic and comorbidities were identified. Moreover, a stepwise logistic regression model was used to reduce them to 3 so that only the significant predictor variables are entered into the regression equation one at a time. Thus, it can be observed that the BMI of females was significantly higher than males (P<0.01), and the higher the BMI of a person, the greater the chance to have hypertension (P<0.01). However, in the outcome, it was observed that with higher BMI, the likelihood of developing shock was reduced (P<0.01). Table 3 presents the univariate and multivariate linear regression analyses of risk factors associated with high BMI for COVID-19 patients.

Table 2. Treatment and Outcome of COVID-19 patients classified by BMI Classes

Variable	Total (n = 260)	Normal (n =54)	Overweight (n = 98)	Obese (n =108)	P value
Treatment (%)					
Steroids	160 (61.8)	31 (57.4)	65 (67.0)	64 (59.3)	0.396
Antibiotics	232 (89.2)	44 (81.5)	91 (92.9)	97 (89.8)	0.093
Hydroxychloroquine	40 (15.4)	12 (22.1)	21 (21.4)	7 (6.5)	0.004*
Azithromycin	162 (62.3)	31 (57.4)	69 (70.4)	62 (57.4)	0.111
Anti-viral	14 (5.4)	3 (5.6)	5 (5.1)	6 (5.6)	0.988
Outcome (%)					
Pneumonia	222 (85.4)	42 (77.8)	84 (85.7)	96 (88.9)	0.167
ARDS	26 (10.0)	5 (9.3)	10 (10.2)	11 (10.2)	0.979
Mechanical Ventilation	60 (23.2)	12 (22.2)	20 (20.4)	28 (26.2)	0.610
Shock	19 (7.3)	8 (14.8)	7 (7.1)	4 (3.7)	0.037*
AKI	62 (23.8)	16 (29.6)	16 (16.3)	30 (27.8)	0.084
HF	15 (5.8)	2 (3.7)	4 (4.1)	9 (8.3)	0.326
ICU admission	136 (52.3)	21 (38.9)	54 (55.1)	61 (56.5)	0.084
LOS (day)	17.9 ± 14.6	14.3 ± 5.3	22.9 ± 18.1	16.1 ± 13.6	0.222
Death	71 (27.3)	14 (25.9)	25 (25.5)	32 (29.6)	0.777

Data are presented as mean ± standard deviation or number (%); * Statistically significant; ARDS- Acute Respiratory Distress Syndrome; AKI- acute kidney injury; HF- heart failure; ICU- Intensive Care Units; LOS-Length of Stay

Table 3. Univariate and multivariate linear regression analyses of risk factors associated with BMI for COVID-19 patients

Risk Factor Variables	Univariate analysis Unstandardized coefficients				Multivariate analysis Unstandardized coefficients			
	B	SE	95% CI	P value	B	SE	95% CI	P value
Age (yr)	0.03	0.03	-0.02, -0.08	0.275	0.01	0.03	-0.05, 0.07	0.750
Male sex (vs female)	3.83	0.84	2.18, 5.49	0.000*	3.59	0.86	1.89, 5.30	0.000*
Smoker (vs non-smoker)	-0.16	1.52	-3.16, 2.83	0.915	1.39	1.49	-1.53, 4.32	0.350
Comorbidity present (vs not present)								
Hypertension	2.95	0.79	1.39, 4.51	0.000*	3.49	0.94	1.65, 5.34	0.000*
Diabetes mellitus	-0.16	0.81	-1.77, 1.44	0.841	-1.45	0.88	-3.18, 0.28	0.099
Ischemic Heart Disease	0.15	1.29	-2.38, 2.69	0.905	-0.78	1.38	-3.51, 1.94	0.571
Chronic Kidney Disease	-0.99	1.37	-3.69, 1.71	0.472	-0.71	1.48	-3.63, 2.21	0.632
Chronic lung Disease	2.50	1.51	-0.48, 5.48	0.100	2.10	1.50	-0.85, 5.06	0.163
Heart Failure	3.44	1.72	0.04, 6.83	0.047*	0.98	1.54	-2.06, 4.01	0.527
Cerebrovascular accident	-2.19	1.59	-5.32, 0.94	0.170	-3.13	1.75	-6.59, 0.39	0.076
Outcome								
Pneumonia	1.61	1.14	-0.64, 3.86	0.160	1.41	1.17	-0.90, 3.73	0.230
ARDS	0.56	1.35	-2.10, 3.22	0.676	1.15	1.49	-1.79, 4.09	0.440
Mechanical Ventilation	0.42	0.96	-1.47, 2.32	0.659	1.78	1.38	-0.94, 4.50	0.199
Shock	-3.64	1.54	-6.67, -0.60	0.019*	-4.70	1.77	-8.19, -1.21	0.009*
Acute Kidney Injury	1.14	0.95	-0.73, 3.01	0.231	0.78	1.03	-1.26, 2.81	0.453
Heart Failure	3.44	1.72	0.04, 6.83	0.047*	2.06	1.92	-1.73, 5.85	0.285
ICU patients	1.22	0.81	-0.37, 2.81	0.131	1.11	0.95	-0.76, 2.99	0.243
LOS (day)	-0.03	0.03	-0.08, 0.02	0.222	-0.04	0.03	-0.09, 0.01	0.144
Death	-0.10	0.91	-1.89, 1.69	0.910	-0.89	1.29	-3.43, 1.64	0.488

Legend: ARDS, Acute Respiratory Distress Syndrome; ICU, Intensive Care Unit; LOS, length of stay; * Statistically significant

Discussion

The findings of the present study showed a high prevalence of obesity among hospitalized patients with COVID-19 in Saudi Arabia particularly among females. In the same line, obese patients with COVID-19 had high probability of hypertension as compared to the non-obese. There was a trend toward adverse outcome among obese patients, however the difference was not statistically significant.

Our findings were in agreement with a previous study from Saudi Arabia which reported that 45.8% of COVID-19 patients were obese (9). Lower prevalence of obesity was reported from China (10) probably reflecting the local prevalence of obesity in different countries. Nevertheless, obese patients in general seem to be more vulnerable to infections. A study conducted in Sweden has reported that there were increased incidence of varying infections in obese men and women as well as subjects with a low level of physical activity compared with more physically active subjects for both genders (11).

In the present study, hypertension was more common among obese patients with COVID-19. A population based cross-sectional study in Al Kharj, Saudi Arabia reported that being overweight was associated with the highest risk of hypertension (OR = 4.98 [95% C.I. = 1.98–12.52], P = 0.001). Those who were classified as class I obese had 3.5 times the risk of hypertension compared with the non-obese group (OR = 3.49 [95% C.I. = 1.42– 8.63], P = 0.007) (12). Another study which was conducted in Saudi Arabia between 1995 to 2005 reported that the prevalence of hypertension was around 26% among the 15–70 years' age group, and by 2010, hypertension was classified as the leading risk factor for death in Saudi Arabia (13,14,15,16). In the present study obese patients were more likely to have hypertension, which can partly contribute to a worse outcome of COVID-19 infection.

More than two thirds of the study patients were males. Numerous reports have been published on gender differences in COVID-19 outcomes (11) and although, varying evidence did not show a strong difference between genders regarding infection with COVID-19, male patients tend to have both higher severity and fatality rates. These variances may be due to higher levels of angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2) in males. Hormonal influences on the immune response as well as differences in behavior can also contribute to the greater severity and fatality in COVID-19 observed among more men than women (17). This study can be compared to previously published studies which observed that the majority of the COVID-19 patients were males (9).

Shock is a clinical state of circulatory failure; it is an indicative of diminished oxygen delivery at the cellular level. It has been reported that patients infected with COVID-19 who required intensive care unit (ICU) admission, had up to 67% probability of developing shock (3,18). A retrospective cohort study of 1,019 COVID-19 patients conducted in New York City at the height of the pandemic, reported that obesity is independently associated with an increased risk for septic shock (19). In the present study, only 7% of the total patients developed shock during the course of their hospital admission, moreover, obesity was inversely related to developing shock as an outcome (p .009).

The potential impact of obesity on the outcome of septic patients is quite controversial. In most animal studies, obesity resulted in altered inflammatory response, higher number of complications, and escalated mortality among obese animals (20,21). On the contrary, some human studies showed that obesity has a beneficial effect wherein, an observational cohort study with 1,400 adult patients analyzed with severe sepsis, found that obesity shielded against death (22). Another study, reported an improved short-term survival in overweight and obese patients with septic shock despite equal severity of illness upon presentation and co-morbidities (20). In addition, overweight and obese patients had lower degree of inflammatory response as shown by lower IL-6 levels, and less coagulation derangement than normal weight patients (20). In the present study we observed that obese patients had a lower level of D-Dimer, PT, APTT and ferritin than patients with normal BMI. This might in part indicate a lower inflammatory response and explain the lower number of obese patients who developed shock, however this needs to be confirmed in larger studies.

Pneumonia, ICU admission, mechanical ventilation and death were higher among obese patients, although the difference did not reach statistical significance. This is probably due to the small number of patients and the high prevalence of DM (50%) in patients with normal BMI, who's average HbA1c was 7.7 mg/dL. DM on its own merit is associated with higher in-hospital complications among COVID-19 patients (7).

An earlier record-based case-series study conducted in Saudi Arabia, reported that ICU admission was significantly higher in obese patients (p=0.001) (23). Similarly, another study reported higher mortality and worse clinical outcome in obese patients (24). A study conducted in France with over 130,000 patients admitted to hospital with COVID-19 validated that obesity, diabetes and arterial hypertension are related to the severity and mortality among patients with existing comorbidities and requiring more invasive mechanical ventilation (18).

Limitations of this study include the small number of patients and the retrospective nature of the study which did not allow measuring adipose tissue-related cytokine concentrations (e. g. interleukin [IL-6], monocyte chemotactic protein [MCP]-1, tumor necrosis factor [TNF]-α, as well as other serum adipokines such as leptin and adiponectin. Other measures of obesity that could be relevant are the visceral fat area (VFA), upper abdominal perimeter, subscapular and triceps fat thickness.

Conclusion

Based on the findings of this study it can be safely contended that obesity is highly prevalent among patients infected with COVID-19 in Saudi Arabia. Given their increased risk toward an adverse outcome when infected with COVID-19, it is vital to recognize the distinctive hazards that obese patients face. This can help to establish a strategy with efficient and effective triaging and clinical evaluation for patients with obesity. This study also highlights the importance of controlling obesity and hypertension at the community level.

Declaration of Competing Interest
The authors of this study has no known competing financial interests or personal relationship that could appeared to influence the work reported in this paper

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Social Anxiety Disorder Among Medical Students at King Abdulaziz University in Rabigh, Saudi Arabia

Naseem Abdulmohi Alhujaili[1], Abdulaziz Abdullah Alghamdi[1],
Iman Mohmad Wahby Salem[2,3], Haya Musaad Altherwi[4], Shahad Musleh Alyaslami[4],
Atheer Talal Aljahdali[4], Sarah Hani Alhajari[4], Abdulrahman Mansour Aldhahri[4].

(1) Department of Medicine, Division of Psychiatry, Faculty of Medicine in Rabigh, King Abdulaziz University, Jeddah, Saudi Arabia.
(2) Family and Community Medicine Department. Faculty of Medicine in Rabigh. King Abdulaziz University, Jeddah, Saudi Arabia
(3) Community and occupational Medicine Department. Faculty of Medicine. Al Azhar University, Egypt.
(4) Department of Medicine, Faculty of Medicine in Rabigh, King Abdulaziz University, Jeddah, Saudi Arabia.

Corresponding author:
Naseem Alhujaili, MD
Child & Adolescent Psychiatrist
Assistant Professor- Department of Internal Medicine
Rabigh Faculty of Medicine - King Abdulaziz University
Email: nalhujaili@kau.edu.sa

Abstract

Background and aims: Social anxiety disorder is documented to have a huge prevalence among young adults and college students, and multiple research references the higher occurrence in medical students. This study is aimed to assess the prevalence of social anxiety disorder among the medical students at King Abdulaziz University- Rabigh branch and its associated risk factors.

Methods: This cross-sectional study was conducted on 218 students aged between 18 and 26, which was managed by sending an online questionnaire that included participants' demographic information and the Liebowitz Social Anxiety Scale (LSAS).

Results: Regarding participants, 52.8% of them are aged between 21 and 23, and most of them (54.6%) were males. About one-third of the students who participated (29.4%) had a marked social anxiety disorder, and only 6.4% of the students were found to have mild to no symptoms. Social anxiety disorder was found to increase in severity in females, younger students, and students with less satisfaction with their weight and appearance.

Conclusion: Social anxiety disorder is found to be significantly common among the participating medical students and correlated positively with multiple relevant factors, showing the effort needed for earlier detection of social anxiety disorder to manage it accordingly.

Keywords: medical students, social anxiety disease, mental health, Rabigh, Saudi Arabia

Introduction

Social anxiety disorder is characterized by a constant fear of embarrassment and humiliation in social situations in which an individual feels as if they are being observed by others, in addition to the fear that they will show symptoms of anxiety in front of others and then be rejected by them. Accordingly, social situations are either tolerated with intense fear or avoided completely (1).

Anxiety disorders are the most common mental disorders in adolescence with a global prevalence that ranges from 15% to over 30%. Furthermore, social anxiety disorder is the commonest anxiety disorder; approximately 9% of adolescents met the criteria for any social phobia in their lifetime. Of these adolescents, 55.8% were affected with the generalized subtype and 44.2% exhibited non-generalized social phobia, compared to the adult state where this prevalence is between 10% and 20%. Furthermore, studies have shown that anxiety disorders with the highest burden are found in both males and females, adolescents and young adults (2,3).

Multiple studies have indicated that social anxiety is a prevalent disorder among university students (5,6,7). A study from Sweden has examined the prevalence of social phobia and its subgroups in a university student population. The point prevalence of social phobia among Swedish university students was 16.1%, comparable with 15.6% previously reported for the general population (5).

A study from Turkey discussed the prevalence of social phobia, and the sociodemographic variables, substance use patterns, and comorbid psychiatric disorders associated with it. The impact of social phobia on quality of life, academic achievement in university students, and identity formation was also examined. They found 20.9% of the participants had social phobia during the previous year and 21.7% had a social phobia for a lifetime. In total, 74.6% of those who had a social phobia during the previous year and 76.5% of those who had a social phobia for their whole lives also had a specific social phobia (6).

A study that was done in Brazil discussed the prevalence of social phobia and the academic impact of this disorder in a large sample of Brazilian college students. The final result of this study showed that the prevalence of social phobia among university students was 11.6% (7).

In a study that finds out the prevalence and determinations of social anxiety disorder among 404 medical undergraduate students of a Medical College in East Delhi, data was collected using a Social Interaction Anxiety Scale (SIAS), and the result found that 5.95% of the study participants hada social anxiety disorder (8).

A study that evaluated medical students of either gender from first to final year attending Allama Iqbal Medical College in Pakistan, concluded that females have a greater tendency for fear and avoidance as compared to males, and students from urban backgrounds have a greater tendency for fear and avoidance resulting in social anxiety disorder, based on the results of 150 included students (9).

In a study conducted in Malaysia on the prevalence of social anxiety problems and potential risk factors that may be associated with the disorder among medical students, the result showed that 56% of the medical students scored >19 in the Social Phobia Inventory (SPIN) suggesting that they had a social anxiety problem (10).

In general, the reported rates of social anxiety disorder in Saudi Arabia vary widely between studies. Previously published studies on social anxiety disorder in Saudi Arabia in undergraduate students showed the following: a study from Taif female university determined the prevalence of social anxiety disorder as 16.3%. Most of the affected students had a moderate degree of the disorder in 43.5% of cases (11). Another study was conducted at Taif university, but the target population was medical students in their clinical years. The result found that 29.3% of the medical students in the clinical years were diagnosed with social anxiety disorder. The students who reported often parental criticism reported the highest rate of social anxiety disorder (43.3%) whereas those who reported no parental criticism showed the lowest rate (19.8%) (12).

The study by the faculty of Medicine at Jazan University assessed the prevalence, severity, disability, and quality of life of social anxiety disorder among undergraduate students. The most commonly reported feared situations in the target sample were acting, performing, or giving a talk in front of an audience followed by taking a test, and the most commonly avoided situations were blushing in front of people followed by having to give speeches; and they found that social anxiety disorder is associated with impairment in the area of work, social life, and family life. The results of this study of 476 students showed that 25.8% were screened positive for social anxiety disorder and 10.5% had severe to very severe symptoms of social anxiety disorder (13).

Another study on medical students at Taibah University in Medina city aimed to assess the prevalence of social anxiety disorder and its associated factors and its effect on the performance of medical students. The study included 504 medical students. The result found that social anxiety disorder was relatively high among medical students and was correlated negatively with academic performance (14). The Clark and Wells (15) model foretold that social anxiety is maintained through a negative feedback loop, consisting of poor self-expectations, anticipatory anxiety, and cognitive impairment. Poor performance and reinforcing negative self-beliefs may be positively interrupted through social and clinical interventions tailored to improve personal confidence, self-awareness, and social skills. Based on this, we think students with social anxiety should engage more in public speaking and group interaction to develop confidence and skills in public speaking and anxiety-management (16). Based on diagnostic interview data from National Comorbidity Survey Replication (NCS-R), an estimated 12.1% of U.S. adults have experienced a social anxiety disorder at some time in their lives.

Data from the Saudi national mental health survey showed a high prevalence of social phobia in Saudi Arabia which is about 5.6% (4). Still, there is a gap in the literature and

a lack of studies assessing this health problem in Saudi Arabia. This makes it mandatory to study social phobia prevalence among medical students at King Abdulaziz University (Rabigh branch).

This study aimed to determine the prevalence and risk factors of social anxiety disorder among medical students at King Abdulaziz University in Rabigh, Saudi Arabia.

Subjects and Methods

Study design, setting, and time frame:
A cross-sectional study was done at King Abdulaziz University in Rabigh, Saudi Arabia from June to August 2022.

Study participants:
The inclusion criteria were all medical students registered at King Abdulaziz University, Faculty of Medicine in Rabigh of Saudi nationality of both genders. The exclusion criteria were non-medical students, non – Saudi students, and those from other universities.

Sample size:
With a 95% confidence level and 5% margin of error and with using Raosoft online (17) sample size calculator, a sample size of 212 participants was the minimum allowed sample.

Data collection:
A pre-designed questionnaire was distributed through an online link and sent to all medical students through class group leaders. The links directed the participants to the consent form and respondents were not able to proceed with the survey unless they agree. The questionnaire included two sections, the first included items about participants' demographic data and the second included the Liebowitz Social Anxiety Scale (LSAS) [Fear or Anxiety] and [Avoidance] (18).

The Liebowitz Social Anxiety Scale (LSAS) is widely used to measure the scale of social anxiety. It has been used in studies of pharmacotherapy of social anxiety and cognitive behavioral group treatment for social anxiety (19,20). The LSAS comprises 24 items that measure fear, and avoidance separately for 24 social situations over the past week. Participants were classified according to the scale score into having no, or mild social anxiety disorder with a score ranging from (0-49), moderate social anxiety disorder (50-69), marked social anxiety disorder (70-89), severe social anxiety disorder (90-109) and very severe social anxiety disorder (≥ 110) (19,20).

Ethical considerations:
Ethical approval for the study was obtained from the research ethics committee at King Abdulaziz University.

Data analysis:
Data were analyzed statistically using (SPSS) version 26. (Armonk, NY: IBM Corp.). For testing different relationships between variables and qualitative data, which were expressed in numbers and percentages, we used the Chi-squared test ($\chi 2$). A p-value of less than 0.05 was considered statistically significant.

Results

(Table 1) shows that from the 218 (total medical students), 52.8% of the participants had an age that ranged from 21-23 years, 54.6% were males and 40.4% had a monthly income > 15000 SR. 18.3% of the participants were in either second, third or the fourth academic year.

(Table 2) shows that only nine participants (4.1%) had psychological disorders, six (66.7%) of them, had depression, and three (33.3%) of them had anxiety. Only 5.5% had chronic diseases. Most of the participants (52.8%, 82.6%, and 56.9%) were satisfied with their weight, facial appearance, and body image, respectively. About 18% had a history of physical or sexual abuse and 20.2% had a family history of anxiety disorders. Only 14.7% tried to access mental health services and 39.9% knew how to access mental health services when they needed help.
Only fourteen participants (6.4%) had no or mild social anxiety disorder, while 204 (93.6%) had several grades of a social anxiety disorder (Figure 1).

(Table 3) demonstrates that participants with an age range from 21-23 years, females, and those with 7000-15000 SR monthly income had a significantly higher percentage of those who suffered from very severe social anxiety disorder (p=< 0.05). On the other hand, a non-significant relationship was found between the level of social anxiety disorders and participants' academic year (p=> 0.05).
(Table 4) demonstrated that participants who had chronic illnesses had a higher percentage of those who suffered from marked social anxiety disorder, this finding was not statistically significant (p=>   0.05). At the same time, participants who had no satisfaction with weight or facial appearance and who did not know how to access mental health services when needed help had a significantly higher percentage of those who suffered from very severe social anxiety disorder (p=< 0.05).

Table 1. Distribution of studied participants according to their demographic characters and academic year (No.=218)

Variable	No. (%)
Age groups (years)	
• 18-20	44 (20.2)
• 21-23	115 (52.8)
• 24-26	59 (27.1)
Gender	
• Female	99 (45.4)
• Male	119 (54.6)
Monthly income (SR)	
• Less than 3000	18 (8.3)
• 3000-5000	18 (8.3)
• 5001-7000	25 (11.5)
• 7001-15000	69 (31.7)
• More than 15000	88 (40.4)
Academic year	
• 2nd	40 (18.3)
• 3rd	40 (18.3)
• 4th	40 (18.3)
• 5th	35 (16.1)
• 6th	33 (15.1)
• Intern	30 (13.8)

Table 2: Distribution of studied participants according to medical history, satisfaction with appearance, and access to mental health services (No.=218)

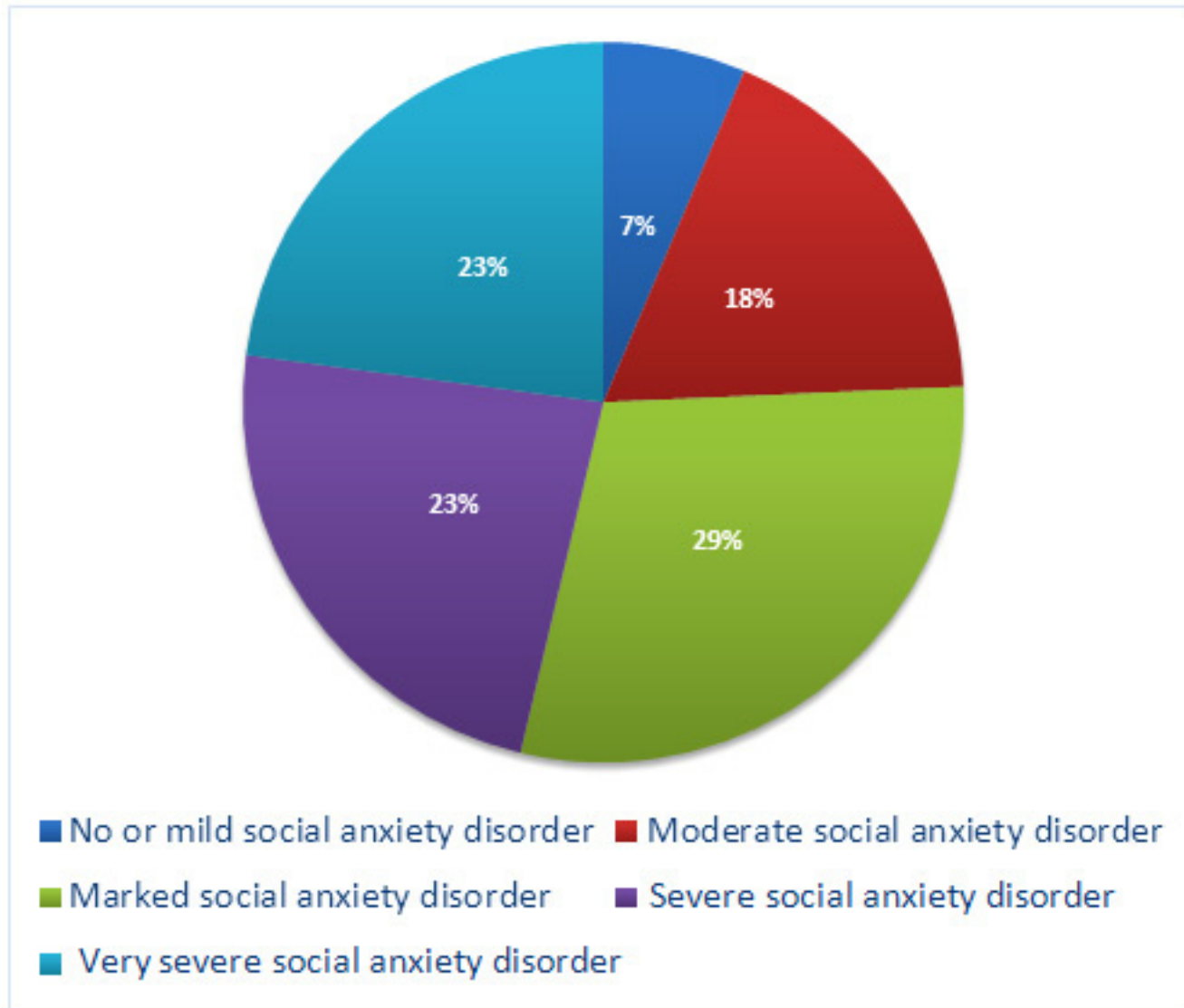| Variable	No. (%)
Psychological disorders	
• No	209 (95.9)
• Yes	9 (4.1)
If yes, specify: (No.:9)	
• Depression'	6 (66.7)
• Anxiety	3 (33.3)
Chronic illness	
• No	206 (94.5)
• Yes	12 (5.5)
Satisfaction with weight	
• No	103 (47.2)
• Yes	115 (52.8)
Satisfaction with facial appearance	
• No	38 (17.4)
• Yes	180 (82.6)
Satisfaction with body image	
• No	94 (43.1)
• Yes	124 (56.9)
History of physical or sexual abuse	
• No	178 (81.7)
• Yes	40 (18.3)
Family history of anxiety disorders	
• No	174 (79.8)
• Yes	44 (20.2)
Tried to access mental health services	
• No	186 (85.3)
• Yes	32 (14.7)
Know how to access mental health services when need help	
• No	131 (60.1)
• Yes	87 (39.9)

Figure 1: Distribution of studied participants according to the level of social anxiety disorder

Table 3. Relationship between the social anxiety disorder levels with participants' demographic characters, and academic year (No.=218)

Variable	Social anxiety disorder levels					Chi -square	P. value
	No or mild No. (%)	Moderate No. (%)	Marked No. (%)	Severe No. (%)	Very severe No. (%)		
Age groups (years)							
18-20	5 (11.4)	5 (11.4)	20 (45.5)	5 (11.4)	9 (20.5)		
21-23	7 (6.1)	24 (20.9)	24 (20.9)	28 (24.3)	32 (27.8)	18.18	0.02*
24-26	2 (3.4)	10 (16.9)	20 (33.9)	18 (30.5)	9 (15.3)		
Gender							
Female	8 (8.1)	22 (22.2)	16 (16.2)	21 (21.2)	32 (32.3)	20.77	0.00*
Male	6 (5)	17 (14.3)	48 (40.3)	30 (25.2)	18 (15.1)		
Monthly income (SR)							
Less than 3000							
3000-5000	0 (0.0)	0 (0.0)	9 (50)	6 (33.3)	3 (16.7)		
5001-7000	1 (5.6)	4 (22.2)	5 (27.8)	4 (22.2)	4 (22.2)	32.26	0.00*
7001-15000	6 (24)	2 (8)	5 (20)	8 (32)	4 (16)		
More than 15000	3 (4.3)	9 (13)	24 (34.8)	15 (21.7)	18 (26.1)		
	4 (4.5)	24 (27.3)	21 (23.9)	18 (20.5)	21 (23.9)		
Academic year							
2nd	5 (12.5)	3 (7.5)	13 (32.5)	8 (20)	11 (27.5)		
3rd	1 (2.5)	5 (12.5)	16 (40)	7 (17.5)	11 (27.5)		
4th	3 (7.5)	10 (25)	7 (17.5)	7 (17.5)	13 (32.5)	28.19	0.10
5th	3 (8.6)	11 (31.4)	7 (20)	8 (22.9)	6 (17.1)		
6th	0 (0.0)	5 (15.2)	12 (36.4)	12 (36.4)	4 (12.1)		
Intern	2 (6.7)	5 (16.7)	9 (30)	9 (30)	5 (16.7)		

* Means the P value <0.05 is statistically significant

Table 4. Relationship between level of social anxiety disorders and psychological & chronic diseases history, satisfaction with weight, facial appearance, body image, and access to mental health services (No.:218)

Variable	Social anxiety disorder					Chi-square	P.value
	No or mild No. (%)	Moderate No. (%)	Marked No. (%)	Severe No. (%)	Very severe No. (%)		
Psychological disorders						2.31	0.67
No	13 (6.2)	36 (17.2)	62 (29.7)	49 (23.4)	49 (23.4)		
Yes	1 (11.1)	3 (33.3)	2 (22.2)	2 (22.2)	1 (11.1)		
Chronic illness						1.64	0.80
No	13 (6.3)	38 (18.4)	59 (28.6)	49 (23.8)	47 (22.8)		
Yes	1 (8.3)	1 (8.3)	5 (41.7)	2 (16.7)	3 (25)		
Satisfaction with weight						10.98	**0.02***
No	1 (1)	20 (19.4)	29 (28.2)	25 (24.3)	28 (27.2)		
Yes	13 (11.3)	19 (16.5)	35 (30.4)	26 (22.6)	22 (19.1)		
Satisfaction with facial appearance						20.89	**0.00***
No	2 (5.3)	2 (5.3)	5 (13.2)	11 (28.9)	18 (47.4)		
Yes	12 (6.7)	37 (20.6)	59 (32.8)	40 (22.2)	32 (17.8)		
Satisfaction with body image						8.6	0.07
No	1 (1.1)	18 (19.1)	27 (28.7)	23 (24.5)	25 (26.6)		
Yes	13 (10.5)	21 (16.9)	37 (29.8)	28 (22.6)	25 (20.2)		
History of physical or sexual abuse						6.31	0.17
No	13 (8.3)	36 (20.2)	49 (27.5)	42 (23.6)	38 (21.3)		
Yes	1 (2.5)	3 (7.5)	15 (37.5)	9 (22.5)	12 (30)		
Family history of anxiety disorders						5.3	0.258
No	16 (8)	31 (17.8)	53 (30.5)	39 (22.4)	37 (21.3)		
Yes	0 (0.0)	8 (18.2)	11 (25)	12 (27.3)	13 (29.5)		
Tried to access mental health services						3.42	0.49
No	14 (7.5)	34 (18.3)	52 (28)	43 (23.1)	43 (23.1)		
Yes	0 (0.0)	5 (15.6)	12 (37.5)	8 (25)	7 (21.9)		
Know how to access mental health services when need help						10.89	**0.02***
No	11 (8.4)	19 (14.5)	34 (26)	29 (22.1)	38 (29)		
Yes	3 (3.4)	20 (23)	30 (34.5)	22 (25.3)	12 (13.8)		

*Means the P value p< 0.05 is statistically significant

Discussion

This study aimed to identify the prevalence of social anxiety disorder among medical students in King Abdulaziz University- Rabigh branch and its associated factors and effect on students. The data was collected from 218 students aged from 18 years to 26 years, from the second academic year to the sixth year, with different socioeconomic levels and variable demographic backgrounds.

The prevalence results are almost evenly distributed among medical students, as it shows that the percentage of the students who reported no to mild social anxiety disorder is 6.4%, students with moderate social anxiety disorder is 17.9%, and students with marked social anxiety disorder is 29.4%, and students with severe social anxiety disorder is 23.4%, and students with very severe social anxiety disorder is 22.9%.

A recent study was conducted in Saudi Arabia which showed that the percentage of medical students with mild social anxiety disorder is 20.22%, students with moderate social anxiety disorder is 18.32%, students with severe social anxiety disorder is 8.21%, and students with very severe social anxiety disorder is 4.21% (19). Another similar study in Saudi Arabia has found the percentage of moderate social anxiety disorder among students is 19.6%, severe social anxiety disorder among students is 8.5%, and very severe social anxiety disorder among 5.0% of medical students which shows how common social anxiety disorder is among medical students (14).

Our study shows that more severe social anxiety disorder is found more among the female participants, in accordance with our presented findings. It is shown in other similar studies referring to higher social anxiety disorder severity results among female medical students as compared to male students (20,22,27), however, other studies found that males have a higher incidence of social anxiety disorder (21), while some studies showed no marked difference between genders (14).

Regarding age-divided groups, we found that students aged between 21 and 23 have a significantly higher number of severe social anxiety disorder, which could be attributed to the fact that the fourth academic year which is within this range of age, is practically the period that they start their clinical years and contact with patients, their families, and supervising professors and doctors, as the fourth academic year shows more severe social anxiety disorder results within our current study too. However, the occurrence of social anxiety disorder gradually decreases in severity and quantity in older students as they progress through higher academic years. This can be explained by the fact that more senior students and house officers gain more experience about the medical field, which is consistent with the findings of multiple studies that show decreased percentage of social anxiety disorder among older students (14,20).

An unexpected finding of our study is that students with higher income are shown to have more severe social anxiety disorder, which can be due to the probability of students with higher income having higher expectations and therefore being pressured by their limited academic accomplishments, yet the study provides no consistent finding to support this claim. On the contrary, another similar study in Taibah University showed students with higher income are less likely to have social anxiety disorder (14).

One interesting finding is that there is an unexpectedly low association between students with previous psychological disorders and students with social anxiety disorder, which could be referred to the lack of access to mental health facilities and services among students, and the lack of mental health awareness among young adults in Saudi Arabia, as it's shown in this study conducted in Jazan University, undergraduate students mostly have an intermediate mental health literacy (23).

Our study has found a relationship between dissatisfaction with weight and body image and severe social anxiety disorder, which are two different factors as the body image category could include certain scars or deformities and not only overweight or an underweight appearance. However, they both have the same outcome. These results could be explained by multiple factors; it could be that a student already having social anxiety disorder develops the habit of overeating as a way to cope with the resulting stress and thus gains more weight which is common in anxiety patients (26), and also that students in both categories are more vulnerable to bullying and having lower levels of self-esteem and are more susceptible to social pressure. These results are mirrored by multiple studies that support an association between dissatisfaction with weight and social anxiety disorder (11,24,25). There was an insignificant finding that there was a weak correlation between dissatisfaction with facial appearance and social anxiety disorder.

Another interesting finding is the negative correlation between the history of anxiety in the family and social anxiety disorder among students in the study, which was not surprising due to the wide range of stigma against psychological cases in Saudi Arabia and the high probability of not telling a family member of a current psychological diagnosis as mentioned by this research (28), and it shows more than half of the patients with a mental disorder try to hide their illness.

The current study has also found that students who reported having access to mental health services had lower severity of social anxiety disorder compared to other students. This can be attributed to specific barriers, one of them being "low perceived need" for mental health services, or in other cases they perceive the need to access mental health services, but barriers could be related to either attitudinal factors (e.g., believing they can overcome their condition alone) or structural factors (e.g., inability to access mental health services or lack of financial freedom), which points

to the necessity of awareness of mental health services among students and faculty (29).

In conclusion, we have collectively found that the prevalence of social anxiety disorder among medical students of King Abdulaziz University-Rabigh branch is relatively high. It was positively associated with age in a major way, and academic year. It was also negatively associated with the diagnosis of psychological disorders, and it was positively associated with satisfaction with body image and weight, and positively associated with their lack of access to mental health services.

We acknowledge certain limitations in our study; one of them is using self-reported questionnaires, which cannot always be depended on in the matters of verifications of minute details, and could certainly provide a small percentage of bias to the study, and we had a conveniently small source of students, since The Medical College in King Abdulaziz University- Rabigh branch is a new and growing college, and the cross-sectional design of the questionnaire could provide more limited detection of a possible relationship between our study variables to a certain degree.

Declaration of Interest:
The authors declare no conflict of interest.

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The Correlation Between Depression and Pseudosciences (Astrology, Tarot Cards, Psychic Readings)

Yara Khalid Alkhalid[1], Bander Haddad[2,3], Ahmed Bandar Alasiri[2] ,
Jamal Sulaiman Alothaim[2], Arwa Mohammed Alamer[2].

(1) College of Medicine, Imam Mohammad ibn Saud Islamic University, Riyadh, Saudi Arabia.
(2) College of Medicine, Imam Mohammad ibn Saud Islamic University, Riyadh, Saudi Arabia
(3) Neuroscience Department, College of Medicine, Imam Mohammad ibn Saud Islamic University, Riyadh, Saudi Arabia

Corresponding author:
Yara Khalid Alkhalid
Riyadh, Saudi Arabia.
Post code: 13317
Email: Yara.alkhalid@gmail.com

Abstract

Introduction: Depression prevalence is increasing worldwide, and so are Astrology, tarot cards, and psychics readings practices, as most people who seek pseudoscience practices tend to seek an answer to life issues that they suffer from, such as relationships, or financial issues for example.

Aim: This study aimed to find the correlation between pseudoscience practices and depression among pseudoscience believers in Saudi Arabia.

Subjects and method: This is a cross-sectional study conducted among the Saudi population who believe in pseudoscience. A self-administered questionnaire was distributed electronically using social media platforms, which adhere to the tenets of the Declaration of Helsinki 2013. The questionnaire was composed of socio-demographic variables, psychic-related practices, and depression questionnaires using Patient Health Questionnaire (PHQ-9).

Results: Of the 409 pseudoscience believers, 41.8% were aged between 26 – 35 years old with females being dominant (94.5%). The most prominent practice of reading was the Zodiac (81.3%). The prevalence of depression among pseudoscience believers was 36.3%. In univariate analysis, depression was significantly associated with the younger age group ($p<0.001$), less educated participants ($p=0.028$), being single ($p<0.001$), student ($p=0.001$), and practicing Zodiac ($p=0.014$). In a multivariate regression model, Zodiac practice reading was determined as the sole independent significant predictor of increased depression rates.

Conclusion: There was a high prevalence of depression among pseudoscience believers. Increased depression was demonstrated more frequently by younger believers who were still single, less educated, and who were currently engaged in Zodiac reading practices. More research is needed to shed more light on the effect of pseudoscience on the mental health condition of its believers.

Keywords: Pseudoscience, psychic reading, depression, astrology

Introduction

Depression is a disorder that can interfere with the patient's life, and results in burden, where the patient cannot function properly during daily activities (19). Depression is increasing worldwide, and so is the prevalence of astrology, tarot cards, and psychic readings practices, as most people who seek pseudosciences practices tend to seek an answer for life in the future, life issues, relationships issues, and financial issues. Pseudosciences like psychic readings, cup readings, tarot cards, astrology, and other Pseudosciences practices profess to help heal the client in becoming a whole, such as energy healing, or guide the person into understanding their personality more, like birth charts in astrology (20).

Psychic Readings, Cup readings and Tarot Cards:
Psychic readings, Cup readings and Tarot Cards profess to provide information about unknown events, emotions and questions. Each one of them uses different ways in providing such an answer. Psychic readings profess to use extra human abilities to provide answers. Cup readings are by reading the cup after drinking coffee, in which the coffee grounds will dissolve in the bottom of the cup giving the psychic reader a shape from which to read about the client's fortune. Tarot Cards on the other hands, uses cards that can represent the client's chances, hidden intentions and potential giving a clue about the client's thoughts about various topics a tarot card reader can provide (21).

Astrology:
Astrology is a type of pseudoscience that has a variety of aspects. but the major aspects and the more commonly used are personality aspects, answers about unknown questions, yearly events by star charts, the person's past, present and future. Astrologists provide the answers by using the person's birthday, birth time and place, with the guide of planets, like Mars, Venus, Mercury, Sun, Moon, Saturn, Jupiter, Uranus, Neptune and Pluto under different kinds of signs, where each person is different from one another and they are called the Zodiac Signs. There are twelve signs in total, for example, Cancer and Gemini according to which time of the year you are born. Astrologists also claim that each person has a unique birth chart, based on the position of the planets when they are born and under what 'house' the date falls into as there are also twelve houses which, it is claimed can influence the person's life in the past, present and future (22). It also provides the seeker advice on the ways that can enhance their mental, physical, economy, as well as health from a point of view of astrologer by complex ways to reduce the hard angles in the client's birth chart for example enhancing the moon in the client's birth chart as moon represents emotions, so astrologists believe that it can help in the case of depression (8).

Energy Healings:
The last branch of pseudoscience types in this research is energy healings that help to enhance the person's wholeness in emotional, social, physical, mental, and many other aspects of life giving the person a chance to become a whole soul. It uses different approaches, like Reiki in the East Asian approach, therapeutic touch (TT) and healing touch in western approaches, and many other different techniques (20).

Statistical Analysis

The assessment of depression was drawn from the patient health questionnaire (PHQ-9) developed by Kroenke, Spitzer, & Williams, (2001). It is composed of a 9-item questionnaire with 4-point Likert scale categories ranging from "Not at all" coded with 0 to "nearly every day" coded with 3. The score has a possible range from 0 to 27. A higher score indicates higher depression. Depression levels were categorized as "depressed" (score <10 points) and "not depressed (score ≥10 points). Minimal depression (score 0 – 4 points), mild depression (score 5 – 9 points), moderate (score 10 – 14 points), moderately severe (score 15 – 19 points), severe depression (score 20 – 27 points) (12).

Descriptive statistics were calculated to present numbers and percentages for all categorical variables while mean and standard deviation were used to present continuous variables. The relationship between the level of depression in regards to the socio-demographic characteristics and psychic-related practices of participants was conducted using the Chi-square test. Significant results were then tested in a multivariate regression model to determine the independent significant predictor of depression. A p-value of 0.05 was used to indicate statistical significance. All data analyses were performed using the Statistical Packages for Software Sciences (SPSS) version 26 (Armonk, New York, IBM Corporation, USA.).

Methodology

This is a cross-sectional study which was conducted among the Saudi population who practice pseudoscience from April 2022 to December 2022. A self-administered questionnaire was distributed electronically using social media platforms, which adhere to the tenets of the Declaration of Helsinki 2013. The questionnaire was distributed to 409 believers including both males and females and was composed of three sections. The first section contained ten socio-demographic variables questions, which give information about the believer, or the practitioner's life, as well as the common denominators between them. The second section contained 14 questions, involving detailed questions about Pseudosciences practices (Astrology, Tarot cards, Psychic Readings, Cup Readings, and Energy healings) such as, the reasons for engaging in them, how frequently, their thoughts, beliefs and outcomes, in order to get better perspectives into the minds of people who are engaged with pseudosciences practices. The last, and the third section was the PHQ9 depression questionnaire, to clarify if there is any correlation between pseudoscience practitioners and depression.

Results

Table 1: Socio-demographic characteristics of the participants (n=402)

Study variables	N (%)
Age group	
• 16 – 18 years	30 (07.5%)
• 19 – 25 years	133 (33.1%)
• 26 – 35 years	168 (41.8%)
• >35 years	71 (17.7%)
Gender	
• Male	22 (05.5%)
• Female	380 (94.5%)
Nationality	
• Saudi	367 (91.3%)
• Non-Saudi	35 (08.7%)
Residence region	
• Central Region	165 (41.0%)
• Eastern Region	52 (12.9%)
• Western Region	129 (32.1%)
• Southern Region	30 (07.5%)
• Northern Region	26 (06.5%)
Educational level	
• Middle school	04 (01.0%)
• High school	60 (14.9%)
• Bachelor's degree	295 (73.4%)
• Master or PhD	43 (10.7%)
Socio-economic status (SAR)	
• <5,000	262 (65.2%)
• 5,000 – 15,000	91 (22.6%)
• 15,001 – 25,000	33 (08.2%)
• 25,001 – 35,000	09 (02.2%)
• >35,000	07 (01.7%)
Marital status	
• Single	275 (68.4%)
• Engaged/Married	76 (18.9%)
• Divorced	51 (12.7%)
Employment status	
• Student	118 (29.4%)
• Unemployed	125 (31.1%)
• Employed	115 (28.6%)
• Free Business	30 (07.5%)
• Working and free business	14 (03.5%)

Table 1: Socio-demographic characteristics of the participants (n=402) continued

| Living Arrangement	
• Alone	31 (07.7%)
• With family	306 (76.1%)
• With husband	21 (05.2%)
• With husband and children	44 (10.9%)
Place residence	
• Apartment (rented)	130 (32.3%)
• Apartment (owned)	37 (09.2%)
• House	235 (58.5%)

A total of 402 respondents were recruited. Table 1 presents the socio-demographic characteristics of participants. 41.8% were aged between 26 to 35 years old with nearly all being females (94.5%) and most were Saudis (91.3%). 41% lived in the Central Region. Respondents who were bachelor degree holders were 73.4%. With regard to socio-economic status, nearly two-thirds (65.2%) were earning less than 5,000 SAR per month. With respect to marital status, 68.4% were single and 31.1% were unemployed. Also, 76.1% were living with family and 58.5% lived in their own house.

Figure 1: Sources of information regarding psychic-related practices
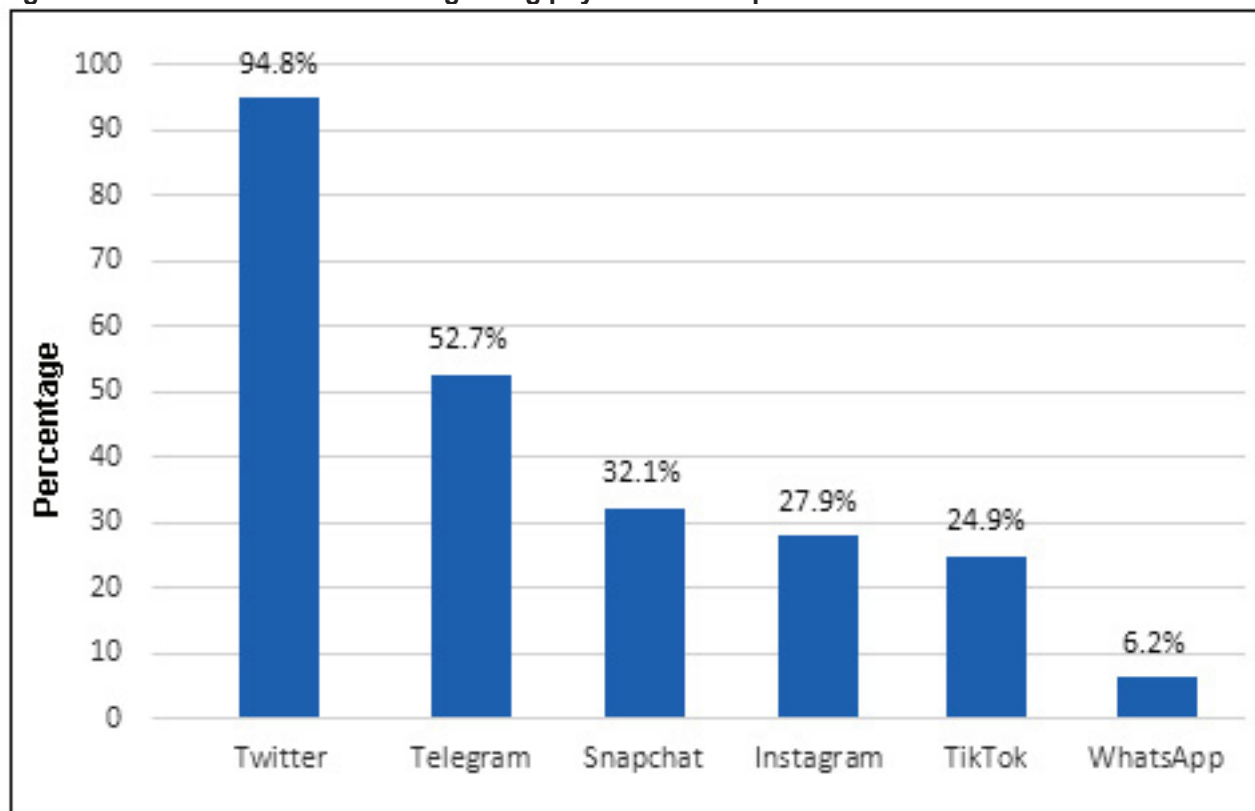
In Figure 1, the common source of information regarding psychic-related practices was Twitter (94.8%), followed by telegram (52.7%) and Snapchat (32.1%).

Figure 2: General mood before and after engagement in psychic-related practices
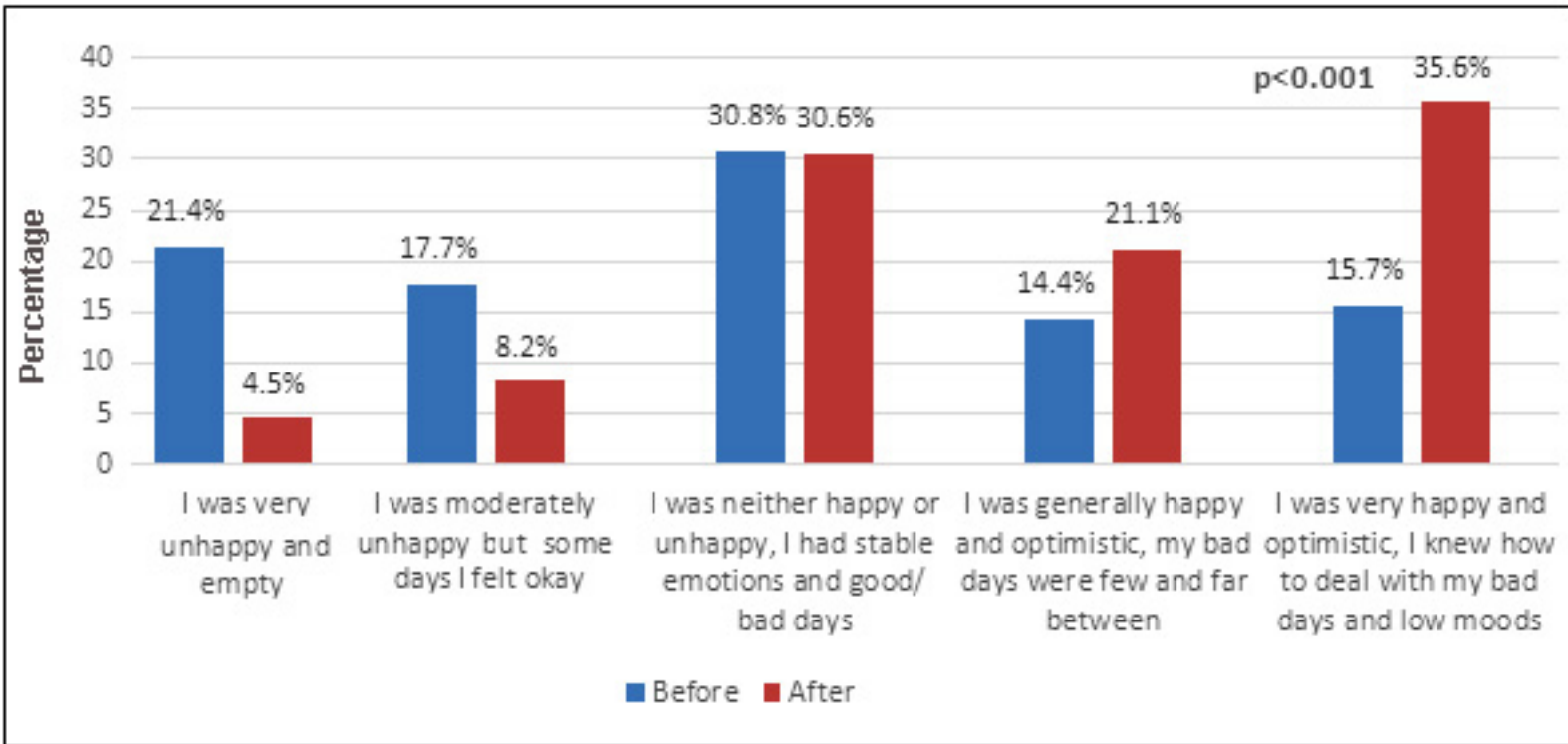
In Figure 2, there was a significant difference between the general mood before and after psychic-related practices engagement (p<0.001).

Table 2: Psychic-related practices (n=402)

Statement	N (%)
What are the practices that you read of? [†]	
• Zodiac (horoscope/astrology)	327 (81.3%)
• Energy healing work (E.g. Theta, Reiki)	212 (52.7%)
• Tarot	201 (50.0%)
• Psychics reading	176 (43.8%)
• Cup reading	82 (20.4%)
How much would you describe your belief in them?	
• I don't believe in them	08 (02.0%)
• I don't believe in them, but I read them for fun	39 (09.7%)
• I believe that sometimes they are right, but also believe that some of them could be untrue	222 (55.2%)
• I believe in them completely	133 (33.1%)
How did you get them?	
• I look for accounts and follow them to stay updated	344 (85.6%)
• I get them sent by friends	50 (12.4%)
• I usually avoid them	08 (02.0%)
How often do you read them?	
• Daily (multiple times a day)	117 (29.1%)
• Daily (once or twice a day)	67 (16.7%)
• Every other day	44 (10.9%)
• Weekly	32 (08.0%)
• Monthly	12 (03.0%)
• When I have a question on my mind	130 (32.3%)
What was your reason behind starting to engage yourself in these practices?	
• Curiosity about the future	65 (16.2%)
• A painful event (Divorce, break-up, death)	46 (11.4%)
• A life aspect that I wanted predictions for (Family issues, income issues)	31 (07.7%)
• Looking for answers about a specific topic	163 (40.5%)
• To feel hope and optimism about the future	97 (24.1%)
Did your engagement with them affect your life?	
• No	91 (22.6%)
• Slightly	106 (26.4%)
• Moderately	101 (25.1%)
• Yes, majorly	104 (25.9%)
Was the effect positive or negative?	
• Positive	276 (68.1%)
• Negative	35 (08.7%)
• No effect	91 (22.6%)
Have any of the readings come true?	
• Yes, all	11 (02.7%)
• Yes, most of them	116 (28.9%)
• Yes, part of it	137 (34.1%)
• No	25 (06.2%)
• I do not practice readings concerned with predicting the future	113 (28.1%)

† Variables with multiple response answers.

Table 2: Psychic-related practices (n=402) Continued

Statement	N (%)
Do you think engaging in these readings can be helpful for other people?	
• Yes	239 (59.5%)
• No	163 (40.5%)
During your low moods/bad days, have you ever sought help from a professional (Psychiatrist, therapist...)?	
• Yes	174 (43.3%)
• No, but I thought about it / wanted to	177 (44.0%)
• Never	51 (12.7%)
If yes, were they helpful? (n=174)	
• Yes	87 (50.0%)
• No	34 (19.5%)
• Probably	53 (30.5%)
If no, what was the reason for not going for a professional? (n=174)	
• Financial issues	82 (36.0%)
• I don't believe they are helpful	61 (26.8%)
• Others	85 (37.3%)

† Variables with multiple response answers.

In Table 2, the most common practice related to a pseudoscience that participants were reading was zodiac (81.3%), followed by energy healing (52.7%) and tarot (50%). 55.2% were of the opinion that people who consult psychics were sometimes right but some of this might not be true. Nearly all (85.6%) indicated that they found these people by searching for their accounts and subscribing to them to stay updated. 29.1% used to read pseudoscience multiple times a day. The most common reason to engage in these practices was looking for answers about a specific topic (40.5%). A quarter of them (25.9%) indicated that engagement in pseudoscience practices affects them majorly wherein 68.1% reported positive effect in their lives. Only 2.7% reported that the obtained readings all came true. Approximately 60% of the respondents believed that engaging in these readings can be helpful. The proportion of respondents who sought professional help during low moods/bad days was 43.3%, wherein 50% indicated that the sought advice was helpful. Of those who did not seek professional help, the most common reason was financial constraints (36%).

Table 3: Prevalence of depression according to PHQ-9 (n=402)

Variables	N (%)
Depression score (mean ± SD)	8.49 ± 6.33
Level of depression	
• Depressed	146 (36.3%)
• Not depressed	256 (63.7%)
Severity of depression	
• Minimal	126 (31.3%)
• Mild	130 (32.3%)
• Moderate	79 (19.7%)
• Moderately severe	40 (10.0%)
• Severe	27 (06.7%)
How difficult has this problem been when performing your work, studying, or carrying out your responsibilities in your home or in harmony with people?	
• Not difficult at all	199 (49.5%)
• Somewhat difficult	139 (34.6%)
• Very difficult	33 (08.2%)
• Extremely difficult	31 (07.7%)

The prevalence of depression has been discussed in Table 3. Based on the results, it was found that the total mean score of depression was 8.49 (SD 6.33) and the prevalence of depressed participants was 36.3%, the rest were not depressed (63.7%). Regarding depression severity, minimal, mild, moderate, moderately severe, and severe were found in 31.3%, 32.3%, 19.7%, 10%, and 6.7% of participants, respectively. Overall, only 8.2% expressed difficulties when performing work, studying, or doing tasks at home or socializing with people while 7.7% had extreme difficulties.

When measuring the relationship between the level of depression in regard to the socio-demographic characteristics and other psychic-related practices of participants (Table 4), it was found that the prevalence of depression was significantly more common among the younger age group (p<0.001), less educated participants (p=0.028), being single (p<0.001), student (p=0.001), and practicing Zodiac (p=0.014) while it was significantly less among those who practiced energy healing (p=0.004). Other variables did not significantly relate to the level of depression including gender, socio-economic status, place of residence engagement in practices that affect life, engagement that can be helpful to others, and visiting a professional during low moods/bad days (p>0.05).

In a multivariate regression model (Table 5), it was revealed that only Zodiac reading was the sole independent significant predictor of depression, compared to participants who were engaged in other psychic readings. Participants who were engaged in Zodiac readings were predicted to increase the risk of depression by almost 2 times higher (AOR=1.965; 95% CI=1.086 – 3.553; p=0.025). Other variables included in the model were not predicted to increase the risk of depression including age, educational level, marital status, and employment status (p>0.05).

Table 4: Relationship between the level of depression according to the Socio-demographic characteristics and psychic-related practices of the participants (n=402)

Factor	Level of depression		P-value §
	Depressed N (%) (n=146)	Not depressed N (%) (n=256)	
Age group			
• ≤25 years	79 (54.1%)	84 (32.8%)	<0.001 **
• >25 years	67 (45.9%)	172 (67.2%)	
Residence region			
• Inside Central Region	56 (38.4%)	109 (42.6%)	0.408
• Outside Central Region	90 (61.6%)	147 (57.4%)	
Educational level			
• High school or below	31 (21.2%)	33 (12.9%)	0.028 **
• Bachelor's degree or higher	115 (78.8%)	223 (87.1%)	
Socio-economic status (SAR)			
• <5,000	104 (71.2%)	158 (61.7%)	0.054
• ≥5,000	42 (28.8%)	98 (38.3%)	
Marital status			
• Single	116 (79.5%)	159 (62.1%)	<0.001 **
• Engaged/Married/Divorced	30 (20.5%)	97 (37.9%)	
Employment status			
• Student	59 (40.4%)	59 (23.0%)	0.001 **
• Unemployed	41 (28.1%)	84 (32.8%)	
• Employed	46 (31.5%)	113 (44.1%)	
Place residence			
• Apartment	59 (40.4%)	108 (42.2%)	0.728
• House	87 (59.6%)	148 (57.8%)	
Practices to psychic readings †			
• Zodiac	128 (87.7%)	199 (77.7%)	0.014 **
• Tarot	68 (46.6%)	133 (52.0%)	0.300
• Cup reading	27 (18.5%)	55 (21.5%)	0.474
• Psychic readings	57 (39.0%)	119 (46.5%)	0.148
• Energy healing	63 (43.2%)	149 (58.2%)	0.004 **
Did your engagement with them affect your life?			
• Yes	107 (73.3%)	204 (79.7%)	0.140
• No	39 (26.7%)	52 (20.3%)	
Do you think engaging in these readings can be helpful for other people?			
• Yes	79 (54.1%)	160 (62.5%)	0.099
• No	67 (45.9%)	96 (37.5%)	
During your low moods/bad days, have you ever sought help from a professional?			
• Yes	62 (42.5%)	112 (43.8%)	0.803
• No	84 (57.5%)	144 (56.3%)	

† Variable with multiple response answers. § P-value has been calculated using Chi-square test.
** Significant at $p < 0.05$ level.

Table 5: Multivariate regression analysis to determine the independent significant factor associated with depression (n=402)

Factor	AOR	95% CI	P-value
Age group			
• ≤25 years	Ref		
• >25 years	0.687	0.376 – 1.257	0.223
Educational level			
• High school or below	Ref		
• Bachelor's degree or higher	0.708	0.398 – 1.258	0.239
Marital status			
• Single	Ref		
• Engaged/Married/Divorced	0.593	0.346 – 1.016	0.057
Employment status			
• Student	Ref		
• Unemployed	0.752	0.384 – 1.472	0.405
• Employed	0.911	0.539 – 1.542	0.730
Practices psychic readings †			
• Zodiac	1.965	1.086 – 3.553	0.025 **
• Energy healing	0.670	0.435 – 1.033	0.070

AOR – Adjusted Odds Ratio; CI – Confidence Interval.
† Variable with multiple response answers.
 ** Significant at p<0.05 level.

Discussion

This study investigated the relationship between depression and pseudoscience-related practices among pseudoscience believers in Saudi Arabia. The findings of this study revealed that among pseudoscience believers, 36.3% were detected to have depression and the rest were not depressed (63.7%). The overall mean depression score based on PHQ-9 was 8.49 (SD 6.33). To our knowledge, this is the first study in Saudi Arabia that discussed the prevalence of depression among people who practice pseudoscience which could be an important contribution to the literature. We estimated that engagement with psychic readings triggered our believers to suffer from depressive symptoms . However, in a study by Doolittle and Farrel (13), where they investigated the association between depression and spirituality, they found out that the prevalence of depression was 62% higher than our report. They also reported that high spiritual scores were correlated with a decreased rate of depression, adding that patients' spiritual healing beliefs may be a helpful alternative solution for the treatment of depression. This account is also true in our study, as we found that energy healing practices are a protective factor against depression. Further investigations are required to determine whether engagement in pseudoscience-related practices causes believers to suffer from depression.

Data in this study indicate that increased depression was significantly more common among believers who were young in age, had lower educational levels, were single, students, and those who were engaged in Zodiac sign practices. Furthermore, we have learned that there was a significant number of believers (35.6%; p<0.001) who indicated that their mood improved and they were very happy and optimistic after psychic reading engagement. These findings are not consistent with that of Escolà-Gascón et al (14). They reported significant differences for the variables depressive symptoms, positive psychotic symptoms, and certain perceptual alterations. Also, a notable increase in pseudoscience beliefs during the COVID-19 quarantine has been shown in the population. Researchers indicated that the high increases might be due to the restrictions during the pandemic which limit their movement and only concentrated with people around the households affecting their mental conditions and paranoid perceptual alterations. Another study published in Turkey (15), reported that the relationship between religiosity and obstructive compulsive symptoms was mediated by magical thinking through punishment and worry. A similar effect on mental health conditions due to engagement in psychic reading had also been recounted by Fenwick et al (16). According to reports, there was evidence to suggest that some psychic experiences were associated with brain dysfunction, however, despite an increased occurrence of head injury, the onset of 'psychic' sensitivity has no clear indication of correlation with the brain disorder. Mystical experience and vagueness about the location of the sensitive's 'psychic helper' showed a trend toward being related to non-dominant brain dysfunction.

Based on multiple response answers, the most common psychic-related practices were Zodiac (81.3%), energy healing (52.7%), Tarot (50%), psychic reading (43.8%), and cup reading (20.4%). Regarding psychic-related practices of believers, more than half (55.2%) of believers indicated that not all readings were true. Nonetheless, most believers (85.6%) were great followers of psychic reading personalities online. Also, nearly 30% of the believers used to read pseudoscience topics multiple times per day looking for an answer about a certain topic (40.5%). Likewise, a quarter of them (25.9%) reported a great influence of psychics on their life, mostly in a positive way (68.1%) though only part of the readings became true (34.1%). In spite of this scenario, a great proportion of them (59.5%) thought that engaging in these readings can be of great help to other people. In addition, citing financial constraints as the major reason for not consulting a professional during low moods/bad days (36%), only 43.3% sought professional help during these occurrences. In India (17), a researcher investigated the negative effect of excessive belief in Astrology. According to reports, some people tend to believe that horoscopes can make predictions turn into reality without providing solid evidence. They frequently make absurd decisions according to their zodiac sign which is purely unreliable astrological predictions. The author then emphasized that people should not concentrate on their future from horoscopes and their predictions of it. They have to shape their own future and not let predictions conquer one's sanity. In UK (18), investigations about misinformation effects on psychic readings and belief in the paranormal lead them to find that believers would be more prone to the misinformation effect and such a way that believers' recall of the reading was imprecise even without exposure to misinformation while non-believers may have better memories of readings when not exposed to misinformation but their recall was comparable to believers upon exposure to misinformation.

Conclusion

There was a high prevalence of depression among pseudoscience believers. Increased depression was demonstrated more frequently by younger believers who were still single, less educat- ed, and who were currently engaged in Zodiac reading practices.

Although, participants who participated in the research mentioned that their life quality has improved after pseudosciences practices, yet the depression prevalence is still high. More research is needed to shed more light on the effect of pseudoscience on the mental health condition of its believers.

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Overview Methicillin-Resistant Staphylococcus Aureus Combination Treatment Options in Vivo and in Vitro

Ahmed Y. Mobarki[1], Ibrahim M. Dighriri[2], Ahmed S. Alotaibi[2], Manal M. Mobarki[2],
Wael M. Alsufyani[2], Sultan F. Almutairi[3], Fahad N. Alharthi[4], Mohammed H. Alessa[4],
Dhafer G. Alqahtani[5], Mohammed S. Almurayt[6], Shoug M. Aljuaid[7], Rahaf A. Alotaibi[7],
Nawaf R. Alsuwayidi[8], Khalaf A. Albaqqar[9], Othayman G. Alqahtani[10]

(1) Department of Molecular Biology, Regional Laboratory and Central Blood Bank, Abha, Saudi Arabia.
(2) Department of Pharmacy, King Abdulaziz Specialist Hospital, Taif, Saudi Arabia.
(3) Department of Pharmacy, King Fahd Specialist Hospital, Al Qassim, Saudi Arabia.
(4) Department of Pharmacy, King Abdulaziz Hospital, Makkah, Saudi Arabia.
(5) Department of Pharmacy, Wadi Aldawaser Hospital, Wadi Aldawaser, Saudi Arabia.
(6) Department of Pharmacy, Armed Forces Hospital Southern Region, Abha, Saudi Arabia.
(7) Department of Pharmacy, Community Pharmacy, Taif, Saudi Arabia.
(8) Pharmaceutical Care Services, Prince Sultan Armed Forces Hospital, Taif, Saudi Arabia.
(9) Department of pharmacy, Prince Mishari bin Saud Hospital, Albaha, Saudi Arabia.
(10) Department of Clinical Service Line, Riyadh First Health Cluster, Riyadh, Saudi Arabia

Corresponding author:
Ibrahim M. Dighriri
Department of Pharmacy, King Abdulaziz Specialist Hospital,
Taif, Saudi Arabia
Email: ibrahimdaghriri1411@gmail.com

Abstract

The spread of multidrug-resistant Staphylococcus aureus continues to threaten global health. Methicillin-resistant Staphylococcus aureus (MRSA) is one of the common causes of bacterial infections in hospitals and communities. Despite vancomycin being an effective treatment for MRSA, from 2006 to 2020, vancomycin-resistant MRSA increased 3.5-fold, from 5% to 7%. Bacterial genome mutations, as well as bacteria's ability to transfer genetic material with other bacteria, allowing them to obtain resistance genes from different strains, are all factors contributing to the development of vancomycin resistance in MRSA. As a result, combination therapy may be a potential treatment for MRSA infection. We searched in PubMed and Google Scholar, and our search yielded 92 articles, out of which 74 full-text articles were reviewed and 56 were selected for this study. This literature review examines combination therapies for MRSA infections, such as β-Lactams with vancomycin, linezolid and imipenem, daptomycin and ceftaroline. The review yielded several studies looking at the synergy between β-lactams and vancomycin. Although linezolid and rifampicin demonstrate synergy against MRSA in vivo and in vitro in various invasion diseases, more clinical research is required to prove their efficacy. Furthermore, daptomycin plus ceftaroline shows synergy for refractory staphylococcal bacteremia in vivo and in vitro. Combining ceftaroline and daptomycin has two benefits: they work synergistically together and make the innate host defense peptide cathelicidin leucine-leucine-37 (LL-37) more sensitizing. Ceftaroline plus daptomycin was recently used in MRSA biofilm infections, demonstrating a potentially promising treatment as the first combination used without side effects in humans.

Keywords: Bacteremia, Vancomycin, Daptomycin, Ceftaroline, Staphylococcus aureus, MRSA.

Introduction

In the last few decades, Staphylococcus aureus has evolved into a form increasingly resistant to antibiotics, called methicillin-resistant Staphylococcus aureus (MRSA). MRSA is resistant to beta-lactams such as methicillin and oxacillin. Resistance to MRSA is caused by the production of penicillin-binding protein 2a (PBP2a); this enzyme attaches to the antibiotic's beta-lactam ring, preventing it from binding to its target and making it ineffective. MRSA infection has become more common over time, especially in people who have undergone surgery, have medical devices installed, or have poor immune systems [1,2]. Staphylococcus aureus is known to colonize the skin in approximately 1 in 30 people and can be transferred by physically touching an infected individual or touching surfaces or objects where the pathogen is present [3].

Colonization with Staphylococcus aureus does not cause symptoms, but it can predispose to deep-seated infections. It can cause redness and swelling, and if it progresses further, it can cause fever, aches, and confusion [3]. Infection with Staphylococcus aureus can cause sepsis and infective endocarditis, as well as septic arthritis, pneumonia, and device-related infections. In England alone, 11,938 cases of MRSA were reported between April 2017 and March 2018 [3], a 3.8% increase over the previous year's figures and a 36.2% increase over the 2011/2012 period [4]. Without adequate treatment, the condition can be life-threatening. A study showed that 23% of patients who are carriers for MRSA will develop MRSA infections within one year, 39% of which were pneumonia, with MRSA contributing to death in 5% of cases [5]. Therefore, MRSA represents a significant and pressing health and community health issue that needs to be addressed through novel and evidence-based management strategies. Therefore, this literature review aims to examine combination therapies discovered against MRSA in vivo and in vitro and analyze their known limitations.

Methods for searching:
We searched in PubMed and Google Scholar for MRSA combination treatment options in vivo and in vitro. We searched using the following search terms: MRSA combination treatment, MRSA and combination therapy, methicillin-resistant Staphylococcus aureus and combination treatment, MRSA triple combination, linezolid and rifampicin, linezolid and fosfomycin, linezolid and imipenem, vancomycin and B-lactams, with all their synonyms. Inclusion criteria were in vivo and in vitro research published in English. Exclusion criteria were articles published in languages other than English. We searched in PubMed and Google Scholar, and our search yielded 92 articles, out of which 74 full-text articles were reviewed, and 56 were selected for this study.

MRSA History

In 1881, Staphylococcus aureus was first described in the papers of Alexander Ogston [6,7]. Following introduction of methicillin in 1961, the first case of MRSA was observed later that year by Jevons and his associated scientists, and the pathogen was widespread throughout Europe in the 1970s [8]. MRSA has emerged increasingly since 1960s and has spread globally to become the leading cause of community acquired bacterial infections [9]. The increasing emergence of MRSA has led to a considerable rise in vancomycin use. Vancomycin-resistant strains of staphylococcus aureus are generated by a change in the peptidoglycan terminal, resulting in diminished vancomycin attachment and the inability to suppress cell wall formation. Resistance is also caused by the creation of aberrant peptides in the cell wall that engage vancomycin and inhibit it from attaching to its receptor or by increased peptidoglycan, leading to thickened cell walls [10,11]. 2 % of MRSA were resistant to vancomycin before 2006, 5 % from 2006 to 2014, and 7 % from 2015 to 2020, indicating a 3.5-fold increase in the prevalence of vancomycin-resistant MRSA from 2006 to 2020 [11].

Current MRSA treatment methods

Current treatment of MRSA includes vancomycin, daptomycin, linezolid, clindamycin, tigecycline, ceftobiprole, bactrim and doxycycline. These agents have advantages and limitations as monotherapy for MRSA [9,12-14]. Daptomycin has been demonstrated effective in treating MRSA infections, including bacteraemia, endocarditis, and complicated skin and soft tissue infections (SSTIs) [14,15]; however, it is not a suitable treatment for pneumonia because it is inactivated by lung surfactant. Daptomycin is also not indicated to treat infections of the central nervous system, due to its poor penetration of tissue into the cerebral spinal fluid [9,15]. Phase III clinical studies have shown that 4 mg/kg of daptomycin in complicated SSTIs and 6 mg/kg in MRSA bacteremia are non-inferior to vancomycin [14]. A case-control study supports switching to daptomycin in MRSA bacteremia patients with high vancomycin minimum inhibitory concentration values (>1 µg/mL) [16].

Linezolid has outstanding tissue penetration and is efficacious for treating pneumonia and SSTIs [17]. Moreover, the treatment time for patients with MRSA complicated SSTIs is shorter than with vancomycin. Itani found that the average length of intravenous treatment with linezolid was much shorter than with vancomycin (5.3 days vs. 9.8 days; P-value = 0.001) [18]. Itani further demonstrated that the median and mean lengths of stay in the linezolid cohort were 5.0 and 7.7 days, respectively, compared to 7.0 and 8.9 days in the vancomycin cohort (P-value = 0.016) [18]. It remains controversial whether it is superior to vancomycin for treating MRSA infections. Side effects of linezolid include several serious complications, such as bone marrow suppression, kidney failure, and lactic acidosis [13,14,19].

Clindamycin is a successful regime for treating SSTIs caused by MRSA and is effective against community associated MRSA. Although clindamycin has been shown to have efficacy in treating joint and bone infections, its resistance rate and bacteriostatic nature have increased [13]. Tigecycline is active in vitro against gram-positive and gram-negative bacteria and is an excellent option for treating MRSA because of its broad coverage. However, it is bacteriostatic, and there are insufficient studies to support its use in clinical practice, especially for MRSA infections. It is also likely not an effective treatment for hospital acquired MRSA (HA-MRSA) pneumonia. Furthermore, it has a huge protein structure, which results in low serum levels, restricting its effectiveness in bacteraemia cases [13,14,19]. According to the Food and Drug Administration's safety warning, patients with severe infections treated with tigecycline have a higher overall mortality rate (4%) than those treated with a comparator drug (3%) [20,21]. Although no significant differences in effectiveness between tigecycline and comparator treatments have been seen in complicated SSTIs, tigecycline is often prescribed as a second- or third-line therapy for MRSA infections when other therapies are ineffective [21,22].

Ceftaroline is bactericidal, broad spectrum, and active against MRSA, as it has a high affinity for MRSA penicillin-binding proteins, mainly PBP2a, as well as gram-negative bacteria. Ceftaroline can treat acute bacterial skin and skin structure infections (SSSI) and community-acquired pneumonia. Although some evidence indicates that it can treat severe MRSA infections, like orthopedic infections and bacteremia, it is noninferior to vancomycin with aztreonam to treat complicated MRSA in SSTIs [23]. Another treatment option is ceftobiprole, which is approved in some European countries. Although ceftobiprole has a spectrum broader than ceftaroline, is bactericidal, and used for treatment in community-acquired pneumonia and hospital-acquired pneumonia, it cannot treat ventilator-associated pneumonia [9,24]. In previous research clinical cure rates for ventilator-associated pneumonia patients were 23.1% with ceftobiprole and 36.8% in patients treated with ceftazidime and linezolid, with ceftobiprole failing to demonstrate non-inferiority [25]. The reasons behind ceftobiprole's inability to demonstrate non-inferiority are not entirely clear. It has been proposed that presence of biofilm-embedded organisms may have an adverse impact [25]. Alternative explanations include need for greater doses and longer infusions to produce appropriate therapeutic concentrations of ceftobiprole in patients with CLCr ≥ 150 ml/min, a condition found in 29% of ceftobiprole-treated patients with ventilator-associated pneumonia [25-27]. Clinical effectiveness data limitations, medication product scarcity, and safety concerns have all hampered use of traditional monotherapies. However, many alternative solutions have been established to overcome the challenges of MRSA infections, like an antimicrobial peptide, bacteriophage therapy, newly discovered antibiotics, antivirulence factors, and antibiotic combination therapy [28,29].

Review of current combination therapy

Combination antibiotics, such as streptomycin and penicillin in the 1950s and trimethoprim with sulfonamides in 1986, are historically proven to be more effective and have a larger range than antibiotic monotherapy [30,31]. A decade ago, Silver reported that most successful antibiotic therapies have multiple targets [32]. Combination therapy is advantageous because it broadens the spectrum of antimicrobial coverage against pathogens. Furthermore, it enables synergistic effects, which improve efficacy. It also decreases development resistance and reduces the toxicity of antibiotics because lower concentrations of drugs are used to attain the synergistic effect. Antibiotic combination therapy can also help improve patient safety and reduce resistance and the cost of discovering new antibiotics [29,33]. Although vancomycin is gold standard for MRSA therapy, monotherapy with a glycopeptide for MRSA has shortcomings, including a slow bactericidal effect, development of drug resistance, and weak tissue penetration. Theoretically, combination therapy might overcome these shortcomings by combining two or three agents to address these deficiencies. Combination treatments can improve tissue and biofilm penetration while reducing resistance and the cost of discovering new antibiotics [12,34,35].

Principally, data on combination therapy have come from in vitro tests. These tests have the following possible results: synergy, antagonism, and indifference. The method used to measure synergy is based on agar diffusions, such as antibiotic discs or E-test strips, checkerboard testing, and time-kill curves. For checkerboard testing, different dilutions of antibiotic combinations are placed in a 96-well plate to achieve a variety of minimum inhibitory concentrations (MICs) for each antibiotic. This method can be used to estimate the degree of synergy, which is expressed as frictional inhibitor concentration index (FICI). A value ≤ 0.5 indicates synergy, whereas a value ≥ 2.0 indicates antagonism; however, the intermediate values indicate indifference.

Time-kill curve assay is a dynamic methodology rather than an assessment of synergy at one time point, which better reflects clinical use. In this method, bacteria are cultured in liquid media with different concentrations: either one antibiotic or a combination of antibiotics. Consequently, the time-kill kinetics and speed of bacterial killing can be calculated over time. In time-kill analysis, synergy (bactericidal and bacteriostatic) is defined as decrease of ≥ 2 log colony forming unit (CFU) of bacteria/mL from the CFU/mL for the strongest component. Eventually, in vitro is used to determine appropriate antibiotic doses in animals and humans. Any synergy is obtained by adding one or two additional drugs, which might increase the bactericidal activity. This method is used to assess existing antibiotics against a target organism [29,34,36].

MRSA Triple combination

One of the most effective combination therapies for MRSA, which was a triple combination of a subclass of β-lactams, studied in vivo and in vitro was reported to display highly synergistic activity. This triple therapy of β-lactams used three old antibiotics, meropenem, piperacillin and tazobactam (ME/PI/TZ) that were clinically approved as monotherapies and found that they act synergistically as a bactericidal agent against MRSA strain N315 and other clinical isolates of MRSA [37]. The FICI of the ME/PI/TZ combination was evaluated in vitro using the checkerboard assay, and a value of 0.11 was obtained, indicating that combination had highly synergistic bacterial killing activity against MRSA N315. However, when only meropenem and tazobactam were used in combination, the FICI was 0.67, indicating that the combination of these two drugs was less synergistic.

In contrast, combination of meropenem and piperacillin was also shown to be synergistic, as was combination of piperacillin and tazobactam [37]. The ME/PI/TZ combination was tested in vivo in a neutropenic mouse model infected with MRSA N315 to determine efficacy of combination. Results of the ME/PI/TZ treatment in the mice model demonstrated that the triple combination had strong killing activity against MRSA N315 and that all mice survived six days post infection. Therefore, combinations of old antibiotics could overcome resistance to MRSA in human infections [37]. Moreover, this triple combination suppressed resistance development in MRSA N315 in vitro and in vivo in 11-day trials [37]. In contrast, treatment with two or one of them resulted in development of resistance in 1-8 days. Mechanism of ME/PI/TZ triple therapy is as follows: Tazobactam inhibits the staphylococcal penicillinase BlaZ, protecting piperacillin from hydrolysis by penicillinase. Then piperacillin can bind to penicillin-binding protein 2 (PBP2) to inhibit transpeptidase activity in MRSA. Meropenem can bind to a penicillin-binding protein (PBP1) and prevent transpeptidation and bind to PBP2a allosteric active site. Therefore, meropenem or other β-lactams open active sites that can affect and inhibit cell wall synthesis machinery in MRSA [37,38]. Despite the fact that MRSA strains are resistant to most β-lactams because of PBP2a, the combination restores efficacy of β-lactams against MRSA [37]. Although in vitro and in vivo studies have shown synergy, resistance suppression over prolonged dose intervals, and collateral antibiotic susceptibility, more human studies are needed to provide additional information on this promising MRSA treatment.

Recently, Yoneda et al. showed that this combination of ME/PI/TZ is highly effective against 207 clinical staphylococcal strain isolates, including MRSA, methicillin-susceptible Staphylococcus aureus, ceftaroline non-susceptible MRSA, and coagulase-negative staphylococci. In this study, ME/PI/TZ combination was found effective, especially against the USA 300-SCCmec (strain of gram-positive coccus bacteria) type IV isolate, which has spread globally. These samples were taken from clinical isolate patients to investigate antibiotic susceptibility testing using MICs. All species demonstrate high sensitivity to triple combination of ME/PI/TZ in MICs [39]. Also, combination of ME/PI/TZ is effective against vancomycin resistant Enterococcus, Staphylococcus epidermidis, and Staphylococcus pseudintermedius [39]. These findings may prove that the combination of ME/PI/TZ might be a novel way to tackle severe MRSA infections. Additionally, combination of ME/PI/TZ is also safe and less expensive than a new anti-MRSA [37-39].

Linezolid combination treatment

Linezolid is antibiotic authorized to treat serious MRSA infections, including endocarditis, pneumonia, meningitis, bacteremia, and SSTIs. Linezolid is a broad-spectrum antibiotic and inhibits protein synthesis in bacteria by binding ribosomal ribonucleic acid involved in the 30S and 50S ribosomal subunits [40,41]. In addition, linezolid might suppress expression of virulence factors and decrease toxin production in gram-positive bacteria [42]. It has been shown highly effective against MRSA infections when combined with other antibiotics because linezolid is bacteriostatic. In 2014, Cabellos et al. studied efficacy of the linezolid and rifampin combination using time-killing curves and rabbit model meningitis [43]. The results revealed that combination had good efficacy, with outstanding antibacterial activity and a synergistic effect after 24 hours in vitro and in vivo at 1/2 the MIC [43,44]. However, the study indicated that there was no antagonism with the combination (linezolid plus rifampin) in vitro and in vivo, the combination mechanism was not explained, and the study's time period was limited; therefore, further investigations are needed.

Linezolid resistance is mediated by plasmid encoding cfr gene [45,46]. Zhou et al. tested the same combination (linezolid with rifampicin) in murine pneumonia infected with cfr-positive and cfr-negative MRSA strains [45,46]. In this study, seven clinical MRSA (ST764) strains were isolated from sputum specimens from patients with pulmonary infections. The effects of combination of linezolid and rifampicin were assessed in vitro using the checkerboard test, and the FICI obtained was equal to or less than 0.5, which indicated a synergistic effect between them. Furthermore, time-killing curves were used to confirm this result, also indicating a synergistic effect over 24 hours. In vivo, the efficacy and dose response of combination have been assessed in neutropenic mice, and the results indicated that linezolid with rifampicin had profound treatment efficacy in vivo over 24 hours. However, this study used only one MRSA genotype, ST764 (HA-MRSA), which is present in Asia, and the number of MRSA strains (seven) examined was small. Therefore, more in vivo investigations are needed, and other infections causing MRSA, such as bacteremia, endocarditis, and SSTIs, should be examined.

In 2020, Zhou et al. studied efficacy of the linezolid plus rifampicin combination against MRSA with or without cfr gene. They tested 10 strains of MRSA isolated from samples from hospitalized patients with pulmonary infections; these

strains included 161402, 161400, 161494, and 161813, as well as ST 5 HA-MRSA lineage, which causes bacteremia and necrotizing fasciitis, and ST 398 MRSA, which causes zoonotic infections that can result in pneumonia and SSSI. In vitro, time-kill curves and concentration-effect tests were performed, and the in vitro results indicated synergy. When the combination was assessed in vivo against murine bacteremia and SSSI, results indicated that the treatment was effective. An advantage of rifampicin is that it decreases fibronectin binding in Staphylococcus aureus when used as a combination therapy [45,47]. This characteristic could be useful in treatment of persistent and recurrent MRSA bacteremia [45,48]. In one report, a patient diagnosed with cellulitis and erythema was treated with a combination of linezolid and rifampicin, and after three days, all symptoms were significantly reduced [44] (Table 1).

Daptomycin with ceftaroline
Daptomycin's mechanism of action involves depolarization, permeabilization, and ion leakage in cell membrane, leading to cell death [51]. In 2014, Sakoulas et al. studied combination of daptomycin and ceftaroline as a possible option to treat refractory staphylococcal bacteremia. The combination was found effective in 26 cases of refractory bacteremia, 20 of which were MRSA. In vitro, checkerboard tests, timekilling, binding assays, and cathelicidin LL-37 killing assays were used to test the combination, which was verified to be synergistic. However, it takes a median of ten days to eradicate bacteremia, with an approximate range of 3 to 23 days. However, a combination of daptomycin and ceftaroline eradicated bacteremia in 2 days (a range of 1 to 6 days). However, ceftaroline alone has also been tested in vitro and was found to kill bacteria slower than daptomycin. Therefore, combining ceftaroline with daptomycin provides dual advantages through synergy and sensitization to cathelicidin LL37, which is an innate host defense peptide. It was reported that sensitization (daptomycin and ceftaroline) to cathelicidin LL37 might help attenuate the virulence of the pathogen. Consequently, combining ceftaroline and daptomycin might be an excellent option for treating refractory staphylococcal bacteremia [52]. However, further human studies are needed to evaluate the resistance mechanism of this combination, as well as its side effects in humans.
In 2015, Barber et al. evaluated daptomycin plus ceftaroline against three clinical biofilm-producing MRSA strains in vitro using a pharmacokinetic/pharmacodynamic model to simulate catheter-related biofilms. Their results indicated bactericidal activity and reduction in bacteria density at 72 hours. They found that daptomycin with ceftaroline improved the killing of biofilm-producing staphylococci in contrast to monotherapy [53]. However, the duration of this study was restricted to 72 hours, and different results might be obtained with other materials, such as prostheses. More in vivo and in vitro examinations are needed, as well as in humans, to clarify the effects against biofilm-producing MRSA [53]. Recently, in 2020, a combination of daptomycin with ceftaroline in humans was evaluated in a cohort study comprised of a 500-bed community teaching hospital to determine its effectiveness in treating

staphylococcal infections associated with medical devices. The study assessed and compared the clinical synergy between rifampin with adjuvant therapy and combination daptomycin and ceftaroline in 116 inpatients aged 18 or older. The primary outcomes for the patients included normal white blood cell count, a temperature less than 38°C, and no remaining symptoms, all of which were achieved with the daptomycin with ceftaroline combination therapy. Furthermore, the secondary outcome was not statistically different in their patient groups, except for a longer hospital stay in the daptomycin with ceftaroline group, 9 vs. 15 days, but there were also no symptoms [54]. Daptomycin with ceftaroline represents a novel combination therapy to treat refractory or relapsing staphylococcal infections associated with medical devices.

Daptomycin with rifampin
In vitro and animal studies have revealed general trends of antagonism or indifference when rifampin is added to daptomycin. For example, a combination daptomycin with rifampin or gentamicin in vitro model was found to antagonize or delay bactericidal activity in daptomycin when used alone [55]. Likewise, combination of daptomycin and rifampin or gentamicin in time-killing experiments and rabbit endocarditis models showed no increase in efficacy of daptomycin against MRSA [56]. However, efficacy of daptomycin plus rifampin in infections associated with prosthetic devices has previously been reported in a rat foreign body infection model and a retrospective review [57,58]. In this combination, rifampin can efficiently penetrate the biofilm and exert its bactericidal activity independently of cell cycle. This combination is suitable for treating slow-growing infections in prosthetic devices. Case studies have also indicated synergy and clinical progress in vitro [59,60]. Rose et al. reported that daptomycin plus rifampin salvage therapy was the most widely used therapy when they examined 12 patients with chronic MRSA infections that usually involved developing biofilms, 10 of whom were treated clinically. Even though a checkerboard test indicated synergy in 75% (9/12) of patients and the anticipated treatment efficacy was 100%, the time-killing curve was not synergistic. These results indicate that the checkerboard test is essential for assessing any combination in future investigations. Furthermore, the finding supports use of daptomycin with rifampin as potential treatment for infections that form biofilms [61], although additional human studies are required.

β-Lactams with vancomycin
Several studies have tested the efficacy of vancomycin with β-lactams against MRSA strains and found indications of synergy in vitro and in vivo. These studies used diverse methodologies, such as disc diffusion assays, E-tests, time-killing tests, or checkboard assays. Most found that the combination is highly effective in killing bacteria, but not all strains, as described in Table 2 [62-68]. Among these studies, there were no clear common characteristics among the strains. However, these studies did show a general trend toward the combination's effectiveness [34]. As a result, additional studies should be performed to examine efficacy of these combinations (Table 2).

Table 1: Combination linezolid therapy for MRSA in vivo and in vitro

Antibiotic combination therapy used	Setting	Procedures	Interaction	Outcomes	Diseases treated	Limitation	References
Linezolid plus rifampicin	In vitro and in vivo (rabbit meningitis model) tests	Time-killing and bacteria counting assays, pharmacokinetic and pharmacodynamic tests	Synergistic	Linezolid with rifampicin showed synergistic anti-bacterial activity at 24 hours	Meningitis	Mechanism of combination has not been determined and further in vivo studies are needed.	[43]
Linezolid plus rifampicin	In vitro and in vivo (murine pneumonia model) tests	Time-killing assay, checkerboard assay, pharmacokinetic profiles	Synergistic	Effective	Pneumonia	Mechanism of combination was not determined in study, and additional in vivo studies on other diseases are needed.	[46]
Linezolid plus rifampicin	In vitro and in vivo murine models of bacteraemia and skin and skin structure infection (SSSI)	Time-killing assay, checkerboard assay, and pharmacokinetic profiles	Synergistic	Linezolid plus rifampicin showed efficacy	Bacteremia infections and skin and soft tissue infection (SSTI)	Further human studies are needed.	[45]
Linezolid and fosfomycin	In vitro and in vivo (biofilm-infection rat model) tests	Time-killing assay, checkerboard assay, and bacteria counting	Synergistic	Linezolid with fosfomycin display anti-biofilm activity against MRSA strains both in vitro and in vivo.	Biofilm associated with MRSA infection, especially catheter infections	Although fosfomycin was shown to destroy the outer layer of bacteria cells and prevent first step in cell wall biosynthesis, more in vivo studies are needed.	[49]
Linezolid and imipenem	In vitro and in vivo (rabbit endocarditis model) tests	Time-killing assay, checkerboard assay, and bacteria counting	Synergistic	Linezolid with imipenem demonstrated synergy and bactericidal activity against MRSA strains after 5 days	Endocarditis	Although this study reports a promising and comprehensive treatment for severe MRSA infections, it did not study the synergistic mechanism between two drugs. Further investigations are needed.	[50]

Table 2: Combination β-lactam with vancomycin

Combination therapy	Setting	Organism	Methods	Outcomes	Disease treated	Limitation	References
Vancomycin + cefpirome, cefoperazone, or ceftazidime	In vitro	MRSA	Checkerboard test	Synergy was observed among cefpirome + vancomycin and cefoperazone + vancomycin but ceftazidime + vancomycin was not synergistic	Not mentioned	The study lacked time killing assays and in vivo studies. Further investigations are needed.	[67]
Vancomycin + piperacillin, tazobactam, ampicillin, sulbactam, imipenem, or nafcillin	In vitro	MRSA	Time-killing curve in infected fibrin clots.	Synergy was observed	Not mentioned	More testing is needed; checkboard tests and in vivo studies are needed.	[66]
Vancomycin + oxacillin, ceftriaxone, ceftazidime, or Augmentin (clavulanic acid + amoxicillin)	In vitro and in vivo (only tested nafcillin for sterilising vegetations and renal abscesses)	MRSA	Checkerboard, disk diffusion, agar dilution, and time-kill tests	Synergy was observed in vitro for all combinations, but in vivo, they only assessed vancomycin with nafcillin. It demonstrated synergy.	Endocarditis	More studies are needed to determine mechanism of action of drugs, and all combinations need to be investigated in vivo.	[62]
Vancomycin + cefepime	In vitro	MRSA	Time-killing assay and checkerboard test	Synergistic according to time killing assay, and the checkboard test indicated additivity or indifference for some strains of MRSA	Not mentioned	More testing is needed in animals and in vitro to confirm the results.	[65]
Vancomycin + cefotaxime	In vitro	MRSA	Checkerboard assay and time kill curves	Synergy was demonstrated in 43 out of 50 MRSA strains	Severe pneumonia	Further examinations in animal model are needed.	[64]
Vancomycin + imipenem	In vitro	MRSA	E-test, time-kill curve method, checkerboard test	Synergistic when using sub-MIC of vancomycin	Not mentioned	Further investigations using the checkboard assay and in vivo studies are needed.	[68]
Vancomycin + piperacillin/tazobactam or oxacillin	In vitro	MRSA	Disk diffusion and E-test studies and time-kill curves over 24 hours	Synergistic	Not mentioned	More examinations in vivo are needed.	[63]

Conclusions

MRSA remains one of the common resistant infections, and vancomycin monotherapy is most effective treatment; however, as MRSA strains become more resistant to antibiotic therapies, combination therapy, such as vancomycin with β-lactam synergy in vitro and in vivo, may be one treatment option for MRSA. Although linezolid and rifampicin demonstrated synergy against bacteremia and SSSI caused by MRSA, more clinical research is required to prove their efficacy. Combination treatment has bactericidal activity, which may compensate for the drawbacks of monotherapy. Ceftaroline and daptomycin were recently utilized in MRSA biofilm infections, suggesting a potentially viable therapy as the first combination tested in people without adverse effects. This could be a unique therapy for staphylococcal device infection. Although combination therapy might be a potential treatment for MRSA invasion infections, more studies are needed before clinical trials. Furthermore, for future studies, a time-killing assay, checkerboard test, and MIC in vitro and in vivo should be used to provide accurate results to demonstrate bactericidal activity. Also, evaluation of a suppressed mechanism and two to three combinations are important to support study of combinations. Importantly, clinical use and controlled studies should be applied to evaluate synergy in humans and identify side effects and limitations.

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The Role of Ultrasound in Poly Cystic Ovaries Assessment

Rana Bakkar [1], **Yusuf Bakkar** [2]

(1) Consultant Radiologist in PHCC, Qatar, Al Thumama HC Primary Health Care
(2) Specialist in Diagnostic Radiology, Gulf laboratory and x-ray, Qatar

Corresponding author:
Rana Bakkar
Consultant Radiologist in PHCC – Qatar,
Al Thumama HC Primary Health Care
Email: rana82sara@gmail.com

Abstract

Current knowledge of polycystic ovarian syndrome is reviewed, with emphasis on diagnostic criteria, the role of imaging, and pertinent imaging parameters.
Polycystic ovarian syndrome (PCOS) is the most common endocrine abnormality in women of reproductive age and carries with it significant health risks, including infertility, endometrial hyperplasia, diabetes, and cardiovascular disease. The workup of PCOS has evolved to include the use of pelvic ultrasonography (US). Ovarian imaging is crucial in the evaluation of patients with suspected PCOS. Although findings of polycystic ovaries are commonly seen at routine US and are frequently not associated with PCOS, awareness of the criteria and definitions used in the diagnosis of PCOS is important, especially in patients who are being evaluated for ovulatory dysfunction or hyperandrogenism. The imaging report should be specific and should include ovarian volumes and antral follicle counts, in addition to other pertinent findings (eg, the presence of a dominant follicle or corpus luteum). Because patients are frequently referred for radiologic imaging as a part of clinical workup, and polycystic ovaries are a common incidental finding in women undergoing US for other gynecologic complaints, radiologists should be aware of the current diagnostic criteria for PCOS, the role of imaging in workup for this abnormality, and the pertinent reporting parameters for pelvic US.

Keywords: Poly Cystic ovaries assessment, Ultrasound

Introduction

Assessment of the ovarian morphology is one of the most commonly performed ultrasound examinations. Polycystic ovarian syndrome (PCOS) is a multifactorial, multifaceted, polygenic disorder with varying phenotypes. It defines a labyrinthine symptomatology including menstrual cycle irregularities, hormonal imbalance, and metabolic disturbance. Historically, this syndrome has been diagnosed clinically with supportive lab parameters. However, the role of ultrasound has mutated from identifying, to mis-defining and finally to re-classifying PCOS[1-4]. At present it seems that the ultrasound identification of the 'string of pearls' has cemented this disease with a misleading name. A supposed increase in the detection of polycystic ovarian morphology on ultrasound has been accredited to advances in technology allowing better visualization of the ovaries/stroma/follicles by higher frequency probes with the possibility of endovaginal imaging. Nevertheless, there is a disparity in what the ultrasound shows, how the clinician interprets the report, and what the patient understands about her diagnosis. Identification of the multifollicular ovary is still quite frequently ascribed to PCOS, while ovarian ultrasound remains ambiguous to the different phenotype of PCOS. Whether morphological disparities represent a normal variation in ovarian anatomy or true precursors of PCOS remains debatable. The absence of definition of a 'normal' ovary with respect to volume and follicular number, makes the diagnosis of PCOS more challenging (5,6).

Over time, ovarian volume remains the most reliable, reproducible and sensitive method for identification of PCOS. However, it has a lower diagnostic accuracy due to considerable overlap with normal women. Confusion prevails in the setting of pelvic infection, hormonal treatment, and ethnic variability. In the setting of poor image resolution, whether due to use of lower frequency probes or patient habitus, volume remains the best usable criterion (3,6). While endorsing the Rotterdam criteria, the recent 2018 International Evidence-Based Guidelines also acknowledged the fact that ultrasound criteria are evolving, and new thresholds need to be established. This development is accredited to both accelerated development in technology, as well as increased availability of ultrasound in widespread populations. However, it should be mentioned that technical skill varies widely, and as such it's important to realize that it is not only the development of 'defined criteria', but also distribution of skill and expertise among practitioners, which will determine the diagnosis of PCOS at a community level (4).

Technical considerations in Pelvic ultrasound examination
Ultrasound examination was performed between cycle days 2 and 7 with a 7 MHz transvaginal transducer (25). This prevents any growing follicle from hiding smaller ones or modifying ovarian volume. In case of oligo or amenorrhoeic women, scanning may be performed at random, or 2-5 days after progesterone-induced bleeding (4).

Scanning should be done with an 'optimally' filled bladder, avoiding extremes in transabdominal sonography (TAS), and empty bladder in transvaginal sonography. Identify the ovaries in relation to iliac vessels. Entire ovary should be scanned in two orthogonal planes. Measurement of ovarian volume (length x width x thickness) should be done precisely, ensuring adequate visualization of the ovarian contour. If possible, a follicular count should be obtained with careful meticulous sweeping of both ovaries individually. This count may not help in the diagnosis of a particular patient, but will help long-term to allow us to redefine criteria. If the setting allows, estimation of stromal area should be done offline. Additionally, it should be ensured to assess the liver and pancreatic fat grade, and have a look on the adrenal areas(4).

Ultrasound measurements were taken in real time, according to a standardized protocol. The highest possible magnification was used to examine the ovaries. After the longest medial axis of the ovary had been determined, the length and thickness were measured and the area was calculated using a manual or automatic ellipse to outline the ovary as described previously (26). Several follicles were measured in two planes of the ovary in order to estimate the size and their position. All follicles of 2 mm, were counted. The diameter of several follicles was measured from the mean of two diameters (longitudinal and anteroposterior), then the number of follicles measuring >5 mm or 80 pg/ml, were also excluded from the study so as not to confound the data with the presence of a dominant follicle (25).

Polycystic Ovarian Morphology

Number and Size of Ovarian Follicles
Assessment of the number of follicles has been upheld to be one of the specific features of PCOS. The concept is to sweep through the entire ovarian volume and count the number of follicles in each ovary in totality, keeping in mind not to measure sonolucencies <2 mm, as they do not represent actual follicles. Grid systems, tagging, and marking have been used in post-processing to accurately measure the follicular number per ovary (FNPO) in order to improve reliability and reproducibility. However, these methods are time-consuming and not widespread. Though there have been documented ethnic variations, generally PCOS patients are seen to have a higher number of follicles per ovary. The FNPO has been found to be the best describing feature in cases of unilateral PCOS. The distribution of follicles has also been proposed to help identify 'classic PCOS', though its accuracy remains in doubt. Disordered follicular growth and recruitment has been identified using ultrasound as well. Transvaginal ultrasound allows a superior assessment of follicles to transabdominal ultrasound, and should be utilized whenever possible. However, in circumstances involving cultural or personal barriers, transabdominal remains the only modality widely accepted (3,4,6-11).

The most common ultrasound definition of a polycystic ovary image, which is included in the Rotterdam criteria, is based on the results obtained by, among others, Jonard et al. who have determined the diagnostic threshold of the number of ovarian follicles using the ROC curve analysis (27). In order to specify ultrasonographic criteria concerning the number of ovarian follicles in PCOS, Jonard et al. compared 112 healthy controls with a group of 214 patients with PCOS. All patients were examined with a transvaginal probe using the two-dimensional technique. The number of follicles measuring 2–9 mm was assessed between the 2nd and 7th day of the cycle. The study revealed a significantly higher mean number of ovarian follicles in PCOS patients compared with the controls (15.5 and 6.0, respectively). The ROC curve analysis demonstrated that the number of 12 follicles measuring 2–9 mm was the best border that differentiated the features of PCOS with the sensitivity of 99% and specificity of 75%. Furthermore, the number of ovarian follicles was also assessed in relation to their diameter in both groups. In this case, no significant differences were found between the groups when analyzing follicles measuring 6–9 mm. However, patients with PCOS presented significantly more follicles with a diameter of 2–5 mm (27). Dewailly et al. (2011) and Lujan et al. (2013) compared the ovarian structure in patients with PCOS and in controls, and specified diagnostic thresholds for follicle count at ≥19 and ≥26, respectively(28, 29). The conflicting results of both studies can result from the selection of controls. In the study of Dewailly et al., women with sonographic features of PCO but without diagnosed PCOS were excluded from the control group, whereas Lujan et al. did not use this exclusion criterion.

Size of an ovary in the assessment of its polycystic morphology
The available studies indicate that ovarian volume does not change much between the age of 20 and 39 (29, 30). The results presented prove that there are natural, age-related changes in ovarian volume, which should be taken into account when diagnosing PCO in adolescents and women older than 40 years of age.

Three-dimensional ultrasound is a recognized diagnostic modality to assess ovarian volume. The mean volume in patients with PCOS ranges from 10.6 and 16.7 ml whereas healthy women present values ranging from 5.2 and 8.7(31, 32). The comparison of ovarian volume measured in two- and three-dimensional images has been the subject of numerous studies. However, the presented outcomes indicate conflicting results(33, 31, 34). This could be caused by non-uniform technical standardization of examinations and different interpretation by different ultrasonographers.

It is believed that the assessment of ovarian volume belongs to the diagnostic criteria of PCO. However, it is characterized by a lower sensitivity compared with the assessment of ovarian follicles. The usage of such assessment is then recommended particularly when the visualization of the ovaries is difficult or it is not possible to conduct an examination with a transvaginal probe(2).

Other parameters used in the assessment of PCO

Vascularization and Morphology Of Ovarian Stroma
Three-dimensional sonography enables the assessment of the volume of the ovary and ovarian follicles. Using the difference between these two parameters, the volume of the ovarian stroma can be assessed. Fulghesu et al. demonstrate the usage of stromal volume to ovarian volume ratio as a diagnostic feature of PCOS that correlates with androgen concentration(30). However, stromal volume is a variable that is strictly correlated with the volume of the entire ovary. That is why its assessment is of little use in clinical practice.

Increased ovarian volume not only correlates with increased stromal volume, but also with its increased vascularization.

However, studies that compare the intensity of vascularization using two- and three-dimensional imaging techniques among patients with features of PCOS and healthy women indicate contradicting results (29, 35). Such discrepancies can result from the lack of the standardization of measurement methods and examinations conducted in small and diversified populations. Currently, because of non-uniform results and the lack of differentiating limit values, the assessment of stromal vascularization is not clinically used in the diagnosis of PCOS.

Bright, echogenic stroma has been subjectively accredited to PCOS. There have been many efforts to correlate qualitative indexes of stromal echogenicity with PCOS; however, it has been found that the intrinsic echogenicity of the ovarian stroma is no different in PCOS than in the normal ovary. 'Feature analysis' objectively measures the brightness, or echogenicity, of the ovarian stroma. This is done by measuring the intensity level of the ultrasound pixels within the stroma displayed on an ultrasonic image. The mean echogenicity of a given area can then be calculated. In a study by Buckett et al.,(12) it was found that even though the stromal index was significantly elevated in polycystic ovaries, the mean stromal echogenicity was not different. The subjective 'bright' stromal echotexture in polycystic ovaries is attributed to a synergistic effect of increase in ovarian stromal volume, and hence a relative lower mean echogenicity of the entire ovary (6,12). The stromal/total area ratio has also been found to have high sensitivity and specificity, albeit with poor reproducibility. With the improvement in ultrasound software, the brightness or echogenicity of the ovarian stroma can be determined much more objectively, and therefore, the quantification of ovarian stroma by computerised reading of ultrasound images has revealed that stromal hypertrophy is a frequent and specific feature in ovarian androgenic dysfunction, with some studies demonstrating that increased stromal volume correlates positively with serum androgen level (6,15). However, no standardised method exists for determining stromal volume. Because overall ovarian volume correlates well with stromal volume in polycystic ovaries, and is more easily measured in clinical practice,

the determination of overall ovarian volume is a reliable surrogate for ovarian stromal assessment (6,13,14).

Elevation of impedance indices of the uterine arteries has been described in patients with PCOS, though it seems a multitude of factors contribute to this finding, including co-existence of obesity. A higher pulsatility Index and systolic/diastolic ratio has also been described. Since most of these studies were performed on patients primarily concerned with infertility, it is not known where exactly these findings fit into the pathophysiology of PCOS (1,16-19).

Anti-Müllerian hormone as a marker of polycystic ovaries

Anti-Müllerian hormone (AMH) is produced in granular cells in the follicular phase and participates in the early follicle recruitment process. AMH secretion is continued until follicles grow to a diameter of 8 mm. The secretion is negligible in larger follicles (36). There is then a good correlation between AMH levels and the number of small follicles as well as ovarian volume. The results of published studies indicate that the level of AMH is higher in patients with PCOS, which can be helpful in the diagnosis in this syndrome (2, 36, 37). Moreover, it has also been shown that there is a correlation between higher AMH concentration, rare menstruation and hyperandrogenism(38). However, due to the usage of various methods to analyze plasma AMH levels, it is difficult to compare previous studies and specify diagnostic norms that would be characterized by high sensitivity and specificity for patients with the features of PCO (2, 38).

Role of sonographic assessment of polycystic ovaries
Currently, the sonographic assessment of ovaries is one of the obligatory criteria in the diagnosis of PCOS according to the Rotterdam consensus (2003) and Androgen Excess & PCOS Society (2006)(39–40). However, because of the presence of ultrasound features of PCO in healthy women, the inclusion of this sign to the diagnostic criteria of polycystic ovary syndrome is still questioned (28). On the other hand, the available publications prove that PCO can be hereditary (41). It has also been confirmed that the coexistence of polycystic ovaries with PCOS is common (over 90% of cases) irrespective of ethnic factors or race(42, 2). The excess of ovarian follicles in this syndrome is strictly associated with hyperandrogenism, which has been demonstrated by Dewailly et al.(42). The authors of this publication also prove that there is a correlation between the presence of PCO features, increased AMH levels and ovulation disorders in patients with PCOS. That is why, the assessment of the features of PCO and increased AMH levels can be useful in the diagnosis of oligoovulation in PCOS patients(43, 44).

The sonographic features of PCO, as included in the Rotterdam criteria, are currently identified in 50% of the general population of women(2). Considering the results of studies, it has been shown that the presence of PCO features in healthy women of child-bearing age is not associated with significant metabolic disturbances, but a slight increase in AMH and androgen levels, compared

with women with the normal ovarian structure, can be observed(43). The presence of PCO in the population of adolescent patients frequently coexists with menstrual disorders and acne. However, these symptoms are not sufficient to diagnose PCOS. However, the polycystic ovarian structure in this age group can be indicative of PCOS in further life. These patients should therefore be monitored clinically and sonographically, and the AMH levels should be controlled. The available studies on the commonness of sonographic signs of PCO have yielded conflicting results. On the one hand, they attest to the heterogeneity of phenotypes in completely healthy and normally ovulating women and in those with mild occult PCOS (44). On the other hand, they reveal the homogeneity of the female population with PCO features as a mild form of polycystic ovary syndrome (45).

Role of MRI in Assessing Polycystic Ovaries

The imaging of ovaries on magnetic resonance is a new and exciting frontier. Ovarian volume on MRI has been shown to be quite sensitive for diagnosis, with high reproducibility. Peripheral follicular distribution and FNPO>28 is supportive, but not as reproducible. Though the advantages of MRI in obese patients with poor quality scans is obvious, MRI cannot be extrapolated to the entire 'PCOS eligible' population due to sheer number and cost (6,22). Artificial intelligence and convolutional neural networks form another exciting area which, however, may not translate to clinical practice soon or enough (23).

Conclusion

Three-dimensional ultrasonography (3D USG) allows accurate measurement of the stromal volume, follicular number, and ovarian volume. Accuracy is comparable to 2-dimensional USG, with ample agreement of the Rotterdam criteria. Although promising, 3D USG is relatively expensive, and not widely available (20,21).
To conclude, it must be emphasized that the influence of the development of new technologies in the sonographic assessment of PCO features is undoubtedly noticeable. This process has caused an increase in the percentage of diagnoses of PCO and PCOS since the Rotterdam criteria were published. It is therefore needed to prepare new commonly accepted diagnostic norms concerning the number of ovarian follicles and the standardization of the technique in which they are counted. However, the application of new examination techniques does not entail the need for the modification of diagnostic norms concerning ovarian volume, which are characterized by lower sensitivity compared with ovarian follicle count. Attention is paid to the need of determining diagnostic norms depending on patients' age and ethnic origin in individual populations of women. The assessment of AMH levels as an equivalent of ultrasound features of PCO is a promising method. However, analytic methods have to be standardized in order to establish commonly accepted diagnostic norms. That is why further studies, conducted on appropriately selected populations of women, are needed to investigate this non-uniform disease entity.

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The Effect of Physical Activity in Preventing Type 2 Diabetes Mellitus in Prediabetes Patients: a systematic review

Rafea Muftah Alghanem

Correspondence:
Rafea Muftah Alghanem
University of Ulster
Email: ralghanem@outlook.com

Abstract

Purpose: To search, analyze and identify evidence regarding the use of physical activity interventions in preventing type 2 diabetes mellitus (T2DM) in the pre-diabetic population.

Method of Research and Design: Studies that focused on physical activities as an intervention and this also included studies that compare physical activity intervention with others. The participants are a high risk group (prediabetes) to develop T2DM. The studies also had to be randomized controlled trials to be included. The databases that were used in searching for the articles include CINAHL, MEDLINE and PubMed database. These studies were analyzed in terms of whether the interventions had a successful or unsuccessful outcome.

Results: Screening process led to the selection of 8 studies relevant to the criteria of inclusion. About six studies compared interventions while the other three examined the effectiveness of one intervention. Most of the physical activity interventions were found to be useful in preventing type 2 diabetes in the high risk group, but with differing levels of effectiveness. The high-intensity-interval training (HIIT) programs were found to be more effective in achieving improvement in body metabolism as well as lower resistance to insulin. They also improved adherence to the intervention. The interventions that were associated with greater energy expenditure showed better outcomes.

Conclusion: This systematic review shows that most of the physical activity interventions are effective and this leaves the healthcare providers to choose one that will show to be more effective. Because of the reported effectiveness, the HIIT programs can prove to be the better choice.

Key words: physical activity, diabetes type 2, prevention

Introduction

Diabetes mellitus (DM) comprises of a group of conditions that have in common a metabolic dysfunction that leads to elevation in blood glucose. It is classified according to the etiology into three main types; type 1, 2 and gestational diabetes (GD). Type 1 is differentiated from type 2 by having total lack of insulin due to the destruction of the beta cells in the pancreases while in type 2 there is resistance to the actions of insulin in the cells. The commonest type of DM is T2DM accounting for 98% of DM cases. The cases of T2DM have been on a constant increase in the world and it has been associated with an increase in industrialization. It is considered to be a lifestyle disease being associated with poor diet choices and reduced physical activity (PA). There is also a role of genetics in the etiology of T2DM having some people more predisposed to having it than others (Edelman & Polonsky, 2017).

T2DM is a preventable condition since the etiology has been well described and the points of intervention have also been identified hence it is easy to prevent its development. Diet and PA have been at the heart of most of the interventions put in place to prevent T2DM. Prediabetic states are when there is impaired glucose tolerance, impaired fasting glucose, or an A1C of 5.7-6.4 % (Knowler et al., 2002). Most T2DM cases are often preceded by a period of prediabetes (Bansal, 2015). The CDC (2017) reports that in America approximately 84 million adults have prediabetes, accounting for about a third of the population. More than 90% of those with prediabetes are unaware of their state. Studies have shown that when the right interventions are put in place the progression of prediabetes to T2DM can be reduced. The aim of this study is to conduct a systematic review of literature on the effectiveness of physical activity (PA) in preventing the development of T2DM. The question that this study asks is among those who have prediabetes, are PA activity interventions effective in preventing the development of T2DM compared to no PA.

Methods

For the conducting and reporting of this review, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were utilized. PRISMA gives the minimum items that can be included in the systematic analyses and meta-analyses and is supported by evidence based studies. It mainly focuses on the reviews that report on randomized trials but the same concepts can be applied in reviewing other studies.

Eligibility Criteria

The studies that were included in this study are those that are peer-reviewed and are based on the prevention of T2DM among individuals who have prediabetes. The studies that were included were those published in English. In establishing the particular inclusion criteria, the PICOS (Participant, Intervention, Comparators, Outcomes, and Study design) guidelines were used. To be included in this study, the article must have had participants that

have been proven to be at high risk for T2DM. The articles should have assessed the use of PA interventions in the prevention of T2DM. In addition, they should be primary experimental studies with a preference for randomized control trials. The studies that were included were also those that provided access to the full details of the study. Articles that contained only the abstracts were excluded. Any study that had a combination of interventions was excluded.

Search Strategy

The databases that were utilized in searching the relevant studies for this review included; Cumulative Index to Nursing & Allied Health Literature (CINAHL), MEDLINE and PubMed. Keywords that were used in searching for the relevant studies included; prediabetes, prevention of type 2 diabetes, physical activity, and randomized control trials.

Method of review

The studies that were considered were those published not later than the year 2013. Duplicates were first removed, followed by articles that contained titles that were irrelevant to this study. A summary of the rest of the studies were reviewed then the eligibility criteria used in the elimination of the irrelevant studies. The final stage was the reviewing of the full texts of the remaining articles.

Data extraction

After choosing the studies that were to be included in the review, a guide was used to gather relevant information from these studies. The guide included the study objectives, the study design, the intervention setting, the study population, the scales and measures that were used and lastly the findings of the study. Elasy et al. (2001) gave a description of the main components for diabetes interventions and these were utilized in the extraction of data from these studies. These main components include; the target for the intervention, the types of assessments that were conducted, the intervention's components, time and intensity, those providing the intervention and the diabetes-related component.

Validity Assessment

Jadad et al. (1996), proposed a criteria which was utilized in assessing validity of the studies selected for this study. First, it assesses whether the study was described as being a randomized study. Secondly, it assesses whether the study described the sequence used for randomization and if it was appropriate and if the cases of dropouts and withdrawals were described. Thirdly it assesses for blinding but in the types of studies included in this review, blinding was not necessary. Therefore, assessment for blinding was not done. Lastly, an assessment for a clear description of the intervention used was done.

Data Analysis

This study used a method described by Kawamoto et al. (2005) that focuses on identifying the associations of success or no success depending on the intervention that was implemented. The analysis was based on the target of the intervention, setting and design, the delivery of the
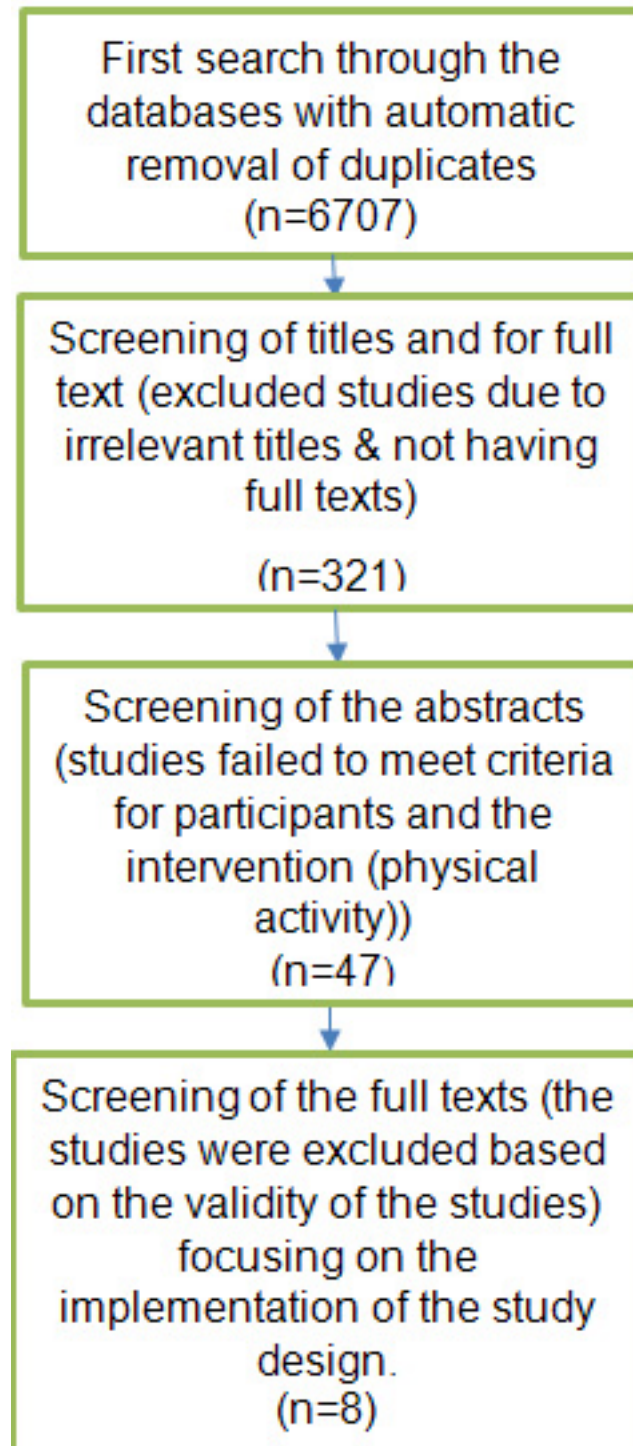
intervention, the duration and intensity of the intervention. These features were used to examine every study. The interventions were reviewed as to whether they led to affirmative results and if it was clinically or statistically significant. Any criteria to describe the clinical importance were absent, but the statistical importance was based on a p-value less than 0.05. Clinical importance was judged based on the findings of each study. The use of this approach made the study more of a descriptive study than a qualitative one. There are two sensitivity analyses that were carried out in this study to assess whether the results were assessed based on the quality of findings. First, only the randomised controlled trials were used in the study.

Second, the randomised controlled studies were limited to those that described the randomization and also the randomization was appropriate for the study. In addition, the studies described the dropouts and the participants who were unwilling to take part.

Findings

Study Description
The study description, search results and process are summarized in the following diagram

First search through the
databases with automatic
removal of duplicates
(n=6707)

↓

Screening of titles and for full
text (excluded studies due to
irrelevant titles & not having
full texts)

(n=321)

↓

Screening of the abstracts
(studies failed to meet criteria
for participants and the
intervention (physical
activity))
(n=47)

↓

Screening of the full texts (the
studies were excluded based
on the validity of the studies)
focusing on the
implementation of the study
design.
(n=8)

Following is a summary of the characteristics of the studies that were included in this paper. All the studies were randomized control studies and they all focused on PA strategies for preventing T2DM. Five of the research items were comparative studies having the aim of showing a better mode for intervention while 3 compared a specific PA with the control. In 7 of the studies, the participants were considered to be high risk by having disorders in glucose metabolism while in one of the studies the participants were considered as high risk by being a child of a diabetic parent.

Study 1: Jung et al. (2015) assessed if high-intensity-interval training (HIIT) has a role in enhancing short term adherence to exercise compared to Moderate-intensity Continuous Training (MICT) . It was a randomized control study. The participants were randomly selected into a HIIT group and MICT group. 32 participants 30-60 years with confirmed prediabetes were included in the study. 17 were in the MICT group and 15 in the HIIT group. Participation was also based on inactivity over the past 6 months and the results from filling the CSEP PA Readiness Questionnaire-Plus and an Exercise Physiologist's clearance to participate in vigorous activity. The measures in the study included Heart rate, training logbook, the activity, duration, intervals, and hardness of the session, accelerometer, cardiorespiratory fitness and anthropometric and blood pressure. According to the study, those in the HIIT group had better adherence to exercise than the MICT group (p=0.05). The time spent working out was higher in the HIIT group (p=0.049). Systolic blood pressure and cardiorespiratory fitness were observed to improve in both groups (p= < 0.05).

Study 2: Philippe et al. (2017) compared the effects of uphill and downhill walking on improving the glucose metabolism and lipids among the prediabetes group in three weeks. Individuals were randomized into a CE group (uphill) and an EE group (downhill). 16 male patients 50-67 years with prediabetes participated in the study. 8 were in the EE group and 8 in CE group. The study measured anthropometric measures, Exercise Capacity, measures of glucose and lipid metabolism and energy expenditure. They found that with uphill walking, there was a significant improvement in glucose tolerance (p=0.05), triglycerides (p=0.036), HDL-C (0.05) and total cholesterol/HDL-C ratio (p=0.012). There were no significant metabolic adaptations with downhill walking.

Study 3: McDermott et al. (2014) had the objective of comparing the effectiveness of Yoga with walking, in preventing T2D among the high risk group. The study was a randomized control study and the participants were placed into a yoga group and a control group (walking) randomly. The study had a total of 41 participants and 20 were in the yoga group while the rest were in the control group. High risk for having T2D was based on a family history of T2D in a first degree relative and glucose tolerance that is impaired. The primary measures were blood pressure, waist circumference, and weight. The

secondary measures were anxiety, affect, perceived stress and depression. The study reported that the yoga group showed a better reduction in weight (p=0.02), BMI (p=0.05) and waist circumference (p= < 0.01). The groups showed no difference that was significant regarding fasting blood glucose, insulin resistance, and postprandial blood glucose. The study also showed a reduction in both groups regarding blood pressure and cholesterol.

Study 4: Patil et al. (2019) had the aim of determining the effects of yoga on insulin resistance and cardiac dysfunction among the offspring of diabetic parents, who are non-diabetic, in 8 weeks. It was a randomized controlled study. A total of 57 participants between 18 and 40 years old, were included with 28 in the yoga group and 29 in the control group. One was considered high risk by being offspring to a diabetic parent. The study measured serum insulin, heart rate variability-low frequency (LF), high frequency (HF) and LF/HF ratio, tolerance to glucose and resistance to insulin. According to the study the yoga group showed a reduction in LF (p=0.005), LF/HF ratio (0.004), insulin resistance (p= < 0.001) and OGTT (p=0.003). There was an increase in HF (p=0.022) in the Yoga group. There was no significant change among the control group.

Study 5: Martins et al. (2018) compared the effects of High-intensity-bodyweight training with combined training on insulin resistance, inflammatory markers, and composition of the body and walking test in postmenopausal women with a high risk for T2DM. The study was a randomized controlled study. There were 16 post-menopausal participants, 8 in the combined training and 8 in the high-intensity-interval-bodyweight training group. They were considered high risk using the levels of HbA1c. The measures in the study included, inflammatory markers, body composition, muscle function, and insulin resistance. The study results were both the groups showed an increase in 6-minute walk test, muscle mass index and Il-1 receptor antagonist (P < 0.05). There was a decrease in fasting blood sugar, HbA1c, insulin, and monocyte chemo-attractant protein (p=0056).

Study 6: Herzig et al. (2014) aimed to determine the threshold of PA that affects glucose, lipid, insulin concentration and body fat composition in prediabetes patients. It was a randomized control study. The study had 68 participants; the intervention group having 33 and the control group having 35. The study measured fasting and 2-hour glucose, insulin, maximal oxygen uptake, daily steps, lipids, fat distribution and body weight. The researchers found that a collected daily steps at an acceleration level of 0.3–0.7 g were 4,434 in control and 5,870 in the intervention group. In the first 3 months, there was no significant change in fasting and 2-hour glucose, body weight and maximal oxygen uptake. The intervention group showed significantly greater changes in fasting and 2-hour insulin (p=0.035 and p=0.003 respectively), insulin resistance (p=0.36), total cholesterol (p=0.041), LDL (p=0.008) and visceral fat (p=0.03).

Study 7: Slentz et al. (2016) had an aim of determining the relative contribution of exercise alone in preventing the progress to diabetes and to determine its effects on the measures of glucose metabolism. It was a randomized control trial. They had 4 intervention groups in which the participants were placed randomly. There were 237 participants 45-75 years who had elevated fasting glucose and they were sedentary non-smokers. The high amount MICT group, high amount vigorous-intensity group and low amount moderate-intensity group had 61 members each and the low amount moderate-intensity training group had 54. The measures were fasting glucose, fasting insulin and Insulin AUCs, cardiometabolic health and glucose tolerance. They reported that the exercise plus diet group was the only one that showed a decrease in fasting glucose (p= <0.001). Fasting glucose showed the following changes: high-amount and moderate-intensity −0.07 (p=0.06); high-amount and vigorous 0.06 (p=0.19); low-amount and moderate 0.05 (p=0.15); and diet and exercise −0.32 (p=−0.18).

Study 8: Lee et al. (2013) had an objective of comparing resistance exercise (RE) against aerobic exercises (AE) regarding their effects on insulin sensitivity and secretion, and abdominal fat adiposity. The randomized control trial had three groups; AE, RE, and control group. The participants were 45 adolescent obese boys; the control group had 13, the exercise group 16 and resistance group 16. The measures were intrahepatic lipid, abdominal fat and intramyocellular lipids and sensitivity to insulin and insulin secretion. They found that both groups showed low weight gain that was significant when compared to the controls. Both the groups also showed a reduction in total and visceral fat and intrahepatic lipids that was significant. The RE group was the only group that showed an improvement in the insulin sensitivity, which was significant.

Methodological quality

All the included studies were randomized control trials. All the studies had a clear description of the randomization process and it was appropriate in all the cases. All the studies also had an account of all the participants and they described the dropouts and the withdrawals.

Interventions

All the studies targeted physical activity-based interventions. The comparative studies compared; interval training of high intensity accompanied by less intense training that is progressive, Yoga and walking, intense interval bodyweight exercise with combined training, PA alone and with combination with diet, resistance exercises with aerobic exercises and uphill walking with downhill walking. The PA interventions that were studied include; yoga, resistance exercises, walking, MICT, HIIT, combined training, and open-air exercise. The main focus of the studies was to show the efficacy of these strategies in preventing progression to T2DM among those who are highly predisposed to developing the condition.

Analysis of features

This study was aimed at determining the effectiveness of PA interventions in preventing T2DM among those who are at high risk. Out of the eight articles, 7 studies had prediabetes participants while one study had individuals that were at high risk due to family history (parents). When each intervention modality is viewed in isolation, it can be inferred that the usefulness of exercise in preventing T2DM is dependent on the type of PA. Although they have different levels of effectiveness, MICT, HIIT, yoga, uphill walking, combined training, resistance exercise, open air activity are effective for preventing T2DM by improving both glucose and lipid metabolism and improving the state of insulin resistance. Downhill walking and no PA were found to be ineffective in T2DM among the high-risk group (McDermott et al., 2014).

Most of the comparative studies were aimed at coming up with an effective mode of PA that also encouraged adherence to the routine. According to Jung et al. (2015), HIIT was found to be more effective compared to the conventional MICT in preventing T2DM among predisposed individuals. In addition, it was observed that the HIIT is useful because apart from improving the metabolic indices, it also encouraged adherence. Philippe et al. (2017) reported that walking uphill is effective in improving the metabolic state in the prediabetic patients while walking downhill is ineffective. McDermott et al. (2014) say that yoga is effective while walking is ineffective in preventing T2DM among the high-risk participants. Lastly, both aerobic and resistance exercises are effective in improving metabolic metabolism in prediabetes. However, it can be noted that resistance exercises would significantly improve insulin sensitivity while the aerobic exercises do not.

Discussion

Adherence
In the current healthcare field, there are many effective interventions that have been developed and most of them are considered to be effective. One of the advantages that some of these interventions bring and makes them a better choice is encouraging adherence. In PA interventions for preventing type 2 diabetes among high-risk groups, there some interventions that have shown to be superior and also encourage adherence. The modalities that were found to be effective in this way are the HIIT and high-intensity-interval bodyweight training. Roy et al. (2018) also conducted a study to demonstrate the usefulness of HIIT compared to the MICT group. They identified that there is higher adherence and better outcomes in the group that did supervise HIIT. HIIT shows better outcomes in a short period of time encouraging participation and the sessions are nicely spaced and that encourages adherence to the intervention (Aamot et al, 2016).

Intensity and Energy Expenditure
One of the ways in which the PA interventions are classified is according to intensity. For the same duration

of time, the high-intensity interventions have been shown to improve the metabolism in the prediabetes group. With increased intensity, there has been shown to be better glucose tolerance, improved fasting blood glucose levels, improved insulin resistance, and improved lipid metabolism as well as weight loss. Cassidy et al. (2017) conducted a study that supported the effectiveness of high-intensity interventions. These interventions are often personalized to fit the individual's physical health status. They have the advantage of requiring less time commitment while having superior effects compared to the traditional methods. There is increased effectiveness in improving cardiorespiratory fitness which is an advantage. Francois & Little (2015) conducted a study that agrees with this study on the effects of HIT on insulin resistance. While some MICT exercises may improve glucose metabolism, most of the time they either fail or take longer to improve insulin resistance. However, the HIIT exercise programs have been associated with improved insulin resistance in a shorter period of time.

One of the factors that have been found to be a common factor in the interventions that are effective, is adequate energy expenditure during the exercise period. While concluding, Philippe et al. (2017) report that downhill climbing could have had the same effectiveness as uphill climbing if the energy expenditure was adjusted. Uphill climbing is part of some HIIT programs and this can show that one of the factors that make the PA interventions effective, is the energy expenditure. Also, while comparing aerobic exercises and resistance exercises, Lee et al. (2013) report that resistance exercises showed higher energy expenditure which was tied to their success.

In summary, this study found that usefulness of physical exercise interventions in preventing T2DM is dependent on individual intervention. While most of them were found to be effective, the comparative studies showed that some of them were more effective than others and some offered the advantage of improving the level of adherence to the intervention.

Conclusion

In conclusion, PA interventions are useful in the prevention of T2DM among a high risk group. The level of effectiveness differs across the interventions and it is important to carry out more studies that will lead to the development of effective models. The current study has shown that interventions that are based on HIIT exercise programs are more effective and have the advantage of enhancing adherence and this makes them good for practice. Energy use forms one of the most important factors in determining the effectiveness of an intervention.

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