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Patients' Attendance to The Virtual Compared to The In-person Complimentary Outpatient Clinics at a Tertiary Care Hospital in Western Saudi Arabia:

A Comparative Cross-sectional Study

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Editorial

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This is the last issue of this year that is rich with papers from the region. At the end of the year , I would like to thank the editorial board , the reviewers and the publishing manager in their great effort for a successful year. At the time, I would like thank you the authors for their trust in our journal and for the valuable readers that we hoped enjoyed reading our papers this year. At the end I wish all a happy holiday season and Happy New Year. Al Qaatri et al., looked at the increased Psychological Disorders among Pediatric Population. The authors stressed that generally, the pediatric population is at a higher risk of developing psychological disorders during COVID-19 than other age groups. Educational status, developmental age, poor economic background, and existing mental health issues are among the vulnerability factors that cause the difference in psychological disorders prevalence between age groups . According to the authors, social distancing and lockdown practices have resulted in anxiety and fear, leading to long and short-term mental health and psychosocial impacts on school-age children. This literature review will focus on examining increased psychological disorders among adolescents and children during COVID-19 and the most effective practices to implement to promote early detection.

Alkubaisi et al., did a retrospective chart review (baseline audit) looking at the clinical effectiveness Department, Directorate of Clinical Affairs, Primary Health Care Corporation, Doha, Qatar. They reviewed 245 health records of children attended well-baby clinic for three months. The aim was to ensure that well-baby services provide clinical care according to children's age as per well-baby service protocol within primary health care centers, to find gaps if any and, generate action plan for further improvement. The authors concluded that impactful audits with actionable recommendation make real difference in practice and compliance. In conclusion, action plan implemented further to the baseline audit are effective in increasing the compliance in most of the areas.

Altaf et al., looked did a comparative cross-sectional study was conducted by comparing patients' demographic information, and compliance to virtual calls and physician arecommendations during 2020 with the regular physical attendance clinics in 2019. Patient data was collected from the electronic medical records after randomly selecting the sample for each year from 6 main outpatient clinics. During the 4-month period of 2020 (March-June), which virtual clinics were implemented in, there was a significant decrease in the attendance compliance when compared to the same period in 2019 conventional clinics. The authors concluded that COVID-19 pandemic had significant negative impact on patient care. Although that impact was seen greatest among those with chronic conditions and oncology patients, it was an essential step towards infection control during this difficult period. However, the pandemic is an opportunity to establish a comprehensive virtual care that will ensure easy access and continuity of patient care.

El-Gamal et al., attempted to identify the major socio-demographic, and health risk factors of stunting in 2-6 years old Saudi children. They did a cross sectional study. It was a convenient sampling method, and was conducted at the outpatient clinics of two general hospitals in Jeddah city. Wasting was encountered among 3.11% of the children, while stunting was found among 22.91%, and underweight among 20.32% of the children. Stunting was more common in early years of life (b=0.015). Short stature of the mothers (b = 0.021), and decrease in her BMI (b= 0.043) were significantly associated with stunting in their children (P < .05). The authors concluded that male gender and very young age are significant risk factors of stunting. Double malnutrition was common among children with stunting. Hereditary may be an important determinant factor of stunting in children.

Al-Jadidi, et al., did a pilot study, weighted and measurable outcome of community service program in decreasing relapse, length of hospital stay and the financial sequel of relapse of the service provided. In this study , there is a statistically significant deference between number of relapse before and after enrolments to community services , the mean number of relapse decreased after enrolment to community and the decreases mean cost per admission for the patients after enrolment to the community program . Decrease in number of admissions among patient enrolled on CMHS from (M 2.68 SD 2.76) to (M 1.51 SD 2.5) with P value 0.001 .The authors concluded that CMHS in Oman is effective in decreasing relapse rate and cost.

Rashed et al., looked at the role of SGLT2 inhibitors and GLP-1analogs in cardiovascular risk reduction in type 2 diabetes. The leading cause of morbidity and mortality in patients with type-2 diabetes mellitus is cardiovascular (CV) disease, that makes it an important target in management. Sodium-glucose cotransporter 2 (SGLT-2) inhibitors and glucagon-like peptide-1 receptor agonist (GLP-1 RA) are both two new antidiabetic drug classes that showed significant reduction in major cardiovascular events (MACE). With the introduction of these drugs, comprehensive CV risk reduction has been achieved in addition to glucose control. Both drugs work in different ways, the SGLT-2 Inhibitors leads to urinary excretion of 60-90 grams of glucose and as well sodium leading to osmotic diuresis. Both the SGLT2 inhibitors and GLP-1 agonists have undergone large trials that have led to massive evidence on their cardiovascular safety and renal benefits. The decision on using which drug from both classes depends on different factors like atherosclerotic disease and chronic Kidney disease.

Almonawar, et al., looked to measure non-compliance and to identify barriers to compliance among hypertensive patients. A total of 200 hypertensive patients attending Al-Qabel Primary Health Care (PHC) Center since at least one year were included in this study. A structured data collection interview questionnaire was used. To assess non-compliance of hypertensive patients, the Hill-Bone Non-Compliance to High Blood Pressure Therapy Scale was used. Only 11% of hypertensive patients were highly compliant. The main barriers for full compliance were forgetfulness (39%) and being asymptomatic (30%). The authors concluded that non-compliance of hypertensive patients attending PHC settings in Abha is high. Main barriers against full compliance of hypertensive patients are forgetfulness, absence of symptoms, dissatisfaction with provided health care and being tired of treatment side effects. Non-compliance is significantly higher among younger, newly diagnosed, Saudi, married, smoker patients. Non-compliance is significantly higher among hypertensive patients on multiple antihypertensive medications.

Alburaidi et al., attempt to assess the level of knowledge among patients with LBP related to their disease. They did a cross-sectional study was conducted at region of Asser, Saudi Arabia and comprised patients presenting with lower back pain. In this study, they used the Arabic version of validated questionnaire called (LBP knowledge questionnaire "LKQ"). we received 183 responses from patients with LBP. Among this sample, male represented 60.7% of the sample. The authors concluded that the level of knowledge among patients toward LBP was inadequate where most of patients had partial level of knowledge about their condition. Age, gender, martial status and monthly income had no effect on this level of knowledge. More investigations should be conducted using another design as prospective design in order to indicate the acutely reasons for this low level of knowledge among patients toward LBP.

Alasmari 1, et al., tried to assess proton pump inhibitors awareness level among physicians and pharmacists and its detriments in PHCCs, Aseer region, Saudi Arabia. They did an analytical cross-sectional study was applied to answer the main research question. The study targeted all physicians and pharmacists in primary healthcare centres in Abha who will be accessible during the study period from 23 May to 27 July. A total of 178 participants completed the study questionnaire. 97 (54.5%) participants were pharmacists, 45 (25.3%) were clinical pharmacists, and 36 (20.2%) were physicians. The authors concluded that the current study showed that medical staff in the primary healthcare centres had moderately low knowledge regarding PPI and its indications. The lowest awareness was mainly among physicians relative to pharmacists especially clinical pharmacists.

Harbi et al., did a cross-sectional study, a self-administered questionnaire was distributed among migraineurs attending primary healthcare centers and hospitals in Riyadh, Saudi Arabia. The survey included questions about

sociodemographic data, number of attacks, and environmental factors triggering migraines in order to assess their prevalence A total of 415 participants were recruited. The most common age group was 31– 50 years old (46.5%), with females dominating the males (84.8% vs 15.2%). The prevalence of migraines that affected activities of daily living (ADL) was 80% (CI=75.7% - 84.3%). The authors concluded that Migraines are highly prevalent in our region, most specifically among women. Noise, outdoor light exposure, indoor lighting, fluorescent lights, and computer systems usage were the most triggering environmental factors of migraines. These factors dissuade patients from doing their daily activities.

Helvaci, et al., tried to understand whether or not there is a disappearance of hepatitis C virus antibodies (anti-HCV) with hydroxyurea therapy in patients with sickle cell diseases (SCD). All patients with the SCD were included, and hydroxyurea therapy was initiated for all of them. The study included 337 patients (169 females and 168 males). Hydroxyurea therapy was well-tolerated with a high majority of cases (80.1%). Mean number of painful crises per year was decreased with the therapy (10.3 versus 1.7 crises per year, p<0.000). The authors concluded that SCD are chronic inflammatory disorders with high morbidity and mortality rates, and hydroxyurea is a well-tolerated and highly effective regimen for them. While hydroxyurea therapy decreases both frequency and severity of painful crises, WBC and PLT counts, total and direct bilirubin, and LDH levels, it increases body weight, Hct value, and MCV. Although hydroxyurea therapy also decreased the anti-HCV positivity, the difference was nonsignificant probably due to the small sample size of the present study.

AlJumail, et al., looked at the satisfaction of health care workers has direct effect on the quality of care. This study aimed to assess the job satisfaction among primary health care (PHC) workers in Buraidah, Saudi Arabia. A cross sectional study was conducted among primary health care workers in Buraidah. Data was collected on socio-demographic and professional characteristics. Job satisfaction was measured using a validated 36 item Job Satisfaction Survey (JSS). A total of 230 PHC workers were included in this study. Among the nine facets of the JSS; Nature of work, Co-workers and Supervision had mean scores in satisfaction category, while, five facets were in the range of ambivalent; Pay, Promotion, Benefits, Contingent rewards and Communication. Only one facet fell under the dissatisfaction range which was Operating Conditions. None of the socio-demographic variables had significant association with job satisfaction. About two thirds of the PHC workers were not satisfied with their job. This calls for policy makers to enhance job and job conditions to increase job satisfaction and improve the quality of care at primary care level.

AlSuqair et al., attempt to measure schoolteacher's perception of epilepsy in school children in Riyadh, Saudi Arabia in 2018. They did an observational, descriptive, cross-sectional study was done and data was collected by online and manual survey from (476) teachers chosen by quota sampling technique. The data was analyzed by using SPSS. Most of the teachers had moderate and good knowledge (81%), Female had better knowledge (85%), teachers with higher educational level had better knowledge (92%) and teachers with more years of experience had better knowledge (83%). The authors concluded that the majority of the teachers had moderate and good knowledge and attitude while only few teachers had moderate and good practice. Teachers' age and years of experience are approved to be factors in acquiring knowledge. t was found that teachers' age has significant effect on their attitude and teachers with higher educational level had better attitude. Teachers' gender and educational level appeared to have a significant effect on their knowledge.

Al-Ahmari et al., attempt to evaluate non-psychiatric physicians' knowledge, attitude and practices regarding management of cases with addiction. Following a cross-sectional study, 126 non-psychiatric physicians in Aseer Region were interviewed. A study questionnaire was used for data collection. It included socio-demographic data; general attitudes and interest toward addictions, addiction psychiatry; knowledge about addictions, addictive disorders, including treatment, and practice about addictions, addictive disorders, and treatment. Age of participants ranged from 26 to 66 years (Mean±SD: 37.1±9.1 years. Most participants (81%) were males. Only 9.5% attended a training course or a conference on management of addiction, while 12.7% attended a training or a course on palliative care. The authors concluded that non-psychiatric physicians in Aseer Region have insufficient knowledge, negative attitude and poor practice about psychoactive substance use disorders. Continuing medical education and training is necessary to promote physicians' knowledge and practices related to prevention and treatment strategies for addiction diseases.

Ballaji, et al., tried to assess risk factors associated with DKA among T1DM children registered at "Heraa Diabetes Center", Makkah Al-Mokarramah City, Saudi Arabia. The authors did a retrospective hospital-based, case-control research design was followed and included 375 diabetic patients aged less than 15 years. There was significantly more positive family history in the DKA group than the control group (78.4% and 68%, respectively, p=0.036). The mothers was the main person who injects her child. Differences between both study groups according to the person who injects the child was statistically significant (p=0.029). DKA occurred more than once in 59.2% of diabetic children, and in 46.4% of children with overactivity. The authors concluded that risk factors for DKA include positive family history of diabetes, less educated or employed mothers, but its incidence is lower among children of parents with health-related jobs. It can be triggered by over-activity. It is caused by eating much sweet, missing blood sugar monitoring, omitting the insulin dose or infection. Noncompliance is associated with higher incidence of DKA.

Ahmed, et al., explored the family physicians' perspectives of the barriers in initiating insulin for adult patients with Type 2 diabetes mellitus (T2DM) in their primary health care settings. Insulin therapy often becomes necessary when oral anti-hyperglycemic agents are not enough, no longer effective or even as an initial choice. This cross sectional study where 102 primary health care physicians (PHCPs) (58 females and 44 males) from multi PHCCs in Tabouk Health Region – Kingdom of Saudi Arabia (KSA), responded correctly to online reliable self-administered questionnaire (Cronbach alpha of 0.77344) to address their perspectives of barriers to insulin initiation for adult patients with T2DM. Despite the free of cost availability of all types of insulin, including the safest and peak less ultra-long (degludec) and long (Glargine), the availability of free of cost glucometers for all people with diabetes, the presence of a well-equipped diabetes clinic at every PHCC, the long list of guidelines and educational courses as well as an appointment system with electronic health information system (HIS), insulin inertia is a common problem among PHCPs working in Tabouk Health Region.

Dr Shasho looked at Diagnostic approach to eosinophilia in children. Blood consists of three types of cells (Erythrocyte – Leukocytes - palates), and plasma. Leukocytes divided into 2 types of granulocytes (including neutrophils, eosinophils and basophils); and agranulocytes (including lymphocytes and monocyte). Eosinophil attack and kill parasites and cancer cells, and help with allergic responses, so their role is to protect the body from bacteria and parasites. However, a dramatic blood and tissue eosinophilia is an important part of adaptive immunity to parasitic helminthic infections, whilst more detrimentally, the eosinophil is thought to make a major contribution to the inflammation underlying the pathogenesis of disorders such as asthma, allergic rhinitis and atopic dermatitis. Eosinophilia is a common finding in clinical practice and presented in broad spectrum of diseases, some of them hematologic disorders and others non – hematologic (infection disease – allergic disease – medication reaction, and autoimmune disease).

Alomary, et al., did a study to determine medical students' perceptions of ML in otorhinolaryngology, head, and neck surgery and its applications in diagnosis and management. Also, to assess medical students' awareness of current challenges facing the application of ML in medical practice in the Kingdom of Saudi Arabia (KSA). They followed a cross-sectional survey was conducted in February–May 2021 among medical students in Saudi Arabia. The participants were provided questionnaires of the survey using electronic forms. Validation of the questionnaire was done using exploratory factor analysis and confirmatory factor analysis. There were 8 validated items on Attitude and 6 items on Knowledge. A total of 538 students completed the questionnaire. The majority of the students were familiar with machine learning in general 308 (57.3%). However, only a few of the participants were familiar with machine learning applications in the field of otorhinolaryngology, head, and neck surgery 184(34.2%). The authors concluded that medical students in the KSA demonstrated a good knowledge of ML in general, although many were not familiar with machine learning applications in the field..

Patients' Attendance to The Virtual Compared to The In-person Complimentary Outpatient Clinics at a Tertiary Care Hospital in Western Saudi Arabia: A Comparative Cross-sectional Study

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Abstract

Background: During the COVID-19 pandemic, outpatient clinics in National Guard-Health Affairs Hospitals, Saudi Arabia, have shifted their health-care services towards virtual clinics to keep up with patient appointments while maintaining infection control precautions. This study aimed to determine if patient attendance compliance has changed by implementing virtual "phone call" appointments compared to the conventional physical appointments in outpatient clinics.

Methods: This comparative cross-sectional study was conducted by comparing patients' demographic information, and compliance to virtual calls and physician recommendations during 2020 with the regular physical attendance clinics in 2019. Patient data was collected from the electronic medical records after randomly selecting the sample for each year from 6 main outpatient clinics.

Results: During the 4-month period of 2020 (March-June), in which virtual clinics were implemented, there was a significant decrease in the attendance compliance when compared to the same period in 2019 conventional clinics. Data were analyzed for 404 and 407 patients' medical records from each year, respectively. The drop in the clinic attendance compliance was the highest in the pediatric oncology clinic. Moreover, physician orders of investigations and medications were significantly reduced.

Conclusion: COVID-19 pandemic had a significant negative impact on patient care. Although that impact was seen greatest among those with chronic conditions and oncology patients, it was an essential step towards infection control during this difficult period. However, the pandemic is an opportunity to establish a comprehensive virtual care system that will ensure easy access and continuity of patient care.

Key words: virtual clinic; patient attendance; telemedicine; telehealth

Introduction

Living in the post digital era virtual healthcare has played a huge role in modern day medicine, especially during the event of COVID-19. A virtual clinic (VC) is a scheduled appointment where the healthcare professional contacts their patients via phone/ video call, to offer the clinical consultation, treatment planning, and advice (ISD Scotland 2020) (1). It may also be defined as an integrated web- based technology that combines self-management, data sharing and communication between patients and professionals (2).

The services that can be provided virtually differ according to the clinic or the virtual system. They could be a simple consultation and plan as mentioned in the definition and they could be more extensive. A prospective evaluation of a virtual urology clinic states that they were able to review imaging, lab results, deal with patient doctor query, refer to imaging or an intervention, and discharge from their clinic all within the VC appointments (3). Virtual healthcare services have been implemented all over the world, and are also known as telemedicine, telehealth, remote medicine, and e-health. After the emergence of the COVID-19 pandemic, National Guard Health Affairs (NGHA) in Saudi Arabia has activated the virtual clinics initiative since April 2020 in their outpatient clinics, in which patient- doctor contact occurs through telephone call (4).

Many other countries have also used virtual clinic appointments but have faced poor attendance. The rate of attendance can be applied to virtual clinics just as it has for conventional clinics. Ellis et al. led a large-scale data analysis on patient medical appointment attendance and stated that the rate of missed appointments at UK hospitals was ~12% until 2012 (5). Although this study is on a smaller scale, it would be interesting to see if the rate of missed appointments is similar to that of other countries. In light of COVID-19, virtual clinics are being implemented more worldwide, and to study their applicability attendance needs to be taken into account. A surgery outpatient clinic considering VOC as an alternative to actual clinics for patient follow-ups found that 91.6% complied with the virtual clinic compared to 81.4% of the actual outpatient clinic. Moreover, a study in Ireland compared the VOC to the conventional OPC patient attendance and satisfaction which found that patients attending the VOC were more pleased with their visit in comparison to patients attending the OPC (6).

Virtual Medicine has its advantages and disadvantages. A local study done in Taif, KSA, reports that physicians believe it could improve the effectiveness of therapeutic interventions in addition to serving stable patients living in remote areas, but for newly undiagnosed patients, the inability to perform physical examination was a setback to reach the correct diagnosis (7). In Saudi Arabia, the COVID-19 outbreak urged the precautionary measures of converting the outpatient clinics to virtual clinics which are somewhat a new technology, not applied prior to the pandemic, and attendance to these clinics is not yet studied.

The aim of the study was to determine if patient attendance has improved using virtual clinics, which could possibly be applicable in the future after the pandemic. The primary objective was to estimate the percentage of patients who were committed to (attend) their virtual appointments during 2020 in comparison to the conventional outpatient physical attendance during 2019 at King Abdulaziz Medical City, Jeddah, in western Saudi Arabia.

Methods

Study Design, Area, and settings

This comparative cross-sectional study was conducted at King Abdulaziz Medical City, Jeddah. This hospital is a tertiary care hospital with 750 beds that serve the national guard employees and their dependents. Patients' medical records numbers (MRNs) were identified through the Health Information Management department. Other patients' data were collected from the Electronic Medical Record (BestCare®).

Identification of study participants and sample details

The patients included in this study were those with appointments at virtual clinics during (March -June) 2020 or conventional in-person outpatient clinic during (March-June) 2019. Exclusion criteria were patients with missing records, or if they were already admitted on the same day of the outpatient appointment.

The sample size was determined by assuming the percentage of attendance of the virtual clinic is 90%, then at 3% margin of error, 95% confidence interval and 80% study power, the estimated sample size was 384. This number was applied to patients in 2020 and 2019 (total sample size was 768). For the sake of simplifying the data collection, the total sample size was increased to 800 (400 from each year). The 400 participants were entered as followed: 100 from internal medicine specialties clinics, 100 from surgical specialties clinics, 50 from obstetrics and gynecology clinics, 50 from pediatric clinics, 50 from adult oncology clinic, and 50 from pediatric oncology clinics.

A systematic sampling technique was applied to select the study sample among patients with appointments since start of the virtual clinic throughout the end of the four-month period in 2020, compared to patients with conventional appointments during the same period in 2019.

Data Collection Process

With the help of medical records, an audit of all patient files with an appointment at a virtual clinic were labeled as show or no show during the 4-month period (during COVID pandemic 2020) - from March to June. The control group were all patients with appointments at the same clinics being evaluated during the same 4-month period, the year before (2019). The percentage of patients who showed in the virtual clinics was compared to the percentage of those who showed to the in-person clinic. The patients were considered as "show" as long as there was a check-in, or a physician note up to 2 weeks after the appointment date for that specific clinic.

Study variables also collected from BESTCare® included patient age, gender, eligibility, main diagnosis, specialty clinic, intervention (medication, investigation). The medication was reported as prescribed or not, and the ordered investigations, if any, were reported to be labs and/or imaging followed by a record if they were done (completed) or not.

Approval of the IRB office of King Abdullah International Medical Research Center (KAIMRC) was obtained (RJ20/180/J). Patient's information was preserved, and no names or sensitive information were taken. All study data collection forms were secured under the responsibility of the study principal investigator.

Data Analysis

Data was analyzed using IBM SPSS version 26. Descriptive statistics (mean, standard deviation, median, interquartile range, frequency, percentage) were applied. Chi square test or Fisher's Exact test, as appropriate was used to compare categorical variables. Student's t test and Analysis of variance (ANOVA) was used to compare means of two or more than two groups, respectively. Level of significance was determined at p value < 0.05.

Results

Attendance and Demographics

Retrospective data from the 2020 sample (N=407) showed a total attendance of 186 patients (45.7%). Demographic data from 2020 virtual clinic sample showed a mean age of 39 years (IQR 14-58), and the appointments were distributed as follows: female (n=251, 61.7%) and male (n=156, 38.3%).

In comparison, data from the 2019 sample (N=404) showed a total attendance of 283 (70.0%). Demographic data from that years' sample showed a mean age of 41 years (IQR 13-60), and the appointments were almost distributed evenly among the subjects where (n=218, 54.5%) were female and (n=182, 45.5%) were male.

Eligibility and Diagnosing Clinic

Military dependents in both the physical and virtual clinic had the most compliance.

Intervention and Medication

Distribution of the sample among the clinics was generally equal among the two groups. However, number of investigations ordered differed between the virtual and physical clinics. The 2019 clinic demonstrated that 184 (65%) of the patients who attended the clinic had investigations ordered for them. Among them, 149 (81.0%) completed the recommended investigations at the hospital while the remaining 35 (19.0%) didn't go for their investigations. The 2020 clinic showed that 83 (44.6%) patients that attended the virtual appointment had investigations ordered, where 67 (80.7%) had completed their investigations at the hospital and 16(19.3%) did not go for their ordered investigations. As for the medication for those who attended, 168 out of 283 (59.4%) of the physical clinic patients were prescriped medication, compared to the virtual clinic patients where only 84 out of 186 (45.2%) of them were prescribed medication.

Virtual appointments had significantly lower attendance compared to conventional appointments (P value 0.001), as demonstrated in Table1. When looking at total appointments, females had more virtual appointments, and males had more physical appointments, but there was no significant difference in the attendance between the genders in the physical clinics (P value 0.71) and a slight significance in the virtual clinics as males had better attendance (P value 0.047).

Fisher exact analysis showed no relation between eligibility and type of clinic, physical and virtual, (P value 0.209), nor did the chi squared analysis for the 6 main departments or clinics (P value 0.998). When looking more closely into the virtual clinic, attendance in the surgery and pediatric clinics were significantly better, while least responses to the calls were from patients with appointments at the pediatric oncology clinic (P value 0.006).

Regarding the variables (investigations and medication) there was a noticeable statistically significant decrease in ordering investigations in the virtual clinic. The "labs/imaging" together was the most ordered in the physical clinic, in contrast, for the 2020 virtual clinic the labs and imaging together were least needed (P value 0.001), and in fact the majority did not have investigations ordered at all. Analysis showed no difference between virtual clinic compared to the in-person clinic (p-value 0.961) when it comes to completing the ordered investigations. As for medication, results display significant decrease in prescriptions in the virtual clinic compared to the physical clinic (p value 0.003).

Discussion

This study demonstrated that the attendance compliance was significantly reduced in the new 2020 virtual clinics, which was different than results of a similar study in the UK done in an otolaryngology outpatient clinic, where the investigators reported a decrease in the "no show" rate in virtual appointments compared to face- to-face visits (8). However, the current study's low attendance was when the outpatient clinics were only operative virtually in 2020 and only operative physically in 2019, and the results could have been different if the virtual clinic was incorporated into the physical clinic , so that both would be running at the same time. McKirdy and Imbuldeniya published a study where they incorporated virtual clinics into the physical clinic when following up with patients, and they reported significant (75%) reductions in the "non attendee" rate (9). Unfortunately, due to the unexpected shift in the method of delivering healthcare during the COVID-19, a telehealth system in the national guard-health affairs prior to this pandemic was not well-established. Thus, the attendance rate has decreased since many of the patients were unfamiliar with virtual appointments and telemedicine, seen especially in the elderly population. Schulz et al. stated that telehealth would be successful during the pandemic only

Table 1: Profile of Study Participants and Healthcare Provided

	Attending Clinic				Total	p-value
	Physically 2019		Virtually 2020			
	n	%	n	%		
Attend clinic or respond to call						<0.001*
Yes	283	60.3	186	39.7	469	
No	121	35.4	221	64.6	342	
Total	404	49.8	407	50.2	811	
Gender						0.039*
Female	218	46.5	251	53.5	469	
Male	182	53.8	156	46.2	338	
Total	400	49.6	407	50.4	807	
Eligibility						0.209**
Military dependents	143	45.7	170	54.3	313	
Letter of Exception	60	48.4	64	51.6	124	
Exception Disease (onc)	54	45.0	66	55.0	120	
Military	37	51.4	35	48.6	72	
HCW dependents	27	58.7	19	41.3	46	
Healthcare worker (HCW)	10	31.3	22	68.8	32	
Business	4	80.0	1	20.0	5	
NGH Non-dependent	2	25.0	6	75.0	8	
Emergency Non-Saudi	1	100.0	0	0.0	1	
Students (College)	1	50.0	1	50.0	2	
Organ Donors	1	100.0	0	0.0	1	
Total	340	47.0	384	53.0	724	
Dx Clinic (sub-specialty)						0.021**
Adult medical oncology	50	50.0	50	50.0	100	
Oncology-pediatrics	46	46.9	52	53.1	98	
Obstetrics and gynecology	45	48.9	47	51.1	92	
Orthopedics	24	49.0	25	51.0	49	
Ophthalmology	22	51.2	21	48.8	43	
Nephrology	13	35.1	24	64.9	37	
Endocrinology & metabolism	23	69.7	10	30.3	33	
Urology surgery	13	40.6	19	59.4	32	
Gastroenterology	18	58.1	13	41.9	31	
Internal medicine	19	65.5	10	34.5	29	
Adult pulmonary	13	46.4	15	53.6	28	
ENT	13	56.5	10	43.5	23	
General pediatric	13	56.5	10	43.5	23	
General surgery	9	45.0	11	55.0	20	
Pediatric diabetic	5	25.0	15	75.0	20	
Pediatric neurology	8	44.4	10	55.6	18	
Neurology	0	0.0	17	100.0	17	
Rheumatology	9	56.3	7	43.8	16	
Neurosurgery	8	53.3	7	46.7	15	
Pediatric neonatology	5	50.0	5	50.0	10	
Vascular surgery	6	60.0	4	40.0	10	
GYN and oncology	5	62.5	3	37.5	8	
Infectious disease	5	71.4	2	28.6	7	

Table 1: Profile of Study Participants and Healthcare Provided (continued)

Pediatric endocrinology	7	100.0	0	0.0	7	
Pediatric gastroenterology	4	57.1	3	42.9	7	
Pediatric oncology	4	66.7	2	33.3	6	
Pediatric pulmonary	1	16.7	5	83.3	6	
Plastic surgery	5	83.3	1	16.7	6	
Pediatric nephrology	2	66.7	1	33.3	3	
Pediatric rheumatology	2	66.7	1	33.3	3	
Pediatric surgery	2	66.7	1	33.3	3	
Pediatric metabolic	1	50.0	1	50.0	2	
Pulmonology	1	50.0	1	50.0	2	
Respiratory	1	50.0	1	50.0	2	
Thoracic surgery	1	50.0	1	50.0	2	
General OB and Gyn	0	0.0	1	100.0	1	
Pediatric asthma	1	100.0	0	0.0	1	
Ped-development	0	0.0	1	100.0	1	
Total	404	49.8	407	50.2	811	
Clinic						0.998*
Surgery	103	50.7	100	49.3	203	
Internal medicine	102	50.5	100	49.5	202	
Peds oncology	50	48.1	54	51.9	104	
Pediatric	49	48.5	52	51.5	101	
OBGYN	50	49.5	51	50.5	101	
Adult oncology	50	50.0	50	50.0	100	
Total	404	49.8	407	50.2	811	
Investigation						**<0.001***
None	99	49.0	103	51.0	202	
Labs	115	61.0	74	40.0	189	
Labs/Imaging	39	90.7	4	9.3	43	
Imaging	30	85.7	5	14.3	35	
Total	283	60.3	186	39.7	469	
Investigation completed						**0.961***
Done	149	69.0	67	31.0	216	
Not done	35	68.6	16	31.4	51	
Total	184	69.0	83	31.1	267	
Medication						**0.003***
Prescribed	168	66.7	84	33.3	252	
Not prescribed	115	53.0	102	47.0	217	
Total	283	60.3	186	39.7	469	

*chi-square test **fisher exact test

if the program was previously established since it would take months to years to have a fully running online health delivery system (10). The implementation of this online outpatient clinic in Australia that started in 2017 resulted in significant reduction in the failure-to-attend rate during the 2020 pandemic (10). Whatever may be the cause of low attendance, justifications are not simply explained by logistics, rather complex psychosocial factor as described in a study conducted to assess non-attendance at diabetic outpatient clinics (11).

In-person appointments can sometimes be inconvenient for the patient for a variety of reasons. Sabit et al. looked at the predictors of poor attendance to a pulmonary rehabilitation program and concluded that attendance was affected by frequent admissions, degree of symptoms, and the long journey time among other causes (12).

This study's findings also revealed that virtual clinics were associated with less investigation orders and less medication prescriptions. The impact of such reduction requires further investigation to assess its cost-effective value on hospital resources and finances. It is well known in any hospital that there is a number of unnecessary laboratory and imaging ordered, as Strockbine et al. applied a clinical decision support system in ordering their lab investigations, they reported significant reduction in required screening, labs, and annual costs (13). Relatedly, Mubaraki et al. report that 44% of physicians included in the study thought the quality of care was enhanced using telemedicine and even with the difficulties that came with it, it should still be a considered medical service for patients living in rural areas (7). Specific applications for telehealth in the commuting population can be used to screen for severe cases and monitor clinically stable patients as stated in a Brazilian study (14).

Telemedicine has been used in the U.S. military for years, and Hwang et al. evaluated the tele-dermatology program documenting that 98% of complaints were consulted within the same day including diagnoses and prescriptions, in addition to avoidable location evacuations (15). This study demonstrated the usefulness of virtual clinics in remote areas. Similarly, Karwowski et al. conducted a study on telemedicine in the Obstetrics and Gynecology field and reported that 10% of their study subjects were in another country at the time of their virtual consultation, demonstrating the convenience of telemedicine systems (16). That convenience is not limited to the patient but to the caregiver as well. An orthopedic clinic evaluated the proportion of patients with simple clavicle fractures that were discharged virtually and followed up with the patients a year later, to find the majority of those patients satisfied with their treatment and recovery. The authors concluded that the virtual appointments benefitted both patient by fewer clinic visits and physician by saving time for complex cases (17).

As for the limitations of this study, they were related to the general acceptance and familiarity of the public toward telehealth care, especially that the data were collected during the early months of the pandemic with first widespread use of the virtual clinics. This observation may have obscured the results towards less attendance when the "call appointments" were first introduced. Social culture in Saudi Arabia is shifting to accept this mode of healthcare delivery among the young to middle aged population, and since the mean age of this study's sample was 40 years, an improvement in the attendance is expected once online or phone appointments are more familiarized. An active way of improving attendance would be to make the online platform user friendly as Li et al. stated (18), and in this case, it would be to prepare the patient for the call and ensure they have access for assistance, especially the elderly. A recent published review emphasized on the importance of the infrastructure to provide a good quality virtual patient-physician confidential session (19).

Cultural familiarity was not the only limitation, as other factors including availability of good communication infrastructure, especially in the rural areas may have also played roles in the low attendance. Although telemedicine provided care for geriatric patients worldwide, a recent review found that these services were limited because of lack of outreach communication facilities, and in order to optimize health care delivery, there needs to be greater government investments to engage the elderly, their care givers and healthcare providers (20).

Conclusion

This study was conducted to determine if attendance was improved using the virtual clinics compared to the conventional physical clinics, however, the findings showed lower attendance compliance. Both male and female patients had almost similar attendance compliance when comparing virtual to physical clinics. Moreover, the association of specialty clinics to virtual attendance differs, for example the pediatric and surgery clinics showed good response, but the oncology and OBGYN clinics had low attendance. Another finding was that lab work up and imaging were ordered less, and prescriptions also decreased when the clinic converted virtually, which raises the question of needing them in the first place, but the rate of completing the investigations in the virtual appointments did not differ from the physical appointments. The low compliance to the virtual clinics may be attributed to poor awareness of patients and families about telehealth care and limitation of infrastructure. Given that virtual appointments are comparatively new to governmental hospitals in Saudi Arabia, they are expected to be used more in the near future and accepted as a mode of healthcare delivery for selected patients. The circumstances to which the virtual appointments system was applied may not have been ideal, and the low attendance rate proves that. But it provided an opportunity to explore how to improve telehealth and deliver care in the best method possible to the patients.

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Knowledge around back pain and spinal disorders among Aseer patients: A cross sectional study

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Abstract

Introduction: Low Back Pain (LBP) is one of the most common health problems and is considered the second highest reason for seeking medical advice. In most cases, LBP is not an indication of serious disorder, however, it can be considered the leading cause of disability and work absence around the world. In Saudi Arabia, it was found that the prevalence of LBP and pattern of its symptoms ranges from 53.2 % to 79.17 %. Aims: to assess the level of knowledge related to their disease, among patients with LBP..

Methods: A cross-sectional study was conducted in the region of Asser, Saudi Arabia and comprised patients presenting with lower back pain. In this study, we had used the Arabic version of validated questionnaire called (LBP knowledge questionnaire "LKQ") which was prepared and validated by Maciel et al. The questionnaire was distributed online using social media such as Facebook and WhatsApp between patients with non – specific LBP from both genders.

Results: We received 183 responses from patients with LBP. Among this sample, males represented 60.7 % of the sample. Furthermore, almost two thirds of the sample were married (57.9 %) and 39.9 % of them were single. Finally, we found that 49.7 % of the sample had monthly income of less than 5000. Considering level of knowledge about LBP in this sample, we found that almost all of the sample (97.8 %) had partial knowledgeable about their disease. Demographic factors such as gender, age, marital status and monthly income had no effect on this level of knowledge (P-value =0.103, 0.467, 0.661, 0.347 respectively)

Conclusion: We found in this study, that the level of knowledge among patients toward LBP was inadequate where most patients had partial level of knowledge about their condition. Age, gender, marital status and monthly income had no effect on this level of knowledge. More investigations should be conducted using another design such as prospective design in order to indicate the exact reasons for this low level of knowledge among patients toward LBP.

Key words: back pain, spinal disorders,

Introduction

Low Back Pain (LBP) is one of the most common health problems [1] where it s considered the second highest reason for seeking medical advice [2]. LBP is defined as pain which is localized between the costal margin and inferior gluteal folds which may be accompanied with leg pain [3]. In most cases, LBP is not an indication of serious disorder [4] however, it can be considered the leading cause of disability and work absence around the world [1] causing destructive economic load on individuals and communities [1]. LBP is common where some studies showed that almost 8 per 10 individuals would experience LBP once in their life [2]. The acute symptoms of LBP in general occur around the age of 30 [5] and peaking in occurrence between ages of 45 and 60 years old which means that this condition is more common in people over 60 years old by a percentage of 25.1 % in males and 35.1 % in the female population [6,7]. In a systematic review conducted to estimate the global prevalence of LBP in 2014, they found that the LBP prevalence was 9.4 % in 2010 where men were more affected than females (10.1 % compared to 8.7 % respectively) [1]. In the same study, when they fixed the age, they found the prevalence of LBP is higher in western Europe than the Middle East and central Latin America and a lower prevalence was noticed in the Caribbean (15 %, 14.8 %, 6.6 and 6.5) [1]. In a systematic review conducted to assess the prevalence of LBP in Saudi Arabia, it was found that the prevalence of LBP and pattern of its symptoms ranged from 53.2 % to 79.17 % [8].

There are many things that can affect the musculoskeletal system of our body and can lead in some cases to LBP while other factors and activities can cause an increase and beginning of these problems especially activities related to work, such as lifting heavy objects, and dealing with sharp objects besides some individual factors including older age, obesity, and stress [9]. In Saudi Arabia, LBP is more related to vitamin D deficiency and obesity [10,11] besides carrying heavy objects, wrong posture when carrying heavy objects such as lifting while twisting and sudden movement of the torso which has an effect on increased prevalence of LBP In Saudi Arabia [12,13].

However, LBP is not serious in most cases. It can however represent an indication of serious conditions such as malignancy, spinal fractures, infections, cauda equina syndrome and aortic aneurisms [14]. Although, malignancy of the spinal cord and fracture are the most common conditions of the spine [9, 14], malignancy is not accompanied by back pain in all cases [15], therefore, more tests such as history of cancer, elevated ESR and clinical judgment are needed [15].

For these reasons, it was important to us to assess the level of knowledge among patients with LBP related to their disease to ensure that patients had the proper level of knowledge about their disease and do not underestimate or overestimate their condition. Many studies have been conducted to assess the same variable, however none of them have been conducted in the region of Asser and most of these studies had found that patients knowledge of the spine and its disorders was low and inadequate [16] as in the study of Tavafian et al., who found that 74 % of his patients had low level of knowledge about their condition and related risk factors [17].

Subjects and Methodology

This cross-sectional study was conducted in the region of Asser, Saudi Arabia and comprised patients presenting with lower back pain. In this study, we used the Arabic version of validated questionnaire called (LBP knowledge questionnaire "LKQ") which was prepared and validated by Maciel et. al [18], in order to assess the level of knowledge of patients about LBP including general aspects, concepts and treatments. The questionnaire also contained questions about basic anatomy, back pain, definition of different causes, diagnosis and treatments. Moreover, demographic factors such as age, gender, monthly income and education were included in this questionnaire.

The questionnaire was online-distributed using social media such as Facebook and WhatsApp between patients with non–specific LBP from both genders. Each participant was told about the objectives of the study and informed consent was obtained before starting the questionnaire and each participant had the ability to withdraw from the study at any time, however incomplete answers of the questionnaire were excluded from this study.

Microsoft Excel 2019 was used for data entry. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 25. Frequencies and percentages were used for the qualitative variables, while measures of central tendency would calculate continuous variables. The data relations between qualitative variables were tested using the chi-square test. To visualize the results, bar and pie charts were used. Statistical significance was defined as p-values of less than 0.05.

Results

In response to our questionnaire, we received 183 responses from patients with LBP. Among this sample, males represented 60.7 % of the sample; most of them were aged between 36-45 years (38.8 %), while 24.6 % of them were 46-55 years old, 19.1 % were between 18 -25 years old, 14.8 % were older than 55 years old and the rest of them were between 26-35 years old. Moreover, 48.1 % of the sample had educational level of university or above while 51.9 % of them had secondary education or below. Furthermore, almost two thirds of the sample were married (57.9 %) and 39.9 % of them were single. Finally, we found that 49.7 % of the sample had monthly income of less than 5000 Saudi Riyal (SR), while 26.2 % had monthly income of 5000-10000SR, 13.7 % had monthly income of 10,000-15,000 SR and only 1.1 % had a monthly income of more than 20,000SR. (Table 1).

Variable		Frequency	Percent
Gender	Male	111	60.7
	Female	72	39.3
Age	18-25	35	19.1
	26-35	5	2.7
	36-45	71	38.8
	46-55	45	24.6
	Older than 55	27	14.8
Education	University education or above	88	48.1
	Secondary education or below	95	51.9
Marital status	Married	106	57.9
	Divorce	4	2.2
	Single	73	39.9
Income SR	Less 5000	91	49.7
	5000-10000	48	26.2
	10000-15000	25	13.7
	15000-20000	17	9.3
	More than 20000	2	1.1
	Total	183	100.0

Table 1: Demographic factors of participants

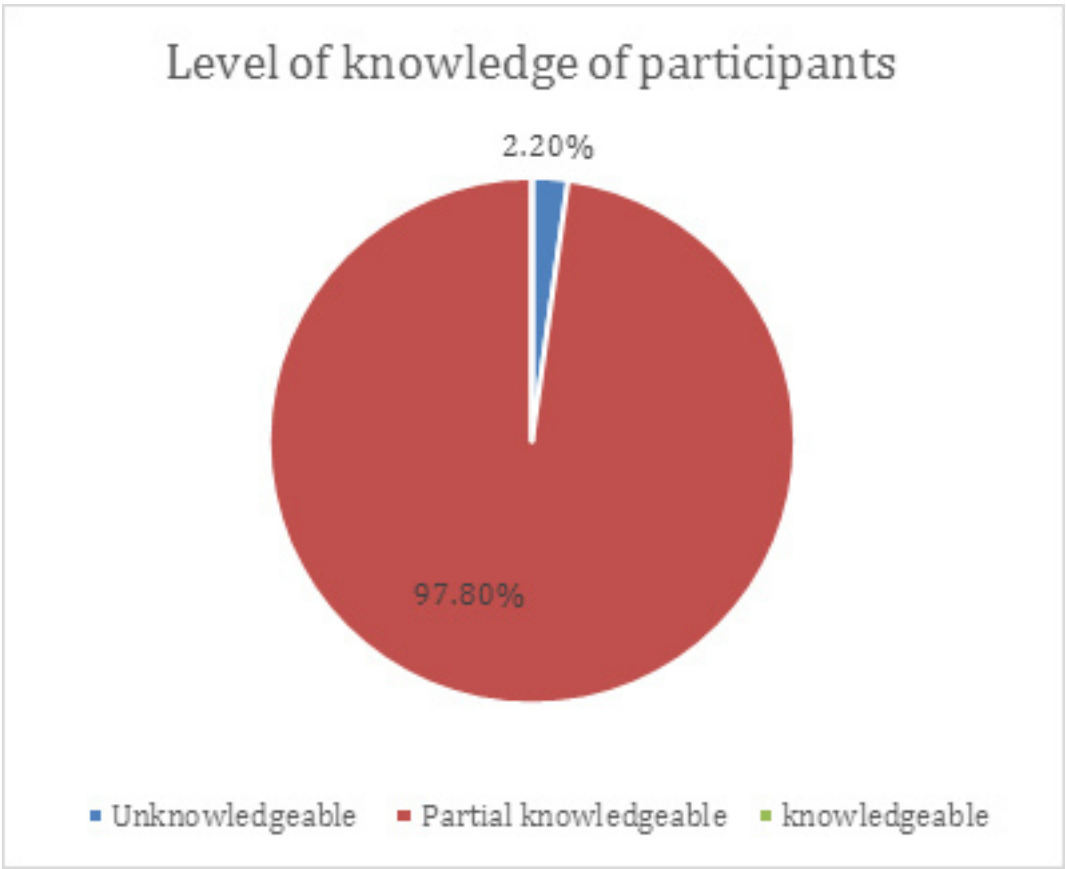

Figure 1

Table2: Relation between level of knowledge and different demographic factors		level of knowledge						
		unknowledgeable		partial knowledgeable		knowledgeable		
		Count	%	Count	N %	Count	N %	p-value
Gender	Male	4	3.6%	107	96.4%	0	0.0%	0.103
	Female	0	0.0%	72	100.0%	0	0.0%	
Year	18-25	0	0.0%	35	100.0%	0	0.0%	0.467
	26-35	0	0.0%	5	100.0%	0	0.0%	
	36-45	3	4.2%	68	95.8%	0	0.0%	
	46-55	0	0.0%	45	100.0%	0	0.0%	
	Older than 55	1	3.7%	26	96.3%	0	0.0%	
State	Married	1	0.9%	105	99.1%	0	0.0%	0.347
	Divorce	0	0.0%	4	100.0%	0	0.0%	
	Single	3	4.1%	70	95.9%	0	0.0%	
	Widow	0	0.0%	0	0.0%	0	0.0%	
Income SR	Less 5000	3	3.3%	88	96.7%	0	0.0%	0.661
	5000-10000	0	0.0%	48	100.0%	0	0.0%	
	10000-15000	1	4.0%	24	96.0%	0	0.0%	
	15000-20000	0	0.0%	17	100.0%	0	0.0%	
	More than 20000	0	0.0%	2	100.0%	0	0.0%	

Considering level of knowledge about LBP in this sample, we found that almost all of the sample (97.8 %) had partial knowledge about their disease, while 2.2 % were unknowledgeable and no one had complete knowledge about PBI (Figure 1).

In Table 2, we compared the level of knowledge among patients according to their demographic factors where gender had no significant effect on this knowledge (p-value= 0.103). Moreover, the age of the patients also had no effect on level of knowledge about LBP however, it seems that older patients had higher level of knowledge (p-value =0.467). Furthermore, neither monthly income nor marital status of patients had an effect on their level of knowledge about LBP.

Discussion

LBP is a common condition that is related with many misconceptions. In this study, we aimed to assess the level of knowledge among patients with LBP in Asser region in Saudi Arabia about their disease using a validated questionnaire. The results in this study revealed inadequate partial level of knowledge among patients where no participants were able to answers all questions correctly. Moreover, we found that age, gender, marital status or monthly income had a significant effect on this level of knowledge.

Similar results had been found in another study conducted in Riyadh, Saudi Arabia in which level of knowledge of patients about their conditions and other problems related to the spine was limited, as no individual in this study had been able to answer more than 37.5 % of the questions correctly however, patients with higher education showed better results [19]. In the study of Machiel et al, among Brazilian patients with LBP, they found the level of knowledge of patients about LBP was low [18]. Moreover, the study of S Ganiyu, Nigeria, found that most of the sample had partial knowledge about LBP (more than 90 %) with less than 10 % who had complete or were not knowledgeable [20]. In another study conducted by Tarimo et, al who used another tool in order to assess the level of knowledge among patients with LBP about their condition they found that most of participants (91.2 %) did not manage to answer all six questions included in their questionnaire and most of the subjects had a partial level of knowledge about the course and causes of LBP [21]. Similar results of low level of knowledge about LBP were also found in the study of Ng'uurah and Frantz conducted in Kenya where most of the patients lacked knowledge about the causes of LBP [22], and study of Allock et al. [23] and study of Mwilila [24] who found in their studies that most patients did not understand the cause of their pain and the main reasons for visiting healthcare providers was to gather more information about their pain.

Many studies found a relation between level of knowledge and attitude and beliefs among patients with LBP where patients with low levels of knowledge had a negative attitude and wrong misconception toward LBP [21]. Therefore, in order to improve the attitude of patients toward correct treatment of LBP, it is important to increase their knowledge about this condition, which can be achieved through preparation of awareness campaigns through TV and social media such as Facebook and WhatsApp, which play a critical role in developing our knowledge nowadays. Moreover, it is important to increase

level of knowledge among medical students as the results of this study revealed inadequate level of knowledge about LBP among them.

This study had un-avoided limitations including depending on a cross-sectional design of which was unable to provide strong evidence of the association between measured variables and level of knowledge. Moreover, this type of questionnaire had many medical terms which may not be known to all patients, however the study was conducted among patients of medical students. Furthermore, the study depended on a self-reported questionnaire which may lead to measurement and recall bias. Finally, the depending on online tools for distribution of the study, decreased the number of the real population who could not use online applications from participating in the questionnaire. On the other hand, this study gives a picture of level of knowledge among patients in Asser region in Saudi Arabia and up to our knowledge, there is no study that has been conducted to assess this variable in Asser region before.

In conclusion we found in this study, that the level of knowledge among patients toward LBP was inadequate where most of patients had partial level of knowledge about their condition. Age, gender, marital status and monthly income had no effect on this level of knowledge. More investigations should be conducted using another design such as prospective design in order to indicate the acute reasons for this low level of knowledge among patients regarding LBP.

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Environmental Triggers in Migraine patients in Riyadh: A Cross-Sectional Study

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Abstract

Background: A migraine is a disabling condition that is characterized by persistent headaches which vary in severity. Migraines are extremely common and represent a major public health concern due to their effect on the quality of life and job performance, which can also lead to a significant financial burden on global economies [1].

Methodology: In this cross-sectional study, a self-administered questionnaire was distributed among migraineurs attending primary healthcare centers and hospitals in Riyadh, Saudi Arabia. The survey included questions about sociodemographic data, number of attacks, and environmental factors triggering migraines, in order to assess their prevalence.

Results: A total of 415 participants were recruited. The most common age group was 31– 50 years old (46.5%), with females dominating the males (84.8% vs 15.2%). The prevalence of migraines that affected activities of daily living (ADL) was 80% (CI=75.7% - 84.3%). The most common environmental factors that triggered migraines were noise (87.7%), followed by outdoor light exposure (81.4%), and indoor lighting, such as fluorescent light, and computer systems (79%). In univariate analyses, migraines that interfered with ADL were more common in patients with a bachelor's degree (p=0.019) and those who were taking migraine medication (p=0.003).

Conclusion: Migraines are highly prevalent in our region, most specifically among women. Noise, outdoor light exposure, indoor lighting, fluorescent lights, and computer systems usage were the most triggering environmental factors of migraines. These factors dissuade patients from doing their daily activities.

Key words: Migraine, environmental factors, patients, primary healthcare center.

Introduction

Migraines are amongst the earliest of diseases introduced to human beings, and specifically, are known to be among the most prevalent diseases of the nervous system [1,2]. Migraines can be defined as a disabling chronic condition that is usually characterized by a periodic, recurrent, and persistent unilateral pulsatile attack of headache, lasting from hours to days. It is often characterized by overstimulation by a sensory stimulus. These symptoms can be associated with increased eye sensitivity to light or photophobia, increased sensitivity to sound, also known as phonophobia, nausea, vomiting, blurred vision, and other cognitive symptoms [1,3]. This type of headache is well-known as a type of primary headache, which mostly begins at puberty and most commonly affects those aged between 35 – 45 years old. In addition, migraines have shown to be favouring one gender more than the other, as it affects women more than men in a ratio of 2:1, which can be justified due the cyclic hormonal influences which females experience on a monthly basis [1]. It is remarkable to mention that hormonal changes are not the only factor provoking an attack of migraine. There are a variety of stimuli which can trigger migraine headaches and lead to their burden of recurrence, such as noises, physical activity, fasting, and air pollution. These factors can be changed according to the location of the population in the surrounding environment [4]. Unfortunately in Saudi Arabia, the number of studies on the basis of migraine triggers are limited [4]. Identifying migraine triggers and tailoring them to the population environment in public health is very crucial due to a migraine's high prevalence and the remarkable temporary disability that it can cause. Migraines represent a major public health concern due to their effect on the quality of life and occupational accomplishments, which can reflect an unfavourable impact on life performance, and thus can lead to a significant financial burden on global economies [5]. Hence, analysing and identifying migraine triggers according to a population environment is extremely vital in order to improve the quality of life for those who suffer from migraine attacks.

Subjects and Method

This cross-sectional questionnaire-based study was carried out among 415 migraine patients attending primary healthcare centers and hospitals during 2021. Participants under the age of 18, or who were not confirmed migraineurs, were excluded to achieve precise results. After obtaining the Institutional Review Board of Princess Nourah Bint Abdulrahman University approval, data were collected from patients by utilizing a validated questionnaire. The data analyses were performed using the Statistical Package for Social Sciences, (SPSS, version 26, Armonk, NY: IBM Corp, USA). Descriptive statistics were presented using numbers and percentages. The environmental factors that are likely to precipitate migraine attacks and affect activities of daily living were correlated with the socio-demographic characteristics of the participants using Chi-square test. Two-tailed analysis with $p < 0.05$ was used as the cut-off for statistical significance. Significant results were placed in a multivariate regression model to determine the highest predictor associated with migraines, where the odds ratio, as well as the 95% confidence interval, were also reported.

Ethical Approval: Ethical approval was granted by the Institutional Review Board at Princess Nourah bin Abdulrahman University before conducting any study procedure.

Results

We recruited 415 patients. Table 1 presents the socio-demographic characteristics of the patients in relation to migraines that interfered with activities of daily life (ADL). The most common age group was 31 – 50 years (46.5%), who were nearly all females (84.8%) and more than half (54.2%) were married. With regards to patients' education, the majority held a bachelor's degree or higher (77.1%), with approximately 41% earning less than 5,000 SAR per month. The proportion of patients who had an associated disease was 18.6%, while the proportion of patients who were taking migraine medication was 60.2%. Regarding migraines that interfered with ADL, it can be observed that migraines were more common among those who had a bachelor degree or higher (p=0.019) and those who were taking migraine medications (p=0.003).

In Figure 1, the most common associated chronic disease was hypertension (9.2%), followed by diabetes (7%) and heart diseases (2.4%).

Figure 2 depicts the perceived environmental factors that triggered migraines. It was revealed that the top 5 most common environmental factors that triggered migraines were: noise (87.7%), followed by outdoor light exposure (81.4%), indoor lighting, fluorescent lights, and computer systems (79%), odours (59.8%), and busy visual environments (58.6%) while electromagnetic fields and sferics were the least (29.4%).

When measuring the relationship between the perceived environmental factors and migraines that interfered with ADL, it was found that the prevalence of migraines was significantly less among those who disagreed that electromagnetic fields and sferics are environmental factors of migraines (p=0.001), while the prevalence of migraines was more common among those who agreed that fasting will trigger a migraine (p=0.001) (Table 2).

In the multivariate regression model, patients who had a bachelor's degree or higher (AOR=2.040; 95% CI=1.148 – 3.626; p=0.015) and those who were taking migraine medications (AOR=2.338; 95% CI=1.338 – 3.938; p=0.001) were twice as likely to have a migraine that interfered with ADL. We also observed that patients who disagreed with the effects of electromagnetic fields and sferics (AOR=0.251; 95%=0.118 – 0.532; p=0.001) and fasting (AOR=0.345; 95% CI=0.198 – 0.603; p<0.001) as migraine triggering factors were significantly less likely to be associated with a migraine that interfered with ADL (Table 3).

Table 1. Socio-demographic characteristics of the patients in relation to migraines that interfered with ADL

Study Data	Overall N (%) (n=415)	Migraine Interfered with ADL		P-value
		Yes N (%) (n=332)	No N (%) (n=83)	
Age group in years				
18 – 30 years	182 (43.9%)	145 (43.7%)	37 (44.6%)	0.882
31 – 50 years	193 (46.5%)	156 (47.0%)	37 (44.6%)	
51 – 70 years	40 (09.6%)	31 (09.3%)	09 (10.8%)	
Gender				
Male	63 (15.2%)	52 (15.7%)	11 (13.3%)	0.584
Female	352 (84.8%)	280 (84.3%)	72 (86.7%)	
Marital status				
Unmarried	190 (45.8%)	150 (45.2%)	40 (48.2%)	0.622
Married	225 (54.2%)	182 (54.8%)	43 (51.8%)	
Educational level				
High school or below	95 (22.9%)	68 (20.5%)	27 (32.5%)	0.019
Bachelor or higher	320 (77.1%)	264 (79.5%)	56 (67.5%)	
Monthly income (SAR)				
<5,000	169 (40.7%)	140 (42.2%)	29 (34.9%)	0.160
5,000 – 10,000	102 (24.6%)	75 (22.6%)	27 (32.5%)	
>10,000	144 (34.7%)	117 (35.2%)	27 (32.5%)	
Associated diseases				
Yes	77 (18.6%)	67 (20.2%)	10 (12.0%)	0.088
No	338 (81.4%)	265 (79.8%)	73 (88.0%)	
Taking migraine medications				
Yes	250 (60.2%)	212 (63.9%)	38 (45.8%)	0.003
No	165 (39.8%)	120 (36.1%)	45 (54.2%)	

Figure 1. Associated Chronic diseases

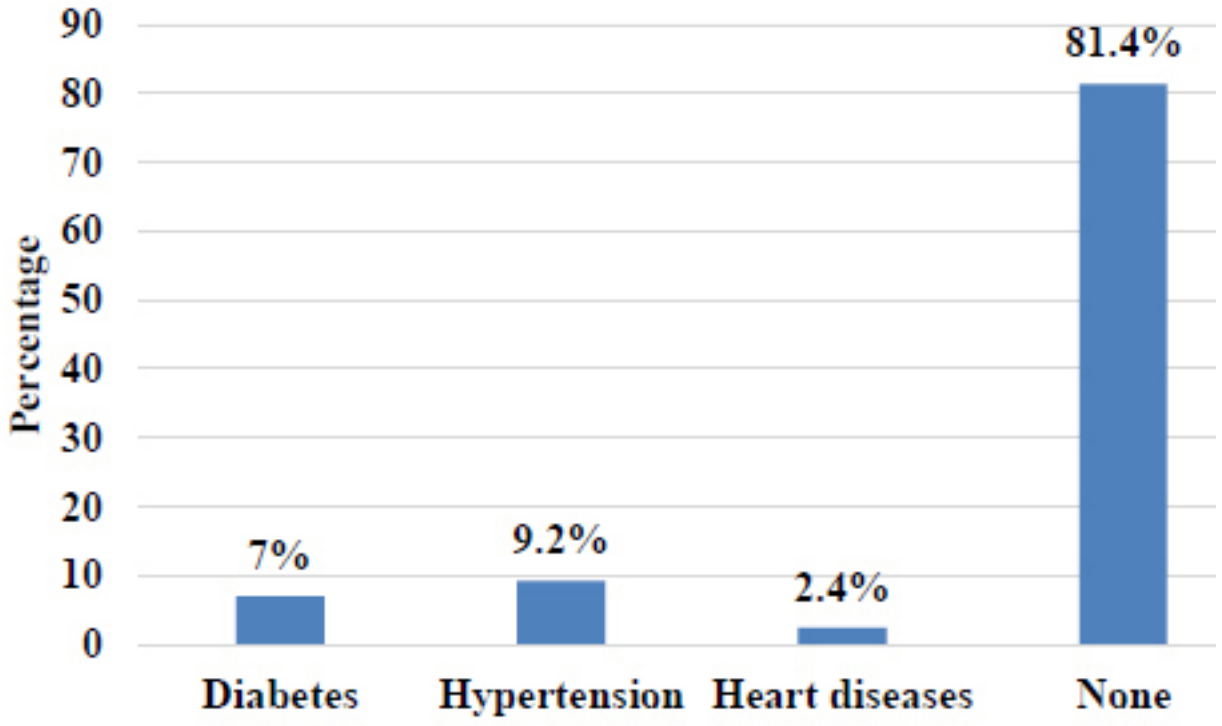

Figure 2. Environmental factors that triggered migraine

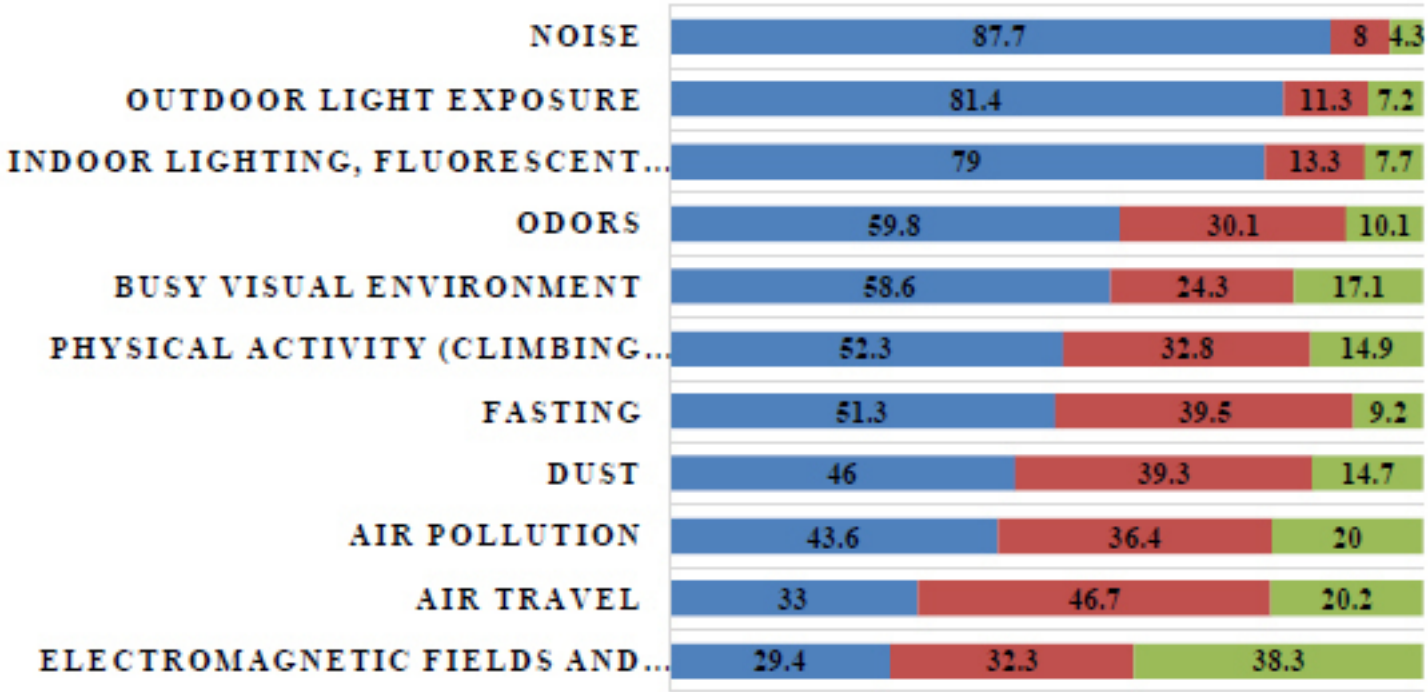

Table 2. Influence of environmental factors toward migraines and their interference with ADL (n=415)

Environmental factors	Migraine interfered with ADL		P-value
	Yes N (%) (n=332)	No N (%) (n=83)	
Air travel			
Agree	111 (33.4%)	26 (31.3%)	0.864
Disagree	153 (46.1%)	41 (49.4%)	
I don't know	68 (20.5%)	16 (19.3%)	
Noise			
Agree	293 (88.3%)	71 (85.5%)	0.103
Disagree	28 (08.4%)	05 (06.0%)	
I don't know	11 (03.3%)	07 (08.4%)	
Electromagnetic fields and spherics			
Agree	111 (33.4%)	11 (13.3%)	0.001
Disagree	98 (29.5%)	36 (43.4%)	
I don't know	123 (37.0%)	36 (43.4%)	
Outdoor light exposure			
Agree	277 (83.4%)	61 (73.5%)	0.111
Disagree	34 (10.2%)	13 (15.7%)	
I don't know	21 (06.3%)	09 (10.8%)	
Indoor lighting, fluorescent lights, Computer screen			
Agree	266 (80.1%)	62 (74.7%)	0.432
Disagree	43 (13.0%)	12 (14.5%)	
I don't know	23 (06.9%)	09 (10.8%)	
Busy visual environment			
Agree	202 (60.8%)	41 (49.4%)	0.111
Disagree	74 (22.3%)	27 (32.5%)	
I don't know	56 (16.9%)	15 (18.1%)	
Odours			
Agree	204 (61.4%)	44 (53.0%)	0.089
Disagree	92 (27.7%)	33 (39.8%)	
I don't know	36 (10.8%)	06 (07.2%)	
Air pollution			
Agree	147 (44.3%)	34 (41.0%)	0.443
Disagree	116 (34.9%)	35 (42.2%)	
I don't know	69 (20.8%)	14 (16.9%)	
Dust			
Agree	156 (47.0%)	35 (42.2%)	0.676
Disagree	127 (38.3%)	36 (43.4%)	
I don't know	49 (14.8%)	12 (14.5%)	

Table 2. Influence of environmental factors toward migraines and their interference with ADL (n=415) (continued)

Fasting			
Agree	186 (56.0%)	27 (32.5%)	0.001
Disagree	118 (35.5%)	46 (55.4%)	
I don't know	28 (08.4%)	10 (12.0%)	
Physical Activity			
Agree	180 (54.2%)	37 (44.6%)	0.283
Disagree	105 (31.6%)	31 (37.3%)	
I don't know	47 (14.2%)	15 (18.1%)	

Table 3: Multivariate regression analysis to determine the independent significant factor associated with migraines that interfered with activities of daily living (n=415)

Factor	Adjusted Odds Ratio (AOR)	95% Confidence Interval (CI)	P-value
Educational level			
High school or below	Ref		
Bachelor or higher	2.040	1.148 – 3.626	0.015
Take migraine medication			
Yes	2.338	1.388 – 3.938	0.001
No	Ref		
Electromagnetic fields and spherics			
Agree	0.679	0.378 – 1.218	0.194
Disagree	0.251	0.118 – 0.532	0.001
I don't know	Ref		
Fasting			
Agree	0.991	0.410 – 2.394	0.984
Disagree	0.345	0.198 – 0.603	<0.001
I don't know	Ref		

Discussion

This study attempted to examine the relationship between environmental changes and their influence on triggering migraines. The findings of this study revealed a high prevalence of environmental triggers for migraines. Approximately 80% of the patients suffered a migraine during the last month. Several published papers reported a high frequency of migraines, varying from 80% to 100% [6-10]. On the other hand, in India, reports indicated that the one-year prevalence of migraines was 14.12%, which was relatively lower than our result [11]. One may argue that the report was based on a one-year prevalence, whereas our study is estimated for a one-month prevalence. Other regions also reported a lower prevalence rate of migraines. For example, in Europe [12], the one-year prevalence rate of migraines was approximately 14%, while in the USA [13], the three-months overall prevalence of migraines was 14.2%. In Latin America, the one-year prevalence of migraines was estimated between 6.1% and 17.4% [14]. Perhaps the differences in prevalence rate depends on the region or it may correlate with patients' history of migraines. The minimal varying rates could be due to the different setup in methodology or the differences in criteria of prevalence and the type of study population [15]. Furthermore, parts of the literature suggest that migraines were more common in women than men [6, 11, 16]. This is consistent with our study, where migraines were more common in females, although, a statistical test revealed that it has no significant impact on the disease after testing their relationship ($p>0.05$).

Of the environmental factors that trigger migraine, our results indicated that the most influential factors were noise, followed by outdoor light exposure, indoor lighting, fluorescent lights, computer screens, and odours. There were varying reports regarding the environmental factors that triggered migraines among patients. For example, in India [8,9,11] as well as in Brazil [10], they reported that prolonged exposure to sunlight and hot humid weather were the most common environmental factors of the disease. This had also been reported by Neut and colleagues [17], where they found that hot and cold weather were the triggering factors of migraines among children and adolescents aged between 7 and 16 years. The researchers explained that in their region the weather is generally mild and rainy unlike in other papers, where hot weather is dominant, such as the study of Chakravarty et al. [8] and Ray et al. [11]. Conversely, Jain and Choudhary [9], denoted that physical activity (43%) and noise (42%) were reported as some of the most common triggering factors of migraines, which is comparable with our study, as 87.7% and 52.3% of the patients agreed that noise and physical activity were the environmental factors that instigated migraines.

Strong odour was also identified as a precipitating factor of migraines. In Kuwait [7], the most common triggers were: the smell of strong odours (62.9%), followed by certain foods (51.8%), which was similarly reported in Brazil [18], where the smell of food was the most common precipitating factor for developing a migraine. In our study, 59.8% of the patients agreed that odours were also an environmental factor that could trigger a migraine, which was consistent with previous reports.

In a study by Ray et al. [11], they found that adverse environmental exposure, long-distance travel, and the use of oral contraception emerged as significant risk factors responsible for the development of migraines.

Moreover, our further investigation noted that patients who were professionals and those who were taking migraine medication were the independent significant predictors associated with an increased risk of migraine that interfered with ADL. Based on our multivariate estimates, we predicted that patients who held a bachelor degree or higher, and those who were taking

medication for the treatment of migraines, were twice as likely to be associated with having migraines ($p<0.05$). These findings are not consistent with Ray et al.'s paper [11]. They documented that lower educational status was the significant risk factor of migraines, while in a paper by Jain and Choudary [9], they indicated that there was no significant difference observed in the prevalence of migraines concerning the socio-demographic characteristics of the patients ($p>0.05$).

Conclusion

Migraines are highly prevalent in our region, most specifically among women. Noise, outdoor light exposure, indoor lighting, fluorescent lights, and computer systems were the most triggering environmental factors of migraines, which dissuaded patients from their activities of daily living. Further, patients who were more educated and those who used treatment methods are likely being affected the most by migraines, which hinder their activities for daily living. An awareness campaign is necessary to educate the patients regarding the influence of environmental factors that could trigger the disease. Proper counseling among the affected is necessary to decrease the burden of the migraine.

List of abbreviations

ADL Activities of daily living
SPSS Statistical package for social sciences
AOR Adjusted Odds Ratio
CI Confidence Interval

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Job Satisfaction among Primary Health Care Workers in Buraidah, Qassim, Saudi Arabia

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Abstract

Satisfaction of health care workers has direct effect on the quality of care. This study aimed to assess the job satisfaction among primary health care (PHC) workers in Buraidah, Saudi Arabia. A cross sectional study was conducted among primary health care workers in Buraidah. Twenty PHC centers were selected by simple random sampling. All the workers including; physician, dentist, nurse, pharmacist and laboratory technician who have been working for at least one year in the same facility were invited to participate in the study. Data was collected on socio-demographic and professional characteristics. Job satisfaction was measured using a validated 36 item Job Satisfaction Survey (JSS). A total of 230 PHC workers were included in this study. Nineteen (8.3%) of them expressed that they were dissatisfied, and almost half of them (55.7%) were ambivalent, and the rest (36.1%) were satisfied with their job. Among the nine facets of the JSS; Nature of work, Co-workers and Supervision had mean scores in the satisfaction category, while, five facets were in the range of ambivalent; Pay, Promotion, Benefits, Contingent rewards and Communication. Only one facet fell under the dissatisfaction range which was Operating Conditions. None of the socio-demographic variables had significant association with job satisfaction. About two thirds of the PHC workers were not satisfied with their job. This calls for policy makers to enhance job and job conditions to increase job satisfaction and improve the quality of care at primary care level.

Key words: Job; Primary care; Satisfaction; Saudi Arabia; Worker

Introduction

Job satisfaction in simple words is the feeling of pleasure and positivity in someone's job experience. It is also determined by what someone wants in a job and what someone has in a job according to Locke Range's Theory of job satisfaction (1976) (1-3). Job satisfaction was found to be linked in a direct way to work productivity and personal wellbeing of workers (4). On the other hand, job dissatisfaction will negatively affect the organization's structure and workflow, for instance, noncompliance to guidelines and procedures of the workplace, increased workers' absence, productivity decline, increased work-related accidents and worsening of physical and mental health of the workers (5). Primary health care workers' satisfaction in their jobs is extremely significant because they are responsible for delivering essential health care for large populations as they are the first line in the health care system that people reach (6). Their satisfaction plays an important role in terms of delivering optimal health care to the patients and having a good clinical outcome as job dissatisfaction was associated with patients' dissatisfaction and more importantly; poor clinical outcome of the patients (1-3). Furthermore, there are several factors which affect job satisfaction, Mausner and Herzberg's views on job satisfaction classified the factors into intrinsic and extrinsic factors. Intrinsic factors include the amount of responsibility that is given to the worker and recognition for the achievements at work as they positively correlate with job satisfaction. On the other hand, extrinsic factors include; working hours, the institute's rules and regulations and salary (7). Salary by itself is considered one of the major reasons that would lead to job dissatisfaction and decreased levels of motivation according to World Health Organization (WHO) which will eventually lead to migration of health care providers (8).

A study was done in the state of Delhi in India regarding job satisfaction among primary health care providers and concluded that the majority of the providers were dissatisfied and it's difficult to point out a single factor as the factors led to dissatisfaction are variable and lay under major groups of factors related to the organization's facilities, organization's polices, interpersonal relationships and job privileges (9). During literature review, it was noticed that there is a scarcity of literature about job satisfaction of primary health care workers in Saudi Arabia. A study from Jazan region in Saudi Arabia, showed that nurses in primary health care were dissatisfied about their work and addressed the factors which influenced their job satisfaction such as working hours, lack of facilities for nurses, lack of professional development opportunities and limited vacation time (10). Another study from Al-Madina region in Saudi Arabia that included physicians and nurses working in PHC centers reported high job dissatisfaction. The domains in which physicians and nurses were mainly dissatisfied were Professional opportunities, patient care, workload, appreciation and financial rewards (11). Primary health care is the corner stone of the health system in Saudi Arabia. Ambitious Vision 2030 of Saudi Arabia requires transformation of the health care system based on primary care. This study will help us to know the job satisfaction among primary health care workers in Qassim region of Saudi Arabia. The findings will also raise policy makers and manager's awareness level and may help them to improve the level of job satisfaction of primary health care providers and ultimately improve the care provided.

Methods

This cross-sectional study was planned to be conducted between November 2019 till October 2020, however, due to the COVID-19 pandemic we extended the data collection period till the beginning of 2021. The study was conducted among primary health care workers who worked in primary health care centers in Buraidah, Qassim region.

Sample size was calculated using OpenEpi. We used finite population correction as the number of PHC workers in Buraidah is estimated to be around 445. We used a proportion of 38% from a previous study to calculate our sample size (12). At 95% confidence level and 5% bound on error the required sample size was 201. We inflated the sample size by 10% to account for non-response and missing data so the final sample required was 221.

1. Sampling procedure:

We used simple random sampling to select the PHCs. The total number of PHCCs in Buraidah city is 40. With about a total population of 445 PHC workers, there are around 11-12 workers in each PHCC, so we needed at least 20 PHCCs to meet the sample size. All the PHCCs were listed in alphabetical order and selected by computerized random numbers. Within each selected PHCC, all the health care workers meeting our eligibility criteria were invited to participate. Any health care worker; physician, dentist, nurse, pharmacist and, laboratory and radiology technicians currently working in primary care for at least one year was eligible for participation in the study. Family medicine trainees and interns were excluded.

2. Data collection tool and procedure:

Data were collected from participants using self-administered questionnaire that consists of three parts. The first part included the informed consent and explanation of the study's purpose and information about the researcher. Contact information was also included for any further inquiry from the participants if required. The second part consisted of demographic data (age, sex, marital status, nationality, job title, working years at the current PHC and total years of work experience). The third part consisted of Job Satisfaction Survey (JSS) questionnaire (13). The Job Satisfaction Survey, JSS is a 36 item, nine facet scale to assess employee attitudes about the job and aspects of the job. Each facet is assessed with four items, and a total score is computed from all items. A summated rating scale format is used, with six choices per item ranging from "strongly disagree" to "strongly agree". Items are written in both directions, so about half must be reverse scored. The nine facets in the JSS were; Pay, Promotion, Supervision, Fringe Benefits, Contingent Rewards (performance-based rewards), Operating Conditions (required rules and procedures), Coworkers, Nature of Work, and

Communication. Scoring system for the 4-item subscales, as well as the 36-item total score, where scores with a mean item response (after reverse scoring the negatively-worded items) of 4 or more represents satisfaction, whereas mean responses of 3 or less represents dissatisfaction. Mean scores between 3 and 4 are ambivalence. Translated into the summed scores, for the 4-item subscales with a range from 4 to 24, scores of 4 to 12 are dissatisfied, 16 to 24 are satisfied, and between 12 and 16 are ambivalent. For the 36-item total where possible scores range from 36 to 216, the ranges are 36 to 108 for dissatisfaction, 144 to 216 for satisfaction, and between 108 and 144 for ambivalent (13).

Statistical analysis was done using IBM SPSS statistics version 28. Descriptive statistics were carried out. Frequency and proportion for categorical variables and mean and standard deviation for continuous variables were calculated. Chi square and ANOVA were used to look for the differences between categorical and continuous variable types respectively. P-values less than 0.05 were considered significant.

3. Ethical Considerations:

This study was reviewed and approved by Qassim Regional Bioethics Committee (Approval number:1441-1064853). Permission to collect data was also obtained from management of primary care in Buraidah city. Informed consent was obtained from all the participants.

Results

A total of 230 participants were included in the study. The mean age of the participants was 35±7.4 years, ranging from 27.6 to 42.4 years. About 83.9% of workers were Saudi. Female workers represented 53.8% of the sample. Nearly half (48.2%) of the participants were nurses, 29.5% were physicians and the rest 22.3% of the workers included pharmacists, dental assistants, lab and radiology technicians. The mean duration of work experience among workers is 10.3±7.3 years. (Table 1)

Table 1. Socio-demographic and professional profile of health care workers in Buraidah, Qassim (n=230)

Characteristics	n (%)
Age (n=195)	
Mean±SD	35±7.4
Gender (n=221)	
Male	102(46.2)
Female	119(53.8)
Nationality (n=223)	
Saudi	187(83.9)
Non-Saudi	36(16.1)
Marital Status (n=182)	
Never married	33(18.1)
Ever married	149(81.9)
Job title (n=224)	
Physician	66(29.5)
Nurse	108(48.2)
others	50(22.3)
Total work experience (years) (n=197) Mean±SD	10.3±7.3
Work experience in the current PHC (n=181) Mean±SD	3.6±3.7

Figure.1 illustrates the overall satisfaction of PHC workers in PHC centers which was calculated from the nine facets of job satisfaction. Only nineteen (8.3%) of the workers expressed that they were dissatisfied, and almost half of them (55.7%) were ambivalent, and the rest (36.1%) were satisfied.

Figure 1. Overall job satisfaction of PHC workers in Buraidah, Saudi Arabia (n=230)

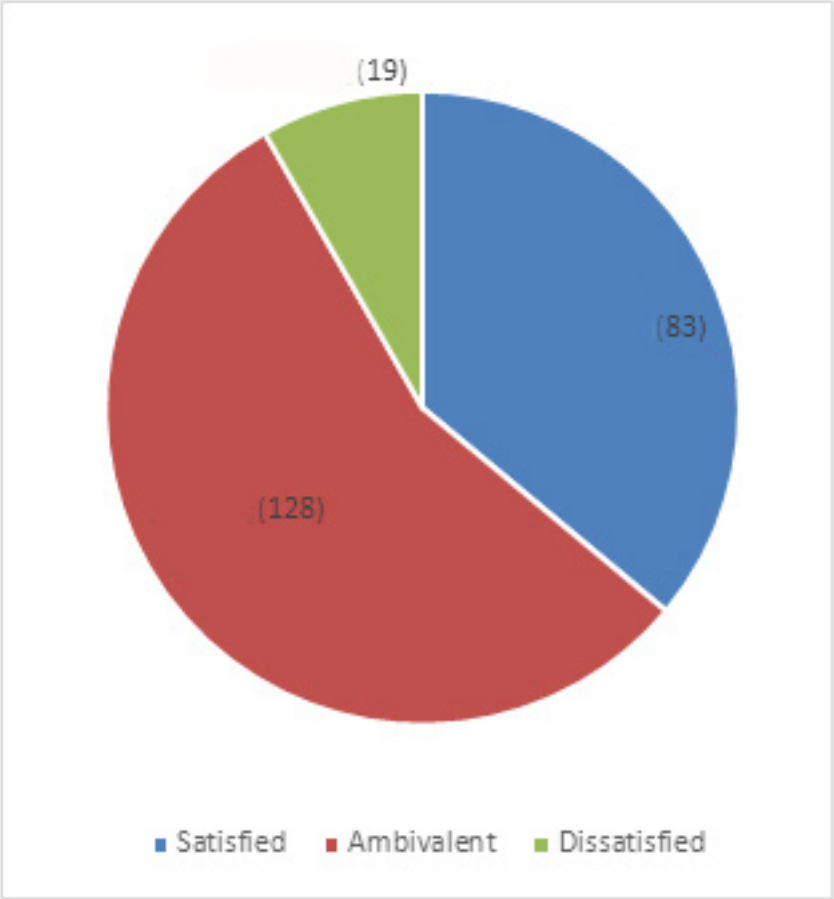

Table 2 shows the mean and standard deviation for each facet of job satisfaction. Means between 16-24 represent satisfaction. The facets which are in the level of satisfaction were; Nature of work (20.1±4.1), Co-workers (18.6±3.8) and Supervision (17.2±4.8). Meanwhile, five facets were in the range of Ambivalent (12-16), and these included; Pay, Promotion, Benefits, Contingent rewards and Communication. Only one facet fell under the dissatisfaction range which was Operating Conditions

Table 2: Level of satisfaction and mean score of PHC workers' responses to Job satisfaction survey's facets

Subscale	Satisfied %(n)	Ambivalent %(n)	Dissatisfied %(n)	Mean(±SD)
Pay	36.1(83)	43.9(101)	20(46)	14.7(±3.3)
Promotion	48.7(112)	26.1(60)	25.2(58)	14.9(±4.3)
Supervision	54.8(126)	31.7(73)	13.5(31)	17.2(±4.8)
Benefits	23(53)	35.7(82)	41.3(95)	13.1(±4.5)
Contingent rewards	24.8(57)	25.2(58)	50(115)	12.9(±4.7)
Operating Conditions	6.1(14)	15.2(35)	78.7(181)	10.4(±2.8)
Co-workers	76.5(176)	18.3(42)	5.2(12)	18.6(±3.8)
Nature of work	83.9(193)	11.7(27)	4.3(10)	20.1(±4.1)
Communication	49.1(113)	23.5(54)	27.4(63)	15.7(±4.9)

Table.3 presents the overall job satisfaction level according to sociodemographic characteristics, duration of work experience in the current PHC and total work experience. Older workers (35.9±7.1) were more satisfied than younger workers. The longer the duration of work in the same PHC, the higher the dissatisfaction. Male workers were slightly more satisfied than female workers, as well as Saudi workers in comparison to non-Saudi. However, none of these characteristics were statistically significant P > 0.05.

Table 3: Differentials of the overall level of job satisfaction according to sociodemographic characteristics and work experiences and duration of work in the same PHCC of PHC workers in Buraidah, Qassim, KSA (n=230)

Characteristics	Satisfied %(n)	Ambivalent % (n)	Dissatisfied % (n)	P-value
Age				
Mean±SD	35.9±7.1	34.9±7.5	31.8±7.8	0.138[a]
Gender				
Male	37.3(38)	54.9(56)	7.8(8)	0.911
Female	35.3(42)	55.5(66)	9.2(11)	
Nationality				
Saudi	36.4(68)	55.1(103)	8.6(16)	0.934
Non-Saudi	33.3(12)	58.3(21)	8.3(3)	
Marital status				
Ever married	35.6(53)	57(85)	7.4(11)	0.548
Never married	39.4(13)	48.5(16)	12.1(4)	
Job title				
Physician	36.4(24)	53(35)	10.6(7)	0.236
Nurse	32.4(35)	62(67)	5.6(6)	
others	44(22)	44(22)	12(6)	
Total work experience				
Mean±SD	10.9±7.6	10.1±7.0	9±7.6	0.570 [a]
Work experience in current PHC Mean±SD	3.4±4.0	3.7±3.2	3.8±4.9	0.876 [a]
[a] P-value derived from ANOVA				

Discussion

To the best of the researchers' knowledge, this is the first study in Saudi Arabia that included all PHC workers who worked in PHCCs of a regional capital to assess their level of job satisfaction. In this study, 36.1% of the workers were satisfied about their job, while only 8.3% were dissatisfied and the rest of participants were ambivalent. The total satisfaction in our study is lower than other similar studies. Bawakid K conducted a comparison study about professional satisfaction among family physicians who worked in PHCCs in both Jeddah and Eastern region, Saudi Arabia and they reported that 62% of the physicians were satisfied (14). Another study conducted by Al-Takroni about job satisfaction among nurses in Qassim found that they were "averagely satisfied", however the study included both hospital and PHC nurses taking into consideration of differences of work duties and work conditions between PHCCs and hospitals (15). The lower satisfaction of PHC workers in our study as compared to Jeddah and Eastern province could be due to fact that former settings were big cities with more opportunity for social and recreational activities compared to Buraidah. There could also be differences in the management and other opportunities compared to our setting. These factors might affect the satisfaction with the job. Nonetheless, this is an important finding which has implications for policy makers for taking actions to improve satisfaction levels of workers in primary care.

According to our study, nature of work and co-workers were the two domains which workers were satisfied the most about. Similarly, a study done by Almalik, in Jazan region showed the majority of nurses in PHC were satisfied with their co-workers and dissatisfied with supervision, professional development opportunities and salary. All of these domains showed to be ambivalent in our study (10). As for nature of work in PHCCs, 83.9% of workers in this study were satisfied. However, 78.7% were dissatisfied with Operating Conditions which is similar to the Allebdi study

which showed that PHC physicians were satisfied about the nature of work and dissatisfied about operating conditions, promotion, contingent rewards and fringe benefits (16). Also, in the AlJuhani et al. study, the domains which physicians were mostly dissatisfied about were financial reward, professional development and patient care. Professional development was also one of the domains that nurses were dissatisfied about in addition to workload and appreciation reward (11). These differences across the various domains of satisfaction might indicate variations in the overall primary care systems across regions within Saudi Arabia. This indicates that there is dire need to improve the working conditions and create opportunities for professional development for PHC workers.

Furthermore, in regards to sociodemographic factors, a previous study (11) showed that male, non-Saudi, older physicians and female non-Saudi older nurses had higher mean scores than their counterparts and were found to be more satisfied. Shah et al. found that older nurses were more satisfied and attributed that to their ability (as mature age-wise) to make better adjustments to the work environment (17). In the current study job satisfaction was slightly higher for older, male, Saudi, workers, however, none of these factors along with other factors like Job title and work experience are statistically significant. Similarly, in Allebdi study where variations of age and gender factor didn't make any statistical significance (16), also, in Kumar study 9 duration of work (experience) has no effect on job satisfaction which in our study, also, showed no statistical significance. Absence of statistical significance in our study could be due to smaller sample which may not have enough power to detect smaller associations.

We used Job Satisfaction Survey (JSS) questionnaire. It is a well-established instrument that has been repeatedly investigated for validity and reliability. Additionally, our sampling criteria was inclusive and included a range of health care workers; physician, dentist, nurse, pharmacist and laboratory technicians. The questionnaire wasn't web-based; therefore, data collectors were available all the time to answer and clarify participants' questions.

On the other hand, our limitations were that the study was done during the COVID-19 pandemic and we faced difficulties in obtaining data due to changes in work conditions. Furthermore, the pandemic may have altered and affected the results of job satisfaction. Finally, the study was done in a single city, Buraidah, due to time and resource limitations which may affect the generalizability of our results to the whole region. Nevertheless, our results are important as we conducted the study in a regional capital while job conditions and social circumstances may be poor in smaller cities and rural areas and we may expect even lower satisfaction in those areas.

Conclusion

Almost two thirds of the workers weren't satisfied with their job which may affect their performance and quality of care. Operating conditions were found to be the factor with lowest satisfaction. On the other hand, Co-workers and Nature of work impacted positively on their satisfaction. Immediate attention is needed from policy makers and planners to implement workplace or job-related changes to improve the satisfaction level of PHC workers and therefore, improve the quality of care at primary care level. We also recommend further large-scale studies to cover PHC workers in the whole Qassim region for generalizable results.

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Barriers to Compliance of Hypertensive Patients in Abha City, Saudi Arabia

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Abstract

Aim of Study: To measure non-compliance and to identify barriers to compliance among hypertensive patients.

Patients and Methods: A total of 200 hypertensive patients attending Al-Qabel Primary Health Care (PHC) Center since at least one year were included in this study. A structured data collection interview questionnaire was used. To assess non-compliance of hypertensive patients, the Hill-Bone Non-Compliance to High Blood Pressure Therapy Scale was used.

Results: Only 11% of hypertensive patients were highly compliant. The main barriers for full compliance were forgetfulness (39%) and being asymptomatic (30%). Some patients were non-compliant as a result of disliking the manner of medical service provided by the primary health care (PHC) team (16%), or they felt the need to take some rest from the daily antihypertensive medication (15.5%). Controlled blood pressure was achieved among 58% of patients. Saudis were significantly more non-compliant than non-Saudis ($p<0.001$). Married patients expressed significantly higher non-compliance than single patients ($p=0.015$). Non-compliance scores were significantly higher among smokers than non-smokers ($p<0.001$); and significantly higher among patients who were treated with multiple antihypertensive drugs ($p=0.019$). Patients with uncontrolled systolic or diastolic blood pressure had significantly higher non-compliance mean scores ($p<0.001$ for both).

Conclusions: Non-compliance of hypertensive patients attending PHC settings in Abha is high. Main barriers against full compliance of hypertensive patients are forgetfulness, absence of symptoms, dissatisfaction with provided health care and being tired of treatment side effects. Non-compliance is significantly higher among younger, newly diagnosed, Saudi, married and smoker patients. Non-compliance is also significantly higher among hypertensive patients on multiple antihypertensive medications.

Recommendations: Health education of hypertensive patients should cover information on the disease, medication, exercise, diet and follow up visits. Patients should be advised to include self-reminders to avoid missing intake of medication and follow up visits. Hypertensive patients should be advised to avoid smoking. PHC physicians should spend enough time with their hypertensive patients listening to their complaints and to meet patients' expectations of a consultation and to avoid any unnecessary over-prescription of multiple anti-hypertensive medications.

Key words: Hypertension, Barriers to compliance, Primary care, Saudi Arabia.

Introduction

Hypertension is an important and prevalent public health problem worldwide, with almost one in three adults suffering from hypertension (1). It is a major risk factor for coronary artery disease and its complications, heart failure, stroke, renal insufficiency, and blindness in diabetic patients. The Global Burden of Disease study estimated that hypertension is the leading risk factor for disability-adjusted life years worldwide, and is considered one of the most significant causes of mortality worldwide (2).

The risk of developing high blood pressure can be reduced by effective medication therapy management and significant lifestyle modifications. Moreover, antihypertensive medication plays an important role in hypertension management. Nevertheless, compliance to hypertension management remains suboptimal (3).

Non-compliance is the main obstacle for controlling hypertension in the community, and a significant barrier to effective hypertension management (4). Therefore, good compliance is crucial to improve hypertension control rates and prevent complications (5). In a global study, the non-compliance rate was 45% and a significant number of hypertensive patients with comorbidities were non-adherent to treatment (6).

Maintaining compliance to multiple medications is a complex issue in patients with chronic diseases. The influence of non-adherence to antihypertensive medications is the most important cause of uncontrolled blood pressure. Consequently, because of non-compliance, nearly three-quarters of hypertensive patients do not achieve optimal blood pressure control (7).

Several approaches have been tried to investigate the medication-taking behavior and the traditional methods, such as pill counts, clinical reports, prescription refills and patient-reported measures are some of the cheap and acceptable methods to provide medication adherence information. However, self-reported questionnaires were often used to assess medication adherence in chronic disease patients (8).

Several self-reported validated questionnaires have been developed to monitor medication adherence in chronic disease patients including hypertension patients. Some of these scales suitable for measuring adherence in hypertension patients include the Hill-Bone Compliance scale (9), and the Morisky medication adherence scale-8 (10).

Several barriers have been associated with non-compliance, such as forgetfulness, lack of motivation due to the incurable nature of hypertension, absence of symptoms, use of herbal preparations, physical disability, presence of complications, low level of education, poor knowledge of the disease and ignorance on the need for long-term treatment (11).

Therefore, a better understanding of these barriers to compliance could help to tailor effective interventions and strategies to improve blood pressure control of hypertensive patients (12).

Study Rationale

Hypertension is a common health problem among adults in Saudi Arabia. Although there has been significant progress in management of hypertension, rates for control of this chronic disease have proved to be very low. An important cause for failure to control hypertension is low compliance with treatment, which remains a universal problem. The identification and characterization of barriers to compliance can potentially lead to better management of hypertension.

Aim of Study

To measure prevalence and extent of non-compliance and to identify barriers to compliance among hypertensive patients in Abha City, Saudi Arabia.

Patients and Methods

This research followed a cross sectional study design and was conducted in Abha City, Saudi Arabia. Following a simple random sample, Al-Qabel primary health care (PHC) center was chosen to conduct this study. It serves a population of about 15,000, most of whom are Saudi. The study population comprised all hypertensive patients registered at the study setting.

A total of 200 hypertensive patients were interviewed by the researchers. Their blood pressure (BP) was measured using a mercury sphygmomanometer. Patients were seated for at least 5 minutes and BP was measured with the patient lying on a couch. A cuff of suitable size was applied evenly and firmly around the right exposed upper arm and was rapidly inflated until the reading is 30 mmHg above the level at which the pulse disappears, then slowly deflated at a rate of 2 mmHg per second. Systolic blood pressure (SBP) was taken at Phase I of Kortokoff's sound disappearance. Diastolic blood pressure (DBP) was taken at Phase V (13). BP control was judged according to the Eighth Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNC VIII) (14).

The researchers designed and used a structured data collection interview questionnaire that included the following items:

1- Patients' characteristics: age, sex, marital status, smoking status, employment and level of education.

2- Data about hypertension: duration of treatment, BP measures, family history of hypertension, type and number of drugs taken for hypertension (1, 2 or > 2 drugs) and the source of drugs (free, subsidized or not).

To assess non-compliance of hypertensive patients, the "Hill-Bone Compliance to High Blood Pressure Therapy Scale" (9) was used. It assesses patients' behaviors for 3 important behavioral domains of high BP treatment: 1) diet (i.e., reduced sodium intake); 2) appointment keeping;

and 3) medication taking. This scale is composed of 14 items in 3 subscales. Each item is a 4-point Likert type scale. Each item is given a score that ranges from "1" for never to "4" for always. Accordingly, the highest total score is 56 while the lowest is 14. Patients were classified as "highly compliant" if their total score is less than 29; "moderately non-compliant" if their total score is 29-42; or "highly non-compliant", if their total score is higher than 42.

Data were collected by direct interview of hypertensive patients. The Statistical Package for Social Sciences (IBM, SPSS ver. 25.0) was used for that purpose. Descriptive statistics were calculated and the appropriate tests of significance (i.e., t-test, F-test) were applied accordingly.

Results

Table (1) shows that more than half of patients were aged 40-60 years (56.5%) and more than one third were aged above 60 years. Male patients were more than female patients (56% and 44%, respectively). Most patients were Saudis (88.5%) and married (94.5%). More than one third of patients were illiterate (37%); almost one quarter attained primary level of education (24.5%), while those who were university graduates constituted 8%. More than half of patients were unemployed or retired (55.5%). In addition, 17% of patients were smokers. Almost one quarter of patients (23%) had a positive family history for hypertension.

Table (2) shows that 52.5% of patients had been treated for more than 5 years. More than half of patients showed controlled BP (58%). Almost one quarter of patients had high systolic and diastolic blood pressures (22%), while 18.5% had isolated systolic hypertension and 1.5% had diastolic hypertension. Beta blockers were administered to more than half of patients (52%), followed by ACE inhibitors (35.5%), diuretics (32%), and calcium channel blockers (15%). More than half of patients received one anti-hypertensive drug (56%), 28% received two different drugs, while 16% of hypertensive patients received three drugs or more. Anti-hypertensive treatment was fully subsidized for most patients (71%). It was partially subsidized for 17.5% of patients while it was covered for 11.5% of patients.

Table (3) shows that only 11% were highly compliant. More than two thirds of patients were partially compliant (68.5%) while one fifth of patients were non-compliant (20.5%). The main reasons for not achieving full compliance were forgetfulness (39%) and feeling normal (30%). Moreover, some patients were non-compliant as they did not like the manner of provided medical service by the health team (16%), or they felt the need to take some rest from the daily antihypertensive medications (15.5%).

Table (4) shows that mean non-compliance scores were almost similar among male and female patients. Saudis showed significantly higher non-compliance scores than non-Saudis (36.2+7.5 vs. 30.9+4.2, $p<0.001$). Married patients expressed significantly higher non-compliance than single patients (35.9+7.3 vs. 30.3+7.1, $p=0.015$). Patients with higher educational status (e.g., university graduates) expressed lower non-compliance scores compared with patients with low educational status (e.g., illiterate or primary level). However, differences were not statistically significant. Mean non-compliance scores were almost similar among employed and non-employed patients. Non-compliance scores were significantly higher among smokers than non-smokers (43.4+6.2 vs. 34.0+6.6, respectively, $p<0.001$). Mean non-compliance scores were almost similar among those with positive family history of hypertension and those with no family history of hypertension. Non-compliance mean scores of hypertensive patients did not differ significantly if ACE inhibitors, calcium channel blockers or beta-blockers were administered. However, patients on diuretics expressed significantly lower mean non-compliance scores, (i.e., higher compliance) ($p<0.001$). Non-compliance was significantly higher among patients treated with multiple antihypertensive drugs ($p=0.019$). Patients who fully paid for their medications expressed the highest non-compliance mean scores (38.1+6.4) compared with those who had partially or fully subsidized treatment. Differences were not statistically significant. Patients with uncontrolled systolic or diastolic BP had significantly higher non-compliance mean scores ($p<0.001$ for both).

Table 1: Characteristics of hypertensive patients

Characteristics (n=200)	No.	%
Age group (in years)		
– <40	15	7.5
– 40-60	113	56.5
– >60	72	36.0
Sex		
– Males	112	56.0
– Females	88	44.0
Nationality		
– Saudi	177	88.5
– Non-Saudi	23	11.5
Marital status		
– Single	11	5.5
– Married	189	94.5
Educational level		
– Illiterate	74	37.0
– Primary	49	24.5
– Intermediate	32	16.0
– Secondary	29	14.5
– University	16	8.0
Smoking status		
– Smoker	34	17.0
– Non-smoker	166	83.0
Positive family history of hypertension		
– No	154	67.0
– Yes	46	23.0

Table 2: Characteristics of treatment received by hypertensive patients

Variables (n=200)	No.	%
Duration of treatment		
– ≤5 years	95	47.5
– > 5 years	105	52.5
Blood pressure control		
– Controlled	116	58.0
– Systolic-Diastolic Hypertension (SDH)	44	22.0
– Isolated Systolic Hypertension (ISH)	37	18.5
– Isolated Diastolic Hypertension (IDH)	3	1.5
Prescribed antihypertensive medications		
– Beta blockers	104	52.0
– ACE Inhibitors	71	35.5
– Diuretics	64	32.0
– Calcium channel blockers	30	15.0
– Other medications	47	23.5
Number of prescribed antihypertensive medications		
– One	112	56.0
– Two	56	28.0
– Three or more	32	16.0
Payment for antihypertensive medications		
– Totally by patient	23	11.5
– Partially subsidized	35	17.5
– Fully subsidized	142	71.0

Table 3: Degrees of non-compliance and reasons for non-compliance among hypertensive patients

Patterns of non-compliance	No.	%
Levels of non-compliance among hypertensive patients (n=200)		
– Highly compliant *(non-compliance scores <29)*	22	11.0
– Moderately compliant *(non-compliance scores 29-42)*	137	68.5
– Non-compliant *(non-compliance scores >42)*	41	20.5
Main reasons for non-compliance†		
– Forgetfulness	78	39.0
– Feeling normal (asymptomatic) without taking medication	60	30.0
– Dissatisfaction with offered health care	32	16.0
– Getting some rest from anti-hypertensive treatment side effects	31	15.5

† More than one reason is possible

Table 4: Association between non-compliance scores (Mean±SD) and patients' personal characteristics

Personal Characteristics		No.	Mean	SD	p-value
Age group	<40 years	15	33.1	2.0	
	40-60 years	113	38.0	8.2	
	>60 years	72	32.2	4.9	<0.001
Sex	Males	112	36.0	7.2	
	Females	88	35.0	7.7	0.369
Nationality	Saudi	177	36.2	7.5	
	Non-Saudi	23	30.9	4.2	0.001
Marital status	Single	11	30.3	7.1	
	Married	189	35.9	7.3	0.015
Educational level	Illiterate	74	36.0	8.3	
	Primary	49	36.6	7.3	
	Intermediate	32	35.5	5.7	
	Secondary	29	34.3	8.0	
	University	16	32.9	4.3	0.415
Duration of treatment	≤5 years	95	36.6	7.4	
	> 5 years	105	34.6	7.4	0.048
Smoking	Non-smoker	166	34.0	6.6	
	Smoker	34	43.4	6.2	<0.001
Family history of hypertension	Negative	154	35.8	7.8	
	Positive	46	34.8	5.7	0.449
Prescribed medications	ACE Inhibitors	71	36.1	6.7	0.408
	Calcium channel blockers	30	36.7	6.4	0.360
	Diuretics	64	32.2	5.4	<0.001
	Beta blockers	104	36.4	8.1	0.096
No. of prescribed antihypertensive drugs	One	112	34.3	7.3	
	Two	56	36.8	6.5	
	Three or more	32	37.8	8.4	0.019
Payment for treatment	Totally by patient	23	38.1	6.4	
	Partially subsidized	35	33.9	5.4	
	Fully subsidized	142	35.5	7.9	0.106
Systolic blood pressure	Controlled	119	32.1	4.1	
	Uncontrolled	81	40.7	8.2	<0.001
Diastolic blood pressure	Controlled	153	32.7	4.8	
	Uncontrolled	47	44.9	6.6	<0.001

Discussion

The present study indicated that non-compliance of hypertensive patients was highly prevalent. Only 11% were highly compliant. More than two thirds of patients were partially compliant (68.5%) while one fifth of patients were non-compliant (20.5%). The main reasons for failure to achieve full compliance were forgetfulness (39%) and being asymptomatic (30%). Moreover, some patients were non-compliant as they did not like the manner of provided medical service by the health team (16%), or they felt the need to take some rest from the daily antihypertensive medication (15.5%).

High non-compliance rates for hypertensive patients were reported by several studies all over the world. Al-Sowielem and Elzubier (15) reported that 34.2% of their hypertensive patients in Al-Khobar, KSA were compliant. Hadi and Rostami-Gooran (16), in Iran, reported that only 39.6% of their hypertensive patients were compliant. Youssef and Moubarak (17), in Egypt, noted that half of their patients were compliant, while nearly half of their hypertensive patients were either non-compliant (25.9%) or partially compliant (22.2%). Thrall et al. (18) added that figures from the United States suggest that non-compliance with medication may reach as high as 50-80%, with compliance decreasing rapidly over time.

Miller et al. (19) stated that barriers to compliance encountered by patients include practical and logistical issues such as lack of transportation and health insurance, inability to take time off from work to keep medical appointments, and lack of a continuing health care provider.

Youssef and Moubarak (17) noted that the most frequently stated barriers to full compliance were feeling that BP was normal (36.2%), followed by forgetfulness (34.8%), wanting a 'drug holiday' (11.8%) and wanting to avoid side-effects (10.5%).

Several studies concluded that the main barriers against compliance among hypertensive are having their antihypertensive medications prescribed more than once a day. Patients' concerns mainly relate to the lifelong need for medication and the possible side effects or risks that may be unacceptable in a largely asymptomatic disease (20-21). Mamaghani (22) added that barriers to effective compliance among hypertensive patients include poor doctor-patient communication, cost of antihypertensive therapy, and side effects of the drugs.

Efforts to control hypertension through the use of antihypertensive medications are considered to be the most effective strategy. Since HBP is mostly asymptomatic, poor patient compliance with anti-hypertensive medication has consistently limited the effectiveness of these interventions (23). Moreover, patient forgetfulness, the number of daily doses, side effects, and/or class of agent, may impair patients' compliance (24-25).

The present study showed that achieving BP control is not easily obtainable. About half of patients showed controlled BP (58%). Almost one quarter of patients had high systolic and diastolic BPs (22%), while 18.5% had isolated systolic hypertension and 1.5% had diastolic hypertension. A similar finding has been described by Youssef and Moubarak (17), who reported that just over half (53.2%) of the participants achieved controlled BP.

The present study showed that non-compliance of hypertensive patients differed significantly according to some of their personal characteristics. Non-compliance correlated positively and significantly with age and education of patients. This study also showed that patients with uncontrolled systolic or diastolic BP had significantly lower compliance. Nevertheless, compliance did not differ between male and female patients or between employed and unemployed patients. However, Saudis showed significantly less compliance than non-Saudis. In addition, married patients expressed significantly less compliance than single patients.

These findings were controversial and sometimes contradicting in different studies. Al-Sowielem and Elzubier (15) reported that the compliance of hypertensive patients was significantly higher among illiterate patients than educated ones and among patients over 55 years of age than those who were younger. There was no significant difference in compliance rates between males and females, or between Saudis and non-Saudis. Hadi and Rostami-Gooran (16) reported that older patients were more compliant. Compliance score was higher in those patients who had taken antihypertensive drugs for longer than 5 years ($p<0.05$).

Wang et al. (26) stated that several studies indicated an association between compliance and BP control (27-29). Some other studies have shown a positive association between compliance and male gender (30) and level of education (31).

Similar findings were reported by Al-Sowielem and Elzubier (15) and Al-Mustafa and Abulrahi (33) in the KSA, who reported lower compliance among cigarette smokers and those with positive family history of hypertension.

This study showed that patients on diuretics expressed significantly higher compliance, while non-compliance was significantly higher among patients who were treated with more than one antihypertensive drug. Variations in patients' compliance may reflect the extent of affordable side effects of anti-hypertensive medications. With increased number of prescribed antihypertensive drugs, it is expected that side effects would also increase, hence discouraging the patient to comply. Moreover, hypertensive patients in the present study who fully paid for their medications expressed the least compliance compared with those who had partially or fully subsidized treatment. However, differences were not statistically significant. This finding can be explained by that hypertensive patients who pay for their treatment would not be able to pay any time they face financial problems.

Miller et al. (19) noted that compliance with recommendations for entering and remaining in care, modifying lifestyle, and taking medications vary according to incentive versus therapeutic intent or goal and ability to pay for care. They added that hypertensive patients need to use self-reminders into their daily routine. Patients also need advice on how to adapt to changes in their schedules and environment. Travel and vacations, for example, may lead to delays or omissions in taking medications and dietary errors such as increased intake of foods high in fat and sodium. Hadi and Rostami-Gooran (16) reported that compliance score was significantly higher among patients with 75% insurance than those who had not been insured ($p<0.05$).

Thrall et al. (18) emphasized that one of the main reasons that hypertensive patients give for complying with their medication regimen is the confidence they feel toward their physician or the health-care system. Moreover, the interaction between the patient and his/her physician significantly affects compliance with medical advice and medication. Factors such as empathy on the part of the physician, adequate time spent with the patient, providing clear information about the diagnosis and medication, and meeting patient's expectations of a consultation, all provide strong positive influences which subsequently potentiate compliance.

The present study concluded that non-compliance of hypertensive patients attending Al-Qabel PHC Center in Abha is high. Non-compliance is significantly more among younger, newly diagnosed, Saudi, married, smoker, and those on multiple antihypertensive medications. Compliance is significantly better among hypertensive patients on diuretics. Main barriers against full compliance of hypertensive patients are forgetfulness, absence of symptoms, dissatisfaction with offered health care and being tired of treatment side effects.

This study recommends that health education of hypertensive patients should cover information on the disease, medication, exercise, diet and follow up visits. Patients should be advised to include self-reminders to avoid missing intake of medication and follow up visits. Hypertensive patients should be advised to avoid smoking. PHC physicians should spend enough time with their hypertensive patients listening to their complaints and to meet patient's expectations of a consultation and to avoid any unnecessary over-prescription of multiple anti-hypertensive medications.

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Disappearance of hepatitis C virus antibodies with hydroxyurea therapy in sickle cell diseases

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Abstract

Background: We tried to understand whether or not there is a disappearance of hepatitis C virus antibodies (anti-HCV) with hydroxyurea therapy in patients with sickle cell diseases (SCD).

Methods: All patients with the SCD were included, and hydroxyurea therapy was initiated for all of them.

Results: The study included 337 patients (169 females and 168 males). Hydroxyurea therapy was well-tolerated with a high majority of cases (80.1%). Mean number of painful crises per year was decreased with the therapy (10.3 versus 1.7 crises per year, p<0.000). Mean severity of painful crises was decreased, too (7.8 versus 2.2, p<0.001). Although the body weight, mean hematocrit (Hct) value, and mean corpuscular volume (MCV) increased, white blood cells (WBC) and platelets (PLT) counts and the total and direct bilirubin, and lactate dehydrogenase (LDH) levels of plasma decreased with the therapy (p<0.000 for all). Similarly, 23 patients (6.8%) with anti-HCV positivity before the therapy decreased to 16 patients (4.7%, p>0.05) with hydroxyurea.

Conclusion: SCD are chronic inflammatory disorders with high morbidity and mortality rates, and hydroxyurea is a well-tolerated and highly effective regimen for them. While hydroxyurea therapy decreases both frequency and severity of painful crises, WBC and PLT counts, total and direct bilirubin, and LDH levels, it increases body weight, Hct value, and MCV. Although hydroxyurea therapy also decreased the anti-HCV positivity, the difference was nonsignificant probably due to the small sample size of the present study.

Key words: Sickle cell diseases, chronic endothelial damage, atherosclerosis, metabolic syndrome, hepatitis C virus antibodies, hydroxyurea

Introduction

Chronic endothelial damage may be the leading cause of aging and death. Probably whole afferent vasculature including capillaries are mainly involved in the process since much higher blood pressure (BP) of the afferent vessels may be the major underlying cause by inducing recurrent endothelial injuries. Thus the term of venosclerosis is not as famous as atherosclerosis in the literature. Secondary to the chronic endothelial damage, inflammation, edema, and fibrosis, arterial walls become thickened, their lumens are narrowed, and they lose their elastic nature, those reduce blood flow and increase systolic BP further. Some of the well-known accelerators of the atherosclerotic process are male gender, physical inactivity, excess weight, smoking, alcohol, and chronic inflammatory or infectious processes including sickle cell diseases (SCD), rheumatologic disorders, tuberculosis, and cancers for the development of irreversible consequences including obesity, hypertension (HT), diabetes mellitus (DM), peripheric artery disease (PAD), chronic obstructive pulmonary disease (COPD), chronic renal disease (CRD), coronary heart disease (CHD), cirrhosis, mesenteric ischemia, stroke, and benign prostatic hyperplasia (BPH) those terminate with early aging and premature death. They were researched under the title of metabolic syndrome in the literature, extensively (1-3). Although the early withdrawal of the causative factors may delay terminal consequences, the endothelial changes cannot be reversed after the development of obesity, HT, DM, PAD, COPD, CRD, CHD, stroke, or BPH due to their fibrotic nature (4-6). Similarly, SCD are systemic microangiopathic processes that are characterized by sickle-shaped red blood cells (RBC) caused by homozygous inheritance of the hemoglobin S (Hb S) (7, 8). Glutamic acid is replaced with a less polar amino acid, valine, in the sixth position of the beta chain of the Hb S. Presence of valine promotes polymerisation of the Hb S. So Hb S causes RBC to change their normal elastic and biconcave disc shaped structures to hard bodies. The decreased elasticity of RBC instead of their shapes may be the central pathology of the diseases. The sickling process is probably present in whole life, but it is exaggerated during various stressful conditions of the body. The RBC can take their normal elastic shapes after normalization of the stressful conditions, but after repeated cycles of sickling and unsickling, they become hard bodies, permanently. The hard cells induced chronic endothelial damage together with tissue ischemia and infactions, even in the absence of obvious vascular occlusions, are the final consequences of the diseases, so life expectancy of such patients is decreased by 25 to 30 years (9). We tried to understand whether or not there is a disappearance of hepatitis C virus antibodies (anti-HCV) with hydroxyurea therapy in the SCD.

Material and Methods

The study was performed in the Hematology Service of the Mustafa Kemal University between March 2007 and September 2013. All patients with the SCD were enrolled into the study. SCD are diagnosed by the hemoglobin electrophoresis performed via high performance liquid chromatography. Their medical histories including frequency of painful crises per year and severity of them as a mean degree between 0 to 10 according to patient's self-explanation were detected. Cases with a history of three pack-year were accepted as smokers, and cases with a history of one drink a day for three years were accepted as drinkers. A check up procedure including body weight, serum creatinine value on three occasions, hepatic function tests, markers of hepatitis viruses A, B, and C, and human immunodeficiency virus, an electrocardiography, a Doppler echocardiography, an abdominal ultrasonography, a computed tomography of brain, and a magnetic resonance imaging of hips was performed. Other bone areas for avascular necrosis were scanned according to the patients' complaints. Cases with acute painful crisis or any other inflammatory event were treated at first, and then the spirometric pulmonary function tests to diagnose COPD, the Doppler echocardiography to measure the systolic BP of pulmonary artery, and renal and hepatic function tests were performed on the silent phase. The criterion for diagnosis of COPD is post-bronchodilator forced expiratory volume in 1 second/ forced vital capacity of less than 70% (10). Systolic BP of the pulmonary artery of 40 mmHg or higher during the silent phase is accepted as pulmonary hypertension (11). CRD is diagnosed with a permanently elevated serum creatinine level of 1.3 mg/dL or higher on the silent phase. Cirrhosis is diagnosed with hepatic function tests, ultrasonographic findings, ascites, and liver biopsy in case of requirement. Digital clubbing is diagnosed with the ratio of distal phalangeal diameter to interphalangeal diameter of greater than 1.0 and with the presence of Schamroth's sign (12, 13). A stress electrocardiography was performed in cases with an abnormal electrocardiography and/or angina pectoris. A coronary angiography was obtained just for the stress electrocardiography positive cases. So CHD was diagnosed either angiographically or with the Doppler echocardiographic findings as the movement disorders of the cardiac walls. Then, the hydroxyurea therapy was initiated to all patients with an initial dose of 15 mg/kg/day, and then the dose was increased up to the final dose of 35 mg/kg/day according to patients' requirement and compliance. Finally, the mean number and severity of painful crises, body weight, white blood cells (WBC) and platelets (PLT) counts, hematocrit (Hct) value, mean corpuscular volume (MCV), and the total and direct bilirubin and lactate dehydrogenase (LDH) levels of the serum were compared before and after the hydroxyurea therapy. Mann-Whitney U test, Independent-Samples t test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 337 patients with the SCD (169 females and 168 males). Their mean ages were 28.4 ± 9.3 (8-59) versus 29.8 ± 9.3 (6-58) years in females and males, respectively (p>0.05). The hydroxyurea treatment was used and well-tolerated with a high majority of cases (80.1%), and the remaining cases could not been followed up. We have not observed any major side effect of the therapy during the follow-up period. The final dose of 35 mg/kg/day was just achieved in 25 cases (7.4%), and the usual dose was 500 mg twice daily during the 7-year follow-up period. During the period, the mean number of painful crises per year was significantly decreased with the treatment (10.3 versus 1.7 crises per year, p<0.000). The mean severity of painful crises was decreased, too (7.8 versus 2.2, p<0.001). Although the body weight, mean Hct value, and MCV increased, the WBC and PLT counts and the total and direct bilirubin and LDH levels of the serum decreased with the therapy, significantly (p<0.000 for all). Parallel to the above developments, 23 patients (6.8%) with anti-HCV positivity before the therapy decreased to 16 patients (4.7%, p>0.05) with hydroxyurea therapy (Table 1). On the other hand, we detected autosplenectomy in 46.8%, avascular necrosis of bones in 18.9% (90.6% at the hip joints), leg ulcers in 12.7%, pulmonary hypertension in 11.5%, CRD in 8.3%, CHD in 7.7%, digital clubbing in 6.5%, stroke in 6.5%, exitus in 5.3%, COPD in 4.7%, and cirrhosis in 3.2% of the patients (Table 2). Although smoking was observed in 6.5% (22) of the patients, there was only one case (0.2%) of regular alcohol consumption, who was not cirrhotic at the moment. Although anti-HCV was positive in two of the cirrhotics, HCV RNA was detected as negative by polymerase chain reaction in both. Prevalences of mortality were similar in both genders (4.7% versus 5.9% in females and males, respectively, p>0.05), and mean ages of such cases were 32.1 versus 29.1 years in females and males, respectively (p>0.05).

Table 1: Characteristic features of sickle cell patients before and after hydroxyurea therapy

Variables	Before hydroxyurea therapy	*p*-value	After hydroxyurea therapy
Mean number of painful crises per year	10.3 ± 10.6 (0-48)	*<0.000*	1.7 ± 1.1 (0-6)
Mean severity of painful crises	7.8 ± 2.2 (0-10)	*<0.000*	2.2 ± 1.7 (0-10)
Weight (kg)	59.1 ± 11.4 (37-95)	*<0.000*	65.2 ± 13.0 (46-107)
WBC* (/µL)	15.050 ± 6.148 (4.890-38.800)	*<0.000*	11.349 ± 5.029 (5.010-31.850)
Hct† value (%)	23.2 ± 4.0 (16-35)	*<0.000*	27.8 ± 3.4 (20-36)
MCV‡ (fL)	88.7 ± 9.6 (57-112)	*<0.000*	105.2 ± 13.6 (66-129)
PLT§ (/µL)	449.840 ± 217.370 (169.000-1.561.000)	*<0.000*	430.840 ± 142.681 (219.000-936.000)
Total bilirubin value (mg/dL)	5.3 ± 5.6 (0.6-38.2)	*<0.000*	3.1 ± 2.2 (0.7-11.0)
Direct bilirubin value (mg/dL)	2.0 ± 3.4 (0.2-15.0)	*<0.000*	0.9 ± 0.9 (0.2-6.0)
LDH¶ value (IU/L)	647.5 ± 265.8 (196-1.552)	*<0.000*	509.9 ± 315.4 (235-2.218)
Patients with anti-HCV** positivity	6.8% (23)	Ns***	4.7% (16)

*White blood cells †Hematocrit ‡Mean corpuscular volume §Platelets ¶Lactate dehydrogenase **Hepatitis C virus antibodies ***Nonsignificant (p>0.05)

Table 2: Sickle cell patients with associated disorders

Variables	Prevalence
Autosplenectomy	46.8% (158)
Avascular necrosis of bones	18.9% (64)
Leg ulcers	12.7% (43)
Pulmonary hypertension	11.5% (39)
CRD*	8.3% (28)
CHD†	7.7% (26)
Digital clubbing	6.5% (22)
Stroke	6.5% (22)
Exitus	5.3% (18)
COPD‡	4.7% (16)
Cirrhosis	3.2% (11)

*Chronic renal disease †Coronary heart disease ‡Chronic obstructive pulmonary disease

Discussion

SCD particularly affect microvascular systems of the body (14, 15), since the capillary systems are the main distributors of the hard bodies to tissues, so they are destroyed much more than the larger vessels. Due to the prominent microvascular nature of the SCD, we can observe healing of leg ulcers with hydroxyurea therapy in early years of life, but later in life the healing process is difficult due to the excessive fibrosis around the capillaries. Eventually, the mean survival was 42 and 48 years for males and females in the literature, respectively (9), whereas it was 29.1 and 32.1 years, respectively, in the present study ($p>0.05$). The great differences between the survival should be searched with further studies, but it may be secondary to the delayed initiation of hydroxyurea therapy in Turkey. On the other hand, the prolonged survival of females with the SCD should also be searched, effectively. As a result of such a great variety of clinical presentation, it is not surprising to see that the mean body weight and body mass index (BMI) were significantly retarded in the SCD cases (16). Probably parallel to the significantly lower mean body weight and BMI, mean values of the low density lipoprotein cholesterol, alanine aminotransferase, and systolic BP and diastolic BP were also significantly lower in the SCD (16), which can be explained by definition of the metabolic syndrome (17, 18).

Painful crises are the most disabling symptoms of the SCD. Although some authors reported that painful crises themselves may not be life threatening directly (19), increased basal metabolic rate with any underlying cause including infections, tissue damage, operations, and depression usually terminate with painful crises and an increased risk of mortality. Probably pain is the result of a severe inflammatory process on the vascular endothelium all over the body, and the increased WBC and PLT counts and the decreased Hct values show presence of a chronic inflammatory process during whole their lives in such patients. For example, leukocytosis even in the absence of an infection was an independent predictor of the disease severity (20), and it was associated with an increased risk of stroke, probably by releasing cytotoxic enzymes and causing endothelial damage (21). Due to the severity of pain, narcotic analgesics are usually required to control them (22), but according to our practice, simple, rapid, and repeated RBC transfusions are highly effective during the severe crises both to relieve pain and to prevent sudden death that may develop secondary to the multiorgan failures on chronic inflammatory background of the SCD.

Hydroxyurea is an effective therapeutic option for the treatment of chronic myeloproliferative disorders and SCD. It interferes with cell division by blocking the formation of deoxyribonucleotides via inhibition of ribonucleotide reductase. The deoxyribonucleotides are the building blocks of DNA. Hydroxyurea mainly affects hyper-proliferating cells. Although the action way of hydroxyurea is thought to be the increase in gamma-globin synthesis for fetal hemoglobin (Hb F) (23, 24), we think that its main action way is the suppression of excessive leukocytosis and thrombocytosis via blocking the DNA synthesis in the SCD. By this way, the continuous inflammatory process of the SCD that initiated at birth on the vascular endothelium all over the body is suppressed with some extent. Due to the same action way, hydroxyurea is also used in moderate and severe psoriasis to suppress hyper-proliferating skin cells. As in viral hepatitis cases, although presence of a continuous damage of sickled cells on the capillary endothelium, the severity of destructive process is probably exaggerated by the patients' own immune system particularly by the actions of WBC and PLT. So suppression of excessive proliferation of WBC and PLT probably limits the endothelial damage-induced tissue ischemia and infarctions all over the body. Similarly, it was reported that lower neutrophil counts were associated with lower crises rates, and if a tissue infarction occurs, lower neutrophil counts may limit severity of pain and extent of tissue damage (25). On the other hand, final Hb F levels in hydroxyurea users did not differ from their pretreatment levels, significantly (25).

Physicians at the National Institutes of Health Consensus Conference agreed that hydroxyurea is underused both in children and adults due to some reasons. Hydroxyurea is a chemotherapeutic agent, therefore it is not taken by

women planning to become pregnant in the near future. Additionally, there is a fear of potentially increased risk of cancers in people (26). However, the cancer risk has not been substantiated by more than a decade of using hydroxyurea for adults (27). Although the investigational and post-marketing data show risk to fetus (28), potential benefits may outweigh potential risk in pregnancy. According to our experiences, there are several female patients with infertility, abortus, or stillbirth in the absence of hydroxyurea therapy in the SCD, and the decreased number and severity of painful crises, increased body weight, decreased WBC and PLT counts, and increased Hct value will probably result with resolution of the above problems with some extent in such patients. It is clear that there is a need for more effective treatment regimens in the SCD, but until they become available, hydroxyurea should be used in all cases, and its dose should be kept as higher in the moderate and severe patients.

Hydroxyurea probably has a life-saving role in the SCD. As a similar result to our study, the Multicenter Study of Hydroxyurea (MSH) studied 299 severely affected adults with sickle cell anemia (Hb SS), and compared the results of patients treated with hydroxyurea or placebo (29). The study particularly searched effect of hydroxyurea on painful crises, acute chest syndrome (ACS), and requirement of blood transfusion. The outcomes were so overwhelming in the favour of hydroxyurea that the study was terminated after 22 months, and hydroxyurea was initiated in all patients. The MSH also demonstrated that patients treated with hydroxyurea had a 44% decrease in hospitalizations (29). In multivariable analyses, there was a strong and independent association of lower neutrophil counts with the lower crisis rates (29). But this study was performed just in severe Hb SS cases alone, and the rate of painful crises was decreased from 4.5 to 2.5 per year (29). Whereas in our study, we used all subtypes of the SCD with all clinical severity, and the rate of painful crises was decreased from 10.3 to 1.7 per year ($p<0.000$) with an additional decreased severity of them (7.8 versus 2.2, $p<0.000$). Parallel to our results, adult patients using hydroxyurea for frequent painful crises appear to have reduced mortality rate after a 9-year follow-up period (30). The underlying disease severity remains critical to determine prognosis, but hydroxyurea may decrease severity of disease (30). Probably the chronic endothelial damage of the SCD is initiated at birth, and complications may start to be seen even in infancy. For example, infants with lower hemoglobin levels were more likely to have a higher incidence of clinical events such as ACS, painful crises, and lower neuropsychological scores, and hydroxyurea reduced the incidence of them (31). Hydroxyurea therapy in the early years of life may also protect splenic function, improve growth, and prevent multiorgan dysfunctions by reversing early capillary damage. Transfusion programmes also reduce all of the complications of the SCD, however transfusions carry many risks including potential infection transmission, development of allo-antibodies causing subsequent transfusions more difficult, and iron overload.

HCV infection is an under-diagnosed and prevalent bloodborne illness, resulting in cirrhosis in up to 20% of those infecteds (32). While the overall prevalence in the United States is 1.7%, high-risk populations may have up to a prevalence of 80% (32). About 170 million people are estimated to be chronically infected, worldwide (33). Additionally, it is the leading cause of hepatocellular carcinoma (HCC) and liver transplantation in developed countries (33). In addition to the hepatic involvement, it seems to be related with mixed cryoglobulinemia, Sjögren's syndrome (SS), rheumatoid arthritis (RA), B-cell non-Hodgkin's lymphoma (B-NHL), and membranoproliferative glomerulonephritis (MPGN) like many autoimmune disorders and malignancies (34). There are 36 reported extrahepatic, prominently autoimmune disorders which are thought to be related with HCV infection (35-40). For example, high prevalences of mixed cryoglobulinemia have been reported with chronic hepatitis C (41, 42). Its prevalence increases by the duration of infection, and the duration of infection is nearly two-fold longer in cases with mixed cryoglobulinemia (43). The prevalence of MPGN is approximately 30% in chronic hepatitis C plus type II cryoglobulinemia cases. In an autopsy study performed on 188 Japanese dominantly cirrhotic patients with chronic HCV infection, the prevalence of histological accumulation of immune complexes in glomeruli is importantly higher than the prevalence of symptomatic glomerulonephritis (GN) (39). The prevalence of histological GN was found as 54.8% ,and the prevalence of MPGN as the most frequently seen type as 11.2%. But only 12.2% of cases, especially the MPGN having ones, were symptomatic for GN during the year just before death. According to a widely discussed hypothesis, the cause of extrahepatic involvement of HCV is the extrahepatic tropism, especially the lymphotropism of the virus. The lymphotropism is thought to be the important factor for the development of B-NHL and the production of autoantibodies. In long term follow up studies, B cell malignancies have been detected in 4-6% of cases with chronic hepatitis C plus type II cryoglobulinemia (44, 45). The prevalence of chronic hepatitis C has been found as higher in B-NHL cases than the controls in six studies performed in Italy and Japan (46-51). Although HCV is not accepted as an oncogenic virus until now, core proteins of HCV may take role in the malign conversion of cells (52). Additionally, oncogenesis and hypermutation of immunoglobulins of infected cells with HCV were shown (53). In addition to above, splenic lymphoma associating with chronic hepatitis C regresses parallel to the regression of viremia achieved by antiviral therapy (54). Additionally, although the detection of HCV specific CD4+ and CD8+ lymphocytes in lesions of lichen planus, they couldn't be detected in blood (55). The prevalence of HCV has been found as higher in patients with porphyria cutanea tarda in South Europa, America, and Japan. This finding supports the idea that HCV is a precipitating factor for porphyria cutanea tarda (56), since infection does not decrease the activity of hepatic uroporphyrinogen decarboxylase which is actually decreased in cases with active porphyria cutanea tarda (57).

HCV is believed not to be directly cythopathic, and the host immune response may be mainly responsible for the viral clearance and cellular injury. HCV persists in patients without any apparent evidence of immune deficits

depending on virus or host-related factors. The recent studies have revealed that both cellular and humoral immunity appear to be active despite the progression of the disease (58). Probably the genetically determined factors are also critical in eliminating hepatitis virus infections, and differences in host susceptibility to infectious disease and eventually the disease severity can't be attributed solely to the virulence of microbial agents. Immunologic factors such as human leukocyte antigens (HLA) may take role in the susceptibility to HCV (59). Class I HLA, which present foreign antigens to cytotoxic T-lymphocytes, are integral components of the early host immune response. Various major histocompatibility complex alleles that are correlated with more favorable outcomes in cases of viral hepatitis have been identified in diverse populations (60, 61). According to our experiences, HCV infection seems to be more frequent in elderlies. The increasing prevalence of HCV RNA positivity by age may indicate that it may eventually terminate with chronic manifestations in every infected if the life span of the individual permits. The anti-HCV persists for years after HCV infection, even in those individuals who present with HCV RNA negativity. Viremia can be intermittent in the first year of infection, and the presence of HCV RNA should be considered when attempting to determine the outcome of an acute HCV infection (62). The degree of liver damage can be semi-quantitatively assessed by a system used to score liver biopsies (63).

As a conclusion, SCD are chronic inflammatory disorders with high morbidity and mortality rates, and hydroxyurea therapy is a well-tolerated and highly effective regimen for them. While hydroxyurea therapy decreases frequency and severity of painful crises, WBC and PLT counts, total and direct bilirubin, and LDH levels, it increases body weight, Hct value, and MCV. Although hydroxyurea therapy also decreased the anti-HCV positivity, the difference was nonsignificant probably due to the small sample size of the present study.

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School Teachers' Knowledge and Attitude toward School Students with Epilepsy

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Abstract

Background: Epilepsy is a chronic disorder of the central nervous system that affects people of all ages worldwide.

Objectives: to measure schoolteacher's perception of epilepsy in school children in Riyadh, Saudi Arabia in 2018.

Methods: an observational, descriptive, cross-sectional study was done and data was collected by online and manual survey from (476) teachers chosen by quota sampling technique. The data was analyzed by using SPSS. Scale of level of knowledge in Table 1.

Results: Most of the teachers had moderate and good knowledge (81%); females had better knowledge (85%); teachers with higher educational level had better knowledge (92%) and teachers with more years of experience had better knowledge (83%). Most of the teachers feel sympathy toward students with epilepsy (67%). Most of the teachers had moderate and good attitude (84%). Those who were 40 years or above had a better attitude (88%). About half the teachers knew about epilepsy from their friends (45%). Most of the teachers had poor practice (85%).

Conclusion: Our study revealed that the majority of the teachers had moderate and good knowledge and attitude while only a few teachers had moderate and good practice. Teachers' age and years of experience are shown to be factors in acquiring knowledge. It was found that teachers' age has a significant effect on their attitude and teachers with higher educational level had better attitude. Teachers' gender and educational level appeared to have a significant effect on their knowledge.

Key words: Teachers, Knowledge, Attitude, Students, Epilepsy, Saudi Arabia

Introduction

Epilepsy is a chronic disorder of the central nervous system that affects people of all ages worldwide (1). Epilepsy seizures are brief episodes of involuntary movement that may involve a part of the body (partial) or the entire body (generalized), and are sometimes accompanied by loss of consciousness and control of bowel or bladder sphincters (1). It is one of the world's oldest recognized conditions. Fear, misunderstanding, discrimination and social stigma have surrounded epilepsy for centuries. This stigma continues in many countries today and can impact on the quality of life for people with the disorder and their families. It is one of the most prevalent, frequent and non-infective neurologic disorders in Saudi Arabia (2). Epilepsy seizures are most likely to occur in schools, and teachers need to know the proper way in which they can deal with them (1,2). Teachers are considered as social leaders and role models thus influencing the child's critical period of social and psychological development (1,2).

The prevalence rate of epilepsy is about 6.54 per 1,000 of population and its psychosocial impact results in depression, huge stigma and cognitive impairment (3).

The school period from elementary to secondary has the greatest role in building up the personality of the students physically, psychologically and socially (4). The proper attitude and practice of teachers toward epileptic students have a significant impact on their academic performance. The findings of this study will help in strengthening the role of the teachers. Very few studies have been done in different cities in Saudi Arabia, and they have reported the need to improve teacher's knowledge and attitude toward students with epilepsy (4).

A study conducted in Ethiopia in 2017 found that 41% of teachers had good awareness about epilepsy, about 74% had a positive attitude and only 60.3% of the respondents had proper first aid training (5).

Another study done in Greece found that 37.75% of the teachers obtained information about epilepsy from personal experience and (34.93%) from the internet. 6.2% referred to courses and 88.1% had the right view about the nature of the illness (6).

A study conducted in Kuwait in 2016 concluded that school teachers have relatively very poor knowledge about epilepsy but have positive attitudes toward students with epilepsy (7).

In the Kingdom of Saudi Arabia (KSA) a study was done in 2014 and found that only 17% of the teachers felt very well informed about epilepsy and teachers with higher education were more likely to have good knowledge. Teacher's attitudes correlated highly with their knowledge (8). Another study done in 2015 concluded that schoolteachers were generally knowledgeable about epilepsy but there is a lack of proper plan of action to deal with epileptic students (9).

It is expected that teachers with high level of education have a better attitude toward the students with epilepsy compared to those with low level of education. This study aimed to measure school teachers' awareness, attitude and practice with epilepsy in school students in Riyadh, Saudi Arabia in 2018 and to evaluate the variation between teachers' characteristics regarding their knowledge, attitude, and practice.

Subjects and Methods

Study design: An observational, descriptive, cross-sectional study was done in 2018.

Study area/population: The study was carried out in Riyadh, Saudi Arabia. According to the last statistics published in 2015, the number of elementary schools in Riyadh region are 7,875; while the number of intermediate schools are 4,844 and secondary schools are 3,939 for both genders. The study population was in elementary, intermediate and secondary school teachers (male and female).

Sample size and techniques: Data was collected online and distributed to teachers in schools with up to (476) teachers. Participants were chosen by quota sampling technique.

Data collection: An online questionnaire was used and included 4 sections. The first was for basic information, the second was for general knowledge, the third was for attitude towards epilepsy and the last was for investigation of major related factors. The questionnaire was initially drafted in English, and subsequently translated into Arabic. Confidentiality was maintained.

The data was collected by two methods: first by creating a web link; the link of the questionnaire was sent to participants through social media for filling in online till they reached a suitable response rate. Second, a hard copy was distributed to teachers in schools and it was retrieved after one week of distribution for analysis.

Data analysis: All the data was cleaned, coded and entered using SPSS. The result was represented in table and graphs as frequencies and percentages. A suitable statistical test was used.

Ethical consideration: Permission was taken from the participant teachers by asking them to participate by clicking on the link. The data was used only for the purpose of the study and confidentiality and privacy was maintained.

Results

Table 2 shows that out of 476 teachers in Riyadh, the survey results revealed that 45% of teachers from different educational levels knew about epilepsy from their friends, and 37% knew about epilepsy from the media, and some of the teachers knew about epilepsy from seminars.

Table 3 shows that more than half of the teachers thought the causes were unknown, and 34% believed that it was genetic, 20% supposed that it was from trauma, the rest of them assumed that it was caused either by spirit possession, evil eye, tumor and infection.

Teachers generally have good knowledge about symptoms of epilepsy. They believe that loss of consciousness (62%), biting of tongue (53%) and foaming of mouth (48%) are the most common symptoms of it. This is shown in Table 4.

Most teachers (67%) feel sympathy and (30%) tolerance toward students with epilepsy, while only 11% of teachers feel hostility toward them. This is shown in Table 5.

In regard to Table 6, practices of teachers during epileptic seizures were poor. Out of 476 participants, only 19% supported the student's head and neck, and 15% called the ambulance. The other 42% of participants did inappropriate practices.

Table 7 shows that teacher's knowledge about managing an epileptic student during the attack was moderate. 53% asked for help and 37% of the participants called the students' parents. The rest of the responses revealed that 54% put something in the student's mouth, 18% restrained the student, and 15% held the student upright.

Knowledge about epilepsy among teachers was investigated across the age groups. Thirteen percent of them were less than thirty years of age. Those forty or above were 54%. The proportion of moderate and good knowledge among teachers amounted to 81%. Of those who were 40 years or more the level of moderate and good knowledge amounted to 85% compared to 77% of those who were less than 40 years of age. \This difference in the proportion of moderate and good knowledge was statistically significant (p=0.0216). This is shown in Table 8.

Knowledge about epilepsy among teachers was investigated across the genders. Forty percent of them were males, and sixty percent of them were females. The ratio of moderate and good knowledge between teachers was 81%. The level of moderate and good knowledge across males was 77%. In contrast, it was 85% percent in females who have good and moderate knowledge. These differences in the proportion of good and moderate knowledge was statistically significant (p=0.0182). This is demonstrated in Table 9.

Knowledge about epilepsy between teachers was investigated in proportion to their nationality, either Saudi or non-Saudi. Eighty percent of them were Saudi while twenty percent of them were non-Saudi. Among those who were Saudi, the level of moderate and good knowledge was 84%. Whilst it was 75% among non-Saudi. These differences in the proportion of good and moderate knowledge were not statistically significant (p=0.084). This is demonstrated in Table 10.

Knowledge about epilepsy between school teachers was measured according to their educational level. Seventy-five percent have Bachelor's degree, the educational level of 6% of them was high school, 2% of those who have a Doctorate degree. Eighty-one percent of those teachers with Doctorate degree have good and moderate knowledge. Of those whose level was high school, teacher institute and Bachelor's degree 80% have good and moderate knowledge in comparison with 92% who have Master's degree and Doctorate degree. This difference was statistically significant (p=0.008), and is shown in Table 11.

Knowledge about epilepsy between school teachers was studied according to their years of experience. The knowledge among those who have less than five years of experience was fourteen percent and 68% in teachers who have more than 9 years of experience. Eighty-one percent of those teachers have good and moderate knowledge. Of those who have less than 5 years of experience about 71% have good and moderate knowledge whereas the percentage of teachers who have more than 5 years of experience and have good and moderate knowledge was 83%. This difference was statistically significant (p=0.0222). This is shown in Table 12.

Regarding teacher's age, teachers who are below 40 years old accounted for 46% of the whole sample, and those who were 40 years or above accounted for 54%. The proportion of moderate and good attitude among those teachers accounted for 84%. The level of good and moderate attitude in those who were below 40 years was 80% compared to 88% of those who were 40 or above years. This difference between teachers' age and attitude was statistically significant (p=0.0198). This is shown in Table 13.

Regarding teacher's gender and their attitude toward epileptic students, about 60% were female teachers and 40% were male teachers. The proportion of moderate and good attitude towards epilepsy was 84% among males and 85% among females, with no statistical significance (P-value = 0.996). This is shown in Table 14.

Attitude towards epilepsy between school teachers was studied according to their nationalities. 80% of those teachers were Saudi, while non-Saudi were 20%. The level of moderate and good attitude amounted to 84%, same proportion for non- Saudi was found. The relation between attitude and nationalities was statistically non-significant. That was shown in Table 15.

Attitude towards students with epilepsy between school teachers was studied according to their educational level. Seventy-five percent have Bachelor's degree, the educational level of 6% of them was high school, 2% of them have Doctorate degree. Of those whose level was high school, teacher institute and Bachelor's degree 84% have good and moderate knowledge in comparison with 89% who have Master's degree and Doctorate degree.

This difference was statistically significant (p=0.006) and is shown in Table 16.

Attitude toward epilepsy and teacher's years of experience was investigated across the age groups. Those who have more than nine years of experience exhibited moderate and good attitude (68%). Those who have experience from five to nine years showed moderate and good attitude (19%) more than those who have less than five years of experience (14%). This difference in proportion of moderate and good attitude was statistically significant (p= 0.019). Seventy four percent of them had less than five years of experience. Those from five to nine were eighty two percent. Eighty seven percent had more than nine years of experience. The proportion of moderate and good attitude from teachers was 85%. This is shown in Table 17.

Regarding the age of teachers and their practices toward epilepsy, those who were 40 years or more showed moderate and good practice (54%). Those who were less than 30 years have a lower proportion of moderate and good practice (13%). This difference in proportion of moderate and good practice was statistically non significant (p= 0.960). Sixteen percent of them were less than thirty years of age. Those forty or above were fifteen percent. The proportion of moderate and good practice among these teachers was 15%. This is shown in Table 18.

Practice toward epilepsy among teachers in Saudi Arabia was investigated. Forty percent of those teachers were males and females were 60%.The proportion of moderate and good practice among those teachers amounted to 15 %. The level of moderate and good practice of those who were females amounted to 13 % compared to 18 % of those who were males. This difference in the level of practice between males and females was statistically not significant. This is shown in Table 19.

Practice toward epilepsy among Saudi and non-Saudi teachers in Saudi Arabia was investigated. Eighty percent of them were Saudi while non-Saudi were 20%. It was found that 15% of those teachers have moderate and good practice. The level of moderate and good practice in Saudi teachers amounted to 15% which is the same for non-Saudi teachers. This association between teachers' nationalities and their level of practice was statistically not significant. This is shown in Table 20.

Practice toward epilepsy among teachers was investigated across the educational level. Fifteen percent of them were high school, teacher institute and bachelor's degree. Those who had master's and doctorate degree had a higher level of practice which amounted to 16% compared to 15% of those who had less educational level. This difference in proportion of moderate and good practice was not significant. The proportion of moderate and good practice among teachers based on educational level amounted to 15 %. This is shown in Table 21.

Practice toward epilepsy among teachers was investigated across the years of experience. Eight percent of them had less than five years of experience, those who had 5 to 9 years of experience amounted to 16 % compared to the same value of those with more than 9 years of experience which was not significant. Nine years and above were 16 %; the proportion of moderate and good practice based on experience among teachers amounted to 15%. This is shown in Table 22.

Table 1: Scale of level of knowledge.

Scale of level of knowledge:	
Good knowledge	By answering >14 questions correctly
Moderate knowledge	By answering 8-14 questions correctly
Poor knowledge	By answering <8 questions correctly
Scale for teacher response:	
Positive response	By answering ≥4 questions correctly
Negative response	By answering <3 questions correctly

Table 2: Teacher's source of knowledge

	Number out of "476"	Percentage.
Media	176	37%
Friends	214	45%
Seminars	86	18%

Table 3: Teacher's knowledge about the cause of epilepsy

	Number out of "476"	Percentage.
Genetic	160	34%
Tumor	42	9%
Infection	8	2%
Trauma	96	20%
Spirit possession	49	10%
Evil eye	44	9%
Unknown	248	52%

Table 4: Teacher's knowledge about epilepsy symptoms

	Number out of "476"	Percentage
Loss of consciousness	297	62%
Falling down	291	61%
Rolling of eyes	147	30%
Foaming of mouth	230	48%
Uncontrolled urination	62	13%
Biting of tongue	254	53%
Far gaze	103	22%

Table 5: Teachers attitude toward students with epilepsy

	Number out of "476"	Percentage
Indifference	70	15%
Tolerance	142	30%
Sympathy	318	67%
Intimidation	33	7%
Confusion	51	11%
Hostility	53	11%

Table 6: Practices of teachers during epileptic seizures

	Number out of "476"	Percentage
Nothing	35	7%
Called ambulance	73	15%
Spilled water on his/her face	28	6%
Sprayed him/her with perfume	6	1%
Open his/her mouth and put something in it	77	16%
Prevented his/her involuntary movement	58	12%
Supported his/her head and neck	89	19%

Table 7: Teacher's knowledge about managing an epileptic student during the attack

	Number out of "476"	Percentage
Do nothing and call his parents.	176	37%
Restrain the student.	87	18%
Put something in his mouth to prevent tongue swallowing.	255	54%
Hold him upright.	73	15%
Ask for help.	252	53%

Table 8: Knowledge among teachers according to their age groups (School Teachers' Knowledge and Attitude toward School Students with Epilepsy 2018-2019).

		Poor	Moderate	Good	Total
	<30	15	28	18	61
	30-39	36	63	58	157
	40 - >40	39	137	82	258
Total		90	228	158	476

Table 9: Knowledge toward epilepsy and teacher's Gender in Saudi Arabia according to their gender (School Teacher's Knowledge and Attitude toward School Students with Epilepsy 2018-2019).

		Poor	Moderate	Good	Total
	male	46	84	61	191
	female	44	144	97	285
Total		90	228	158	476

Table 10: Knowledge about epilepsy and teacher's nationality in Saudi Arabia according to their gender (School Teacher's Knowledge and Attitude toward School Students with Epilepsy 2018-2019)

		Poor	Moderate	Good	Total
	Saudi	66	191	123	380
	non Saudi	24	37	35	96
Total		90	228	158	476

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Table 11: Knowledge about epilepsy among teachers according to their educational level (School Teachers' Knowledge and Attitude toward School Students with Epilepsy 2018-2019).

		Poor	Moderate	Good	Total
	High secondary	14	10	4	28
	Teacher Institute	4	32	18	54
	Bachelor's degree	69	168	119	356
	Master's degree	3	15	12	30
	Doctorate degree	0	3	5	8
Total		90	228	158	476

Table 12: Knowledge about epilepsy among teachers according to their years of experience (School Teachers' Knowledge and Attitude toward School Students with Epilepsy 2018-2019).

		Poor	Moderate	Good	Total
	<5	19	26	20	65
	5-9	15	43	31	89
	>9	56	159	107	322
Total		90	228	158	476

Table 13: Attitude towards epilepsy and teacher's age (School Teacher's Knowledge and Attitude toward School Students with Epilepsy 2018-2019)

	Poor	Moderate	Good	Total
<30	15	21	25	61
30-39	29	50	78	157
40->40	30	61	167	258
Total	74	132	270	476

Table 14: Attitude toward epilepsy and teacher's gender (School Teacher's Knowledge and Attitude toward School Students with Epilepsy 2018-2019)

	Poor	Moderate	Good	Total
Male	30	53	108	191
Female	44	79	162	285
Total	74	132	270	476

Table 15: Attitude toward epilepsy and teacher's nationality (School Teacher's Knowledge and Attitude toward School Students with Epilepsy 2018-2019).

		Poor	Moderate	Good	Total
	Saudi	59	108	213	380
	non Saudi	15	24	57	96
Total		74	132	270	476

Table 16: Attitude toward epilepsy and teacher's educational level (School Teacher's Knowledge and Attitude toward School Students with Epilepsy 2018-2019)

		Poor	Moderate	Good	Total
	High secondary	10	5	13	28
	Teacher Institute	4	12	38	54
	Bachelor's degree	56	107	193	356
	Master's degree	3	4	23	30
	Doctorate degree	1	4	3	8
Total		74	132	270	476

Table 17: Practice by teachers according to their age groups (School teacher's knowledge and attitude toward school student with epilepsy (2018-2019)

		Poor	Moderate	Good	Total
	<30	53	5	3	61
	30-39	131	18	8	157
	>40	220	25	13	258
Total		404	48	24	476

Table 18: Attitude of teachers according to their experience (School teacher's knowledge and attitude toward school student with epilepsy) (2018-2019).

		Poor	Moderate	Good	Total
	<5	17	22	26	65
	5-9	16	24	49	89
	>9	41	86	195	322
Total		74	132	270	476

Table 19: Practice toward epilepsy among teachers in Saudi Arabia according to their gender (School Teachers' Knowledge and Attitude toward School Students with Epilepsy 2018-2019).

		Poor	Moderate	Good	Total
	Male	156	25	10	191
	Female	248	23	14	285
Total		404	48	24	476

Table 20: Practice toward epilepsy among teachers in Saudi Arabia according to their nationality (School Teachers' Knowledge and Attitude toward School Students with Epilepsy2018-2019).

		Poor	Moderate	Good	Total
	Saudi	322	38	20	380
	non Saudi	82	10	4	96
Total		404	48	24	476

Table 21: Practice toward epilepsy and teacher's educational level in Saudi Arabia according to their gender (school teachers' knowledge and attitude toward school students with epilepsy 2018-2019).

	Poor	Moderate	Good	Total
High secondary.	25	2	1	28
Teacher institute.	46	6	2	54
Bachelor's degree.	301	35	20	356
Master's degree.	26	3	1	30
Doctorate degree.	6	2	0	8
Total.	404	48	24	476

Table 22: Practice toward epilepsy and teacher's years of experience in Saudi Arabia according to their gender (school teachers' knowledge and attitude toward school students with epilepsy (2018- 2019

		Poor	Moderate	Good	Total
	<5	60	2	3	65
	5 - 9	75	8	6	89
	>9	269	38	15	322
Total		404	48	24	476

Discussion

The finding that the teachers 40 years old and above had better knowledge about epilepsy than the younger ones was expected. According to this study, age proved to be a factor in acquiring knowledge. This finding is different from a study conducted in Nepal in 2015 which found that teacher's age did not correlate significantly with their knowledge about epilepsy (10). This can be verified by further studies.

The result that the male teachers had less knowledge about epilepsy than females was expected. This might be because females have more free time, which in turn, reflected their ability to search, and read more about everything. In addition, females tend to show more empathy in dealing with students. However, in a study conducted in Saudi Arabia in 2014 found that gender had no significant difference as reported in this study. Gender was shown to be a factor in acquiring knowledge (8). This could be proved by upcoming studies.

Regarding the nationality of teachers, there is no significant relation between the knowledge of Saudi teachers and non-Saudi teachers. This finding might be because improving knowledge depends on the person's personality and efforts. This finding is different from a study conducted in Jeddah in 2014 which found that Saudi teachers are more likely to report good knowledge when compared to those of other nationalities (8). We hope that this will be verified in the upcoming studies.

The results that showed higher level of knowledge about epilepsy with teachers who have higher educational level was expected. This can be explained by expanded education and interaction with people who have more knowledge and longer years of experience. In a study conducted in Saudi Arabia in 2014 the same finding was reported (8). Regarding the results, educational level contributes to teachers' level of knowledge. This can be confirmed in coming studies.

The finding which reported higher level of knowledge about epilepsy with teachers who have more years of experience than those who have less years of experience was expected. This could be due to encountering more cases which make them more aware about the seriousness of the condition. A study conducted in Saudi Arabia in 2014 reported no relation between knowledge and years of experience (8). According to the results, years of experience affect teacher's knowledge. This can be proven by further studies.

Good and moderate attitude toward epileptic students was higher among teachers who are 40 years and above. This was expected. It can be explained by their increased experience and knowledge about epilepsy. A previous study in Turkey found that young teacher's age was predictive of good attitudes. This difference between these studies results might be due to the difference of study population (11).

The results that showed that teachers in both genders have good attitude was expected. This might be due to influence of good morals and character. A previous study in Turkey found that male teachers have more positive attitude. This difference between these studies results might be due to the difference of the study population (11).

The results which reported that teachers with different nationalities have the same attitude was expected. This may be the effect of good attitude that is mainly influenced by morals and character. As a result, there is no effect of nationality on the attitude of teachers. However, there was no specific study that focuses on the relation between nationality and level of attitude and we hope to see that in future studies. In conclusion, nationality has no effect on the attitude of teachers towards epilepsy.

The results which reported people with high educational level have good attitude toward students with epilepsy, were expected. In addition, we can infer that teachers with high educational level have a better perception of life, and can deal better with different manners of students which in turn reflected on their good attitude. According to a study conducted by Abulhamail in Saudi Arabia in 2014 teachers with higher education were more likely to have good knowledge when compared to those with less education. Overall, teacher's attitudes correlated highly with their knowledge. Those with good knowledge were less likely to mind having a child with epilepsy in their class. To sum up, teachers with high educational level have a better attitude (8).

The correlation between the level of practice and age groups was not significant. It may be because teachers who were less than thirty tried to practice hard. The opposite finding was in a study conducted in Saudi Arabia (9).The results showed that practice toward epilepsy had no significant effect comparing the age groups. The teachers should practice more to improve how to deal with epilepsy.

The findings are that teachers who had more than nine years of experience had better attitude toward epilepsy than the ones who had less years. It may be due to longer years of experience. This finding in this regard is different from a study done in Sudan (4). Years of experience have a significant effect on the attitude of teachers. This can be verified by further studies.

The findings of this study showed that most of the teachers, whether they are males or females had poor practice level, which was expected. The reason for this finding could be that there are not enough educational courses given to teachers in schools. This finding is different from a study conducted in Sudan in 2017 by Elhassan which showed that females have a better practice level than males (4).
The majority of both Saudi and non-Saudi teachers had poor practice level which was expected. This finding could be due to the lack of adequate instructions given to teachers about epilepsy. This finding is similar to a study conducted in Saudi Arabia in 2015 by Alqahtani which illustrated that there's a lack of proper plan of action to deal with epileptic students (9).

The finding that the teachers had master and doctorate had better practice toward epilepsy than the lesser educational levels like high school and Bachelor's degree could be due to more information and knowledge. A study in Saudi Arabia shows 66% have a college or university degree. Only 17% of the teachers felt very well informed about epilepsy on the Likert scale, with information mostly from the media, relatives, and personal experience. However, teachers with higher education (college or university degrees) were more likely to have good knowledge (moderate or very well on the Likert scale) when compared to those with less education (57% vs. 21%). Overall, teacher's attitudes correlated highly with their knowledge (8). According to this study educational level proved to be a factor in acquiring knowledge. This can be verified by future studies.

Another finding was that the teachers who had more years of experience had better practice toward epilepsy than those who had less years of experience. This could be due to more knowledge and practice toward epileptic students and more cases that they may face. In a study in South Korea the knowledge scores accounted for 50.1% of the variance in the attitude scores, and experience teaching a student with epilepsy accounted only for 1.0%. In contrast, teachers' knowledge was the most important factor influencing teacher's attitudes toward epilepsy (12).

According to this study teacher's practice proved to be a factor in acquiring knowledge, not the years of experience. Further study should be conducted.

Limitations

A major limitation of this study was the difficulty in taking permission from some schools to distribute our questionnaire to their teachers.

Conclusion

This study revealed that there is a relatively high level of knowledge, especially regarding the age and years of experience of the teachers, which result in a better attitude toward epileptic students. Female teachers had better knowledge and attitude than the male teachers. There was significant poor practice among teachers toward epilepsy. Based on the results of this study, health education programs about epilepsy should be directed to all teachers. Future research on larger samples, and older age groups should be done and cover other aspects of epilepsy such as psychological aspects.

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Increased Psychological Disorders among Pediatric Population during Covid

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Abstract

A review of the literature on psychological disorders aming the pediatric population during the Covid 19 pandemic.

Key words: Covid 19, psychological disorders, paediatric population

Literature Review

Generally, the pediatric population is at a higher risk of developing psychological disorders during COVID-19 than other age groups. Educational status, developmental age, poor economic background, and existing mental health issues are among the vulnerability factors that cause the difference in psychological disorders prevalence between age groups (Singh et al., 2020). According to the authors, social distancing and lockdown practices have resulted in anxiety and fear, leading to long and short-term mental health and psychosocial impacts on school-age children. This literature review will focus on examining increased psychological disorders among adolescents and children during COVID-19 and the most effective practices to implement to promote early detection.

While most people often associate psychological disorders among the pediatric population with socioeconomic challenges and media influence, COVID-19 has resulted in different stressors in children's lives. For instance, different governments' orders to reduce the virus spread, such as quarantine have led to isolation and loneliness among adolescents, which are among the common risk factors that cause mental health problems (Rosen et al., 2021). Rosen et al. (2021) discuss how the pandemic affects children's wellbeing by examining how it disrupts their structure and routine. Lack of a structured setting limits innovation and increases boredom. Interaction levels have reduced because of limited outdoor activities and inadequate socialization. Empirical evidence shows a positive relationship between loneliness and depression and anxiety among the pediatric population (Loades et al., 2020). The findings align with research by Sprang & Silman (2013) that focused on post-traumatic stress among youth following health-related disasters. However, the studies were cross-sectional, making it difficult to infer the association direction. Similarly, social loneliness or isolation and mental health dependent measures increased the risk of bias. Nonetheless, the literature review indicates that isolation and loneliness caused by COVID-19 mitigation measures are likely to result in psychological disorders among children and adolescents.

Most parents and caregivers experience mental health-related challenges during the COVID-19 pandemic period because of various factors. For example, there have been increased cases of job loss and increased expenses, reducing most households' income levels. Parents' poor mental health status can have an adverse impact on children's distress and long-term psychological disorders. Children experiencing poor parental mental health are at higher risk of becoming distressed in adulthood (Kamis, 2021). It implies that negative experiences during childhood lead to poor health in the child's life course. The outcome aligns with stress process literature that indicates a positive association between past stressors and current stress levels. However, research has shown that the association between stress during childhood and the development of psychological disorders in the future is not deterministic. Such stressors' effect is likely to wane throughout the life course (Kamis, 2021). Regardless of the availability of adequate information on parental mental health issues' influence on youth during their adolescence

and childhood stages, the primary concentration should be on how the stressors continue to affect their mental health in adulthood.

Poverty can cause an adverse impact on the pediatric population's psychological wellbeing through community and family-level factors. Children from poor backgrounds experience different stressors like poor housing and food insecurity (Hodgkinson et al., 2017). Such challenges can exacerbate the risk of parents to substance abuse and mental health issues, reducing their ability to adopt positive parenting practices. It increases the probability of neglect and child abuse. Some of the characteristics of parents and children from low-income communities include child abuse, increased violence, and inadequate resources. These factors have a positive relationship with adverse mental health outcomes. Thus, available evidence proves that low-income households are at a higher risk of developing psychological disorders and are unlikely to access the necessary mental health care than their counterparts from high-income families.

There are different evidence-based strategies to ensure the early detection of psychological disorders among the pediatric population in the primary care setting. Continuous mental health screening is one of the most effective ways of determining likely concerns in the initial development stages of a child (Hodgkinson et al., 2017). It will play a crucial role in addressing low sensitivity rates among pediatricians in detecting psychological disorders. Furthermore, screening is vital in reducing healthcare disparities since all children and adolescents will access the same assessment despite social or economic status. Hence, universal screening expansion to assess the adverse experiences during the pandemic and parents' mental health can help determine families that require additional support in dealing with psychological disorders. Weitzman & Wegner (2015) noted that despite the benefits of continuous mental health screening, a significant percentage of pediatricians are yet to implement it in their primary care setting fully. Some of the reasons the authors attribute to this slow adoption of routine screening include insufficient mental health resources, limited reimbursement, and insufficient time.

Moreover, integrating behavioral health care in various facilities can foster access to mental health care among the pediatric population. Such models of care are critical in decreasing stigma, promoting collaboration between behavioral health and medical providers, and eliminating the barriers that hinder children from low-income backgrounds from accessing care (Hodgkinson et al., 2017). Thus, the available evidence supports the effectiveness of continuous mental health screening and integrating behavioral health care in institutions in detecting psychological disorders.

Various researchers have focused on psychological disorders among the pediatric population during the pandemic. Available literature indicates that orders and practices implemented by governments to reduce COVID-19 spread are among the novel stressors that negatively impact the pediatric population's lives. Similarly, the literature review shows increased mental health-related challenges among parents, causing children's distress. Thus, pediatric healthcare providers must conduct continuous mental health screening to detect psychological disorders. Additionally, it is vital to integrate behavioral health care in mental health facilities.

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Patterns and determinants of Z score of Height for Age, Weight for Age and Weight for Height among Preschool children in Jeddah city, Saudi Arabia

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Abstract

Background: Stunted growth could lead to increased morbidity and mortality during childhood.

Objectives: To identify the major socio-demographic, and health risk factors of stunting in 2–6 years old Saudi children.

Design: Cross sectional study. Sampling and setting: It was a convenient sampling method, and was conducted at the outpatient clinics of two general hospitals in Jeddah city. Patients and methods: Total sample size was 748 preschool children. Data was collected on the children via personal questionnaire, ISAAC questionnaire on asthma and allergy in children, and anthropometric measurements. Indices for stunting (Height for age), underweight (weight for age), and wasting (weight for height) were compared to WHO reference values for normal children and Z scores for the indices were calculated. Multi-nominal Logistic regression and linear multiple regression were used. Odds ratio (OR) and 95% confidence intervals (95% CI) were calculated. The level of significance for this study was 0.05.

Results: Wasting was encountered among 3.11% of the children, while stunting was found among 22.91%, and underweight among 20.32% of the children. On the other hand overweight/obesity was found among 19.7% of the children. An obese child is 8 times more likely to be stunted (OR: 7.845; 95%CI: 4.103, 15.001), and child with under-weight was 17 times more likely to be stunted (OR: 16.782; 95%CI: 7.517, 37.470). Female child was less likely to be stunted compared to male (OR: 0.607; 95% CI: 0.374; 0.985, P < .043). Stunting was more common in early years of life (b=0.015). Short stature of the mother (b = 0.021), and decreased her BMI (b= 0.043) were significantly associated with stunting in their children (P < .05).

Conclusions: Male gender and very young age are significant risk factors of stunting. Double malnutrition was common among children with stunting. Hereditary may be an important determinant factor of stunting in children.

Key words: Malnutrition, Stunting, Children, Saudi Arabia.

Introduction

During early years of life proper nutrition is a major factor for sound growth, an efficient immune system, perfect function of organs, and nervous system development (1).

Survival of children is dependent to a great extent on nutritional condition, as poor nutrition increases likelihood of acquiring infections and other diseases (2 – 6).

In Saudi Arabia, the prevalence of stunting and other malnutrition disorders in children lies between the figures for developing and developed countries (7). Impairment of growth in early childhood has bad consequences in adulthood, namely impaired fertility, decreased body size, impaired work productivity, and liability for getting chronic disorders (8). About fifty percent of deaths among children worldwide are related to malnutrition (9). One of the indicators of community health and development is the nutritional status of under-five children (10). Growth of the child can be used to evaluate their nutritional status. Under weight, wasting and stunting are different forms of under-nutrition, and can be assessed by anthropometric indicators. Current nutritional status and chronic malnutrition are measured by wasting and stunting. Underweight is a sign of both chronic and acute malnutrition (11). Worldwide the prevalence of stunting (26%), wasting (8%) and underweight (16%) among children are common. Irreversible stunting is associated with poor nutrition in children less than 3 years of age (12). Stunting is significantly associated with increased death of under-five children (13, 14). This study focused on exploring the occurrence of under-nutrition, and investigating the association between its parameter and possible determinants, among preschool children in Jeddah City.

Methods

This cross sectional study was undertaken at the outpatient clinics of two general hospitals; one in a relatively high socioeconomic standard region (North of Jeddah city), and the other in a relatively lower Socio-economic standard region (South of Jeddah city). The total number of children enrolled in this study (748 children) was greater than the necessary minimum number needed for such a study (220 children, as assessed by G*power software, 15 for $\alpha = 0.05$, Power = 0.95, effect size is 0.3, and degree of freedom = 5).

Data were collected from the child's mother after taking informed written consent. The following tools were used to collect data:

1- Interviewing questionnaire which provided information on personal and socio-demographic characteristics of the parents; and feeding pattern, vaccination coverage, and clinical history of the child.

2- Anthropometric measurements: Weight and height of the child and the mother were measured. Anthropometric analysis: the variables age, sex, weight and height were used. These measurements were used to provide the following indices: weigh-for-age (WA), height-for-age (HA), and weight-for-height (WH), and body mass index for age (BMI /A). The indices generated were compared with standard reference values of WHO to obtain the Z-scores (16). From the z-scores, the nutritional status of the child was determined.

3- Operation definitions:

4- Stunting: A child whose height-for-age Z-score is below - 2 standard deviation (SD) from the median value of the reference population.

-Wasting: A child whose weight-for-height Z-score is below - 2 SD from the median value of the reference population.

-Underweight: A child whose weight-for-age Z-score is below - 2 SD from the median value of the reference population.

-Overweight/obese: A child whose BMI for age Z-score is more than 2 SD from the median value of the reference population is classified as overweight; and if it is more than 3 SD is considered obese.

4- ISAAC core questionnaire on asthma and allergy: was used to diagnose bronchial asthma, allergic rhinitis and atopic eczema (17-20).

Data analysis and statistical tests: Statistical Package for Social Sciences (IBM SPSS, version 22, Armonk, NY: IBM Corp.) was used. Linear Multiple Regression, and Multi-nominal Logistic regression method were used. Odds ratios (OR), 95% confidence interval (95% CI), and p values were calculated. The level of significance was 0.05.

Ethical considerations

Ethical clearance was obtained from the Institutional Review Board (IRB). Permission was obtained from the directors of the outpatient clinics for collecting data on preschool children. Informed consent was obtained from the mother of each child after providing information about the purpose of the study. In order to keep confidentiality of any information provided by study participants, the data collection procedure was anonymous.

Results

Characteristics of the studied children are shown in Table 1. The cases with stunting were 34 mild stunting (41.2 %), and 48 severe stunting (58.5% %). Both conditions were considered as one group: children with stunting (response variable). Males were more encountered among children with stunting (57.3%) compared to females (42.7%); this difference was statistically significant where Fisher's Exact Test was 4.56, and $P < .039$. Table 1 revealed that male children had 1.65 times the odds of suffering from stunting than females (OR: 0.607; 95% CI: 0.374, 0.985, and $P < .04$), when adjusting for other factors. Table 2 revealed that mean height of the mothers of children with stunting was significantly lower than mean height of mothers of the control children ($P < .007$). It revealed also that mean BMI of mothers of children with stunting was significantly lower than that of the mothers of children without stunting

(P < .001). Table 3 showed that decreased HAZ score was significantly associated with decreased age of the child (b = 0.015), decreased height of the mother (b= 0.021) and decreased BMI of the mother (b= 0.043). Table 4 depicted that smoking habit of the parents, environmental factors, gestational period and type of feeding in infancy and childhood were irrelevant to stunting of the children (P >.05). Table 5 revealed that children with excess weight had 7.8 times fold risk of stunting than those with normal BMI Z score (OR: 7.845; 95%CI: 4.103, 15.001). It shows, also, that children with under-weight had 16.78 times fold risk of stunting than those with normal weight (OR: 16.782; 95%CI: 7.517, 37.470).

Table 1: Multi-nominal logistic regression for socio-demographic independent factors on the dependent Stunting variable

Independent variables	B	Sig.	Exp (B)	95% Confidence Interval for Exp (B)	
				Lower Bound	Upper Bound
Intercept	1.96	<.000			
Place of study	0.195	<.480	1.215	0.708	2.086
Gender	-.499-	<.043	0.607	0.374	0.985
Nationality	-.241-	<.338	0.786	0.48	1.287
Educational level of the father	0.035	<.899	1.036	0.605	1.774
Educational level of the mother	-.391-	<.16	0.677	0.392	1.167
Occupation of the father	0.005	<.986	1.005	0.568	1.779
Occupation of the mother	0.371	<.23	1.449	0.791	2.656
Family history of allergy	0.205	<.409	1.228	0.754	1.999
Monthly income of the family	0.15	<.598	1.161	0.666	2.024

Table 2: Mean values of personal characteristics of the children and the mothers

Variables	Stunting	Mean	SD	t-test	*P*-value
Age (Months)	No	45.64	15.48	1.408	<.160
	Yes	43.07	12.96		
Number of children in the family	No	2.78	1.35	1.178	<.240
	Yes	2.59	1.23		
Rank of the child among his siblings	No	2.42	2.33	0.806	<.420
	Yes	2.20	1.17		
Duration of main feeding in infancy	No	17.63	8.62	0.571	<.568
	Yes	16.94	9.34		
BMI of the mother	No	28.25	6.68	3.314	<.001
	Yes	25.69	4.50		
Height of the mother	No	159.51	8.01	2.694	<.007
	Yes	156.15	17.77		

Table 3: Linear Multiple regression analysis of some continuous independent variables and dependent HAZ score variable

Independent variables	Unstandardized Coefficients		Standardized Coefficients	t-test	Sig. *P-value*
	B	Std. Error	Beta		
(Constant)	-5.256-	1.431		-3.672-	<.000
Age (Months)	0.015	0.006	0.13	2.569	<.011
Number of children in the family	0.086	0.066	0.067	1.313	<.190
Duration of main feeding in infancy	-.007-	0.01	-.039-	-.763-	<.446
BMI of the mother	0.043	0.013	0.166	3.238	<.001
Height of mother [cm]	0.021	0.008	0.136	2.659	<.008

Table 4: Multi-nominal logistic regression for environmental and dietary independent factors on the dependent Stunting variable

Independent variables	B	Sig. *P*-Value	Exp(B)	95% Confidence Interval for Exp(B)	
				Lower Bound	Upper Bound
Intercept	3.008	<.012			
Smoking of the father	0.026	<.927	1.026	0.591	1.781
Smoking of the mother	-.025-	<.966	0.976	0.319	2.983
Keeping animals at home	0.309	<.666	1.362	0.335	5.531
Keeping birds at home	-.716-	<.278	0.489	0.134	1.78
Keeping plants at home	-.017-	<.973	0.984	0.373	2.591
House nearby industrial city	-.158-	<.719	0.854	0.361	2.019
Gestational period of the child	-.757-	<.17	0.469	0.159	1.382
Vaccination coverage of the child	0.057	<.882	1.059	0.498	2.251
Main feeding in infancy	0.244	<.342	1.277	0.772	2.112
Eat food with preservatives, daily	-.376-	<0.175	0.687	0.399	1.182
Eat sweet food, daily	0.084	<.759	1.088	0.636	1.862
Drink milk, daily	-.160-	<.595	0.852	0.472	1.537
Eat fruits and vegetables, daily	-.340-	<.180	0.712	0.433	1.17

Table 5: Multi-nominal logistic regression for clinical disorders independent factors on the dependent Stunting variable

Independent variables	B	Sig. *P*-value	Exp(B)	95% Confidence Interval for Exp(B)	
				Lower Bound	Upper Bound
Intercept	0.398	<.665			
Repeated URT infections	-.353-	<.377	0.703	0.321	1.537
Treatment for parasitic infection	-.973-	<.107	0.378	0.116	1.233
Treatment for anemia	0.528	<.242	1.695	0.7	4.103
ISAAC diagnosed asthma	0.458	<.218	1.581	0.763	3.278
ISAAC diagnosed rhinitis	-.531-	<.178	0.588	0.272	1.273
ISAAC diagnosed eczema	-.277-	<.511	0.758	0.332	1.732
Obesity	2.06	<.000	7.845	4.103	15.001
Underweight	2.82	<.000	16.782	7.517	37.47
Wasting	-1.718	<.000	0.18	0.073	0.439

Discussion

Stunting is one of the most important measures of children's overall heath, and it indicates the quality of care provided to different community sectors in nations. Millions of children around the world suffer from diminished linear growth due to lack of adequate nutrition and neglected child health care (21). Screening for stunting among at risk population should be asserted in order to discover stunting and hence enhance the current health conditions. Nowadays, in developing countries, due to changes in lifestyle, socio-demographic pattern, type of diet, and increased prevalence of infectious diseases, the problems of over nutrition and different types of under nutrition have become major health problems (22-23). Prevalence of severe stunting in Saudi Arabia was 2.8%, and it was 10.9% for moderate stunting. This indicates that more care should be done to raise standard of nutritional status of Saudi children (7).

This case-control study analyzed 496 children aged 2 – 6 years for risk factors associated with stunting. This is one of the first studies in Saudi Arabia looking at risk factors associated with stunting and the first study to link stunting with a much higher increased risk of being overweight in KSA.

The present study depicted the gender of the child to be a strong risk factor for stunting among young children. There are contradicting results in the literature about whether boys or girls are more vulnerable to stunting (7, 24-27). However, our findings are in line with a previous study (28). Many studies found boys to be more prone to stunting compared to girls in such a young age. In line with these conclusions, our data identified male children to be at a greater risk of stunting compared to females. The reason behind such a difference is not clear. Our study did not find significant association of stunting among children and socio-economic status of their families, or paternal education. The reasons behind that could be due to the similarity of the living condition which does not allow the impact of socioeconomic factor to influence the linear growth of the children. The present study found that HAZ score increased progressively as age increased i.e. stunting was more common in the second and third year and decreased from the 4th to the 6th years. This is in line with other studies (29-32). This particular young age group is vulnerable to infectious diseases as they start to reduce breast feeding, with its protective immunity, as well as exposure to food with its possible contamination, together with increasing dietary requirements (33-36).

Low birth weight children are significantly more likely to be stunted, as they are born with deficient reserves of Vitamin A, iron and zinc as well as low reserves of nutrients essential for growth (25, 37–39). In the present study we didn't find significant association between gestational period and decreased linear growth of the children, particularly after controlling for the confounding factors. This could be explained by the fact that Jeddah is an economically developed city, and most of the people are well off and hence mothers, in both regions, may have better healthcare knowledge, and health care resources. Similarly, in the present study paternal education, occupation, and monthly income were not significant predictors of stunting among children. This is inconsistent with the results of previous studies (25, 29, 30, 40–45).

Undernourished mothers usually have children with stunting. Studies from countries with low socioeconomic conditions reached to similar conclusions (29, 40, 42). Maternal nutritional deficiency is usually associated with deficiency in vitamin A, iodine, vitamin B2, vitamin B1, and

others (7). Consequently, infant nutritional deficiency is a result of maternal nutritional deficiency for these nutrient elements (38, 46). The present study revealed that 43.9% of cases had double nutritional problems (stunting and overweight/obese), compared to 11.4 % of the controls (X2=51.85, P < .000). This is in line with several other studies (40-48). The multi-nominal logistic regression in the present study revealed, also, that the children with stunting were 7.8 times more likely to be overweight/ obesity than those with normal linear growth (OR: 7.8; 95% CI: 7.517, 34.47), after allowing for the confounding factors. This could be explained by the hypothesis of poor diet quality (47). The present study showed that short stature of the mothers was significantly associated with decreased linear growth in 2 – 6 years children. This is in line with other studies (49, 50). This could be explained by the small uterine size which may lead to deficient nutrition supply to the fetus (51).

In conclusion our results provide evidence that male children and those aged between 2 to 4 years are more likely to suffer from stunting. It revealed, also, that an increase in stunting proportion was significantly linked to decrease in mother's height and her BMI. Moreover, overweight and underweight of the children were associated significantly with increasing risk of stunting. Accordingly, it is recommended that more care should be done by concerned health care personnel to prevent malnutrition and control its consequences among under six years Saudi children.

Limitations of this study

The questionnaire data were completed by the parents of the 2- 6 years old children, and were obtained retrospectively. It was also a hospital-based case control study, we can't exclude self-selection bias.

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Effectiveness of Community Mental Health Service in Oman: A Pilot Study

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Abstract

In Oman the Community Mental Health Service (CMHS) was implemented in 2013. CMHS includes home based services such as outreach team, including, crisis response, recovery team and rehabilitation. The community mental health program in Oman is multidisciplinary, however no study has yet evaluated the effectiveness of community mental health in Oman.

Aims: A pilot study was a weighted and measurable outcome of the community service program in decreasing relapse, length of hospital stay and the financial sequelae of relapse of the service provided.

Objective: was to compare readmission rate, length of stay and total hospital cost per admission for the patients before and after enrolment to the CMHS program.

Results: In this study there is a statistically significant difference between number of relapses before and after enrolments to community services. The mean number of relapses decreased after enrolment to CMHS and the decreases mean cost per admission for the patients after enrolment to the community program. Decrease in number of admissions among patients enrolled on CMHS was from (M 2.68 SD 2.76) to (M 1.51 SD 2.5) with P value 0.001 . Duration of stay also decreased from (179.83 SD 471.2 day) to (61.62 SD 102.14 day) with P value approximately <P=0.01 indicating high statistical significance. which reflects also on the cost of care which dropped from (17900.83 SD 47100.2 OMR) to (6100.62 SD 10200.14 OMR. Further demographic variable results showed that males, illiterate, never been employed, single and divorced get benefits from CMHS and schizophrenia. < 10 years of illness and good family support got more benefits compared to other diseases

Conclusion: CMHS in Oman is effective in decreasing relapse rate and cost.

Key words: Community Mental Health Service, Oman

Introduction

Mental disorders are associated with a considerable burden of disease directly because of relative high estimates of prevalence, mortality, disabilities, and costs (WHO, 2004 and Baxter et. al., 2011). Considering this serious burden, accurate and effective management has been believed to be an essential component of any mental health programs. However, most of the patients experience prolonged hospitalization and repeated readmissions that impose grave burden not just on a patients' quality of life, but on fragile financial resources of mental health programs (Botha et. al., 2010).

After beginning of deinstitutionalization reform, clear changes happened in the strategy of mental health services. One of the essentials of deinstitutionalization reform is the principle of "continuity of care" (Bachrach, 1979). Body of evidence attests to the importance of aftercare programs for patients' continuity of care.

Regarding aftercare, different services have been designed to discuss possible solutions, such as intermediate settings ("step-down" services), residential treatment centres, or home-based facilities (Foster, 1999). Of the home-based services, case management, (Dieterich, et. al., 2010) follow-up phone calls (Van den Berg et. al., 2011) or home visits are the most common (Burns et. al.,2002 and Sharifi, 2006).
A retrospective analytical study in Bahrain assessed the outcome of home visit in cases with schizophrenia, and revealed that there is reduction of hospital admission by 62% for those enrolled in community services. The effectiveness of Community mental health services is evidence based. Simmonds et al. 2001 in their systematic review, reported that community mental health team management is superior to standard care in promoting greater acceptance of treatment and may also reduce hospital admission and avoid deaths by suicide. This model of care is effective and deserves encouragement.

In addition, among older adults with mental illness Van Citters and Bartels (2004) concluded in their systematic review, that home-based mental health treatment is effective in improving psychiatric symptoms in older adults with home visits who didn't require admission at all (Heussein et al., 2009).

In Oman Dr. Saleha Al-Jadidi at AlMasarra Hospital implemented the Community Mental Health Service (CMHS) in 2013. CMHS included home based services such as outreach team, including, crisis response, recovery team and rehabilitation. Community mental health program in Oman is multidisciplinary. However, Nursing community services became a base of the services in visiting patients in their community (particularly in Muscat Governorate), two times per week, which has extended now to three times per week depending on the cases and types of medications used. Multidisciplinary teams depending on clinical needs of the patients are also involved in CMHS in Oman, including psychiatrists, consultant, specialists, nurses, medical officers, psychologists, social workers, clinical pharmacists, general practitioners, occupational therapists, physiotherapists, dietitians and medical orderlies (20,21). The service provides home based assessments, providing medications or administering them, managing the cases and conducting investigations such as blood investigations (Saleha Al-Jadidi et al 2015).

CMHS in Oman showed effectiveness in reducing relapses and length of stay in the hospital etc. For better organization, Oman CMHS enrolled patients were divided into four phases from the implementation to date; phase one including chronic schizophrenia with / without long acting injections phase two other psychotic disorders (e.g severe schizoaffective disorder, and severe bipolar affective disorder. Phase three was for chronic major depressive disorder and phase four severe anxiety disorder which has not yet been reached. There are 54 cases that have been enrolled in CMHS so far.

In 2016, CMHS was expanded, and it became a National Program to include general psychiatry cases with the same inclusion and exclusions criteria (15). In order to follow progress of the patients the program was added to MOH A'shifa system (electronic file system) for all local regions, in order for any psychiatrist to refer to the mentioned program, however some regions are still under implementation.

Unit cost for AlMasarra Hospital , for inpatients is (148.2 RO). Unit cost is one for inpatient or inpatient curative care and one for "outpatient defined visit" for patient curative care. Curative care includes the cost of medical and paramedical staff, the agnostic services, both laboratory and imaging services, and medical goods that include prescribed medicines and nondurable and durable goods. Unit cost per bed day was estimated using an Ordinary Least Squares regression model developed by WHO-CHOICE and published by Adam et al. (2003). As per the WHO model, Al Masarra hospital is considered a Tertiary-level psychiatry hospital equipped with highly specialized staff and technicians; clinical services are highly differentiated by function; and have teaching activities. So, the unit cost would be relatively high compared to another regional hospital with different medical specialties. The formula below is used to calculate the unit cost for both inpatient and outpatient services

Unit Cost for Patient Services = Overhead Expenses + Capital Investments/Total Revenue per year

Hospital Costs per Bed Day on average cost every inpatient RO 148.2 per day during their stay in AlMasarra hospital. The cost of the medical and paramedical staff and providing curative care for one inpatient per day amounts to RO 111.3 (about 75.1 % of unit costs). Every inpatient costs RO 16.75 (8%) for medicine and RO 8.3 (5.6%) other medical goods; and costs RO 11.9 for diagnostic services, daily. The total length of stay for admitted patients in year 2019 was 25,774 service days (which cost MOH approximately RO 3,819,706 per year for total admitted patients) and the mean length of stay was 24.7 service days (which cost MOH approximately around RO 3,660 per single patient year). Unit Cost for each inpatient service day Item Percentage was Prescribed Medicine 11.3% Imaging Services 1.7% Laboratory Services 6.3% Non-durable and durable Goods 5.6% Salaries 75.1 %.
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Hospital Costs per Patient Visit at AlMasarra hospital which accommodates more than 25,774 outpatients visit (in 2019):

Each outpatient visits costs on average 86.3. Costs for medical and paramedical staff make the most of this cost (RO 58.9 or 68.2 %). On average, each outpatient visit costs RO 12 of medicine, the rest of the cost goes to diagnostic services. The approximate cost of patient visits in 2019 was RO 2,224,296 (Prescribed Medicine 13.9 %, Imaging Services 3.5 %, Laboratory Services 6.3% ,Non-durable and durable Goods 8.1 %, Salaries 68.2 %).

Methods

A retrospective analysis was done of the data from January 2015 to January 2020 on A'Shifa system of community mental health service and community mental health documents before A'Shifa system implementation for all CNHS patients (54 comprehensive patients were enrolled), who were in CMHS at Al Masarra Mental Hospital, Oman, for the mentioned period.

The study hypothesis was that CMHS, improves the patients' outcome.. (The current unit cost for AlMasarra Hospital, for inpatients is (148.2 RO). The aim was to study the positive outcome of the community service program in Oman in decreasing relapse and the financial sequelae of relapse and the service provided. The objectives of this study, were to compare the relapse rate of hospital admission/per relapse and total hospital cost per admission for the patients before and after the enrolment to the CMHS program.

Inclusion criteria was to enrol all patients enrolled in CMHS (age 18+, chronic mental illness with/without long acting injections Exclusion criteria any mental illness not enrolled in the program which are (substances misuse disorders, personality disorders, pure social problems, forensic cases and severe dysfunction of family dynamic). This study was approved by the Directorate of Health Services Muscat governorate , MOH , Oman research ethics committee.

Data analysis

Statistical Package for Social Science program (SPSS, Inc., USA) V 25 was used for statistical analysis. For quantitative variables, mean and standard deviation (mean ± standard deviation) were calculated. For qualitative variables, frequency and percentage n (%) were described.

Wilcoxon test was used to compare between variables before and after the program. P-values were considered significant when P-value <0.05.

The data was analysed by comparing the outcome measures (the relapse rate, readmission rate, duration of hospital admission/per relapse, severity of episodes, total hospital cost per admission for the patients) after enrolment to CMHS from January 2015 to January 2020 and before the enrolment of the services, using SPSS version 20.

Results

In this pilot study we examined the effectiveness of community interventions among a sample (n=54) of psychiatry patients at A-Masarra Hospital (Table 1). Participants in the study were relatively young, mean age 47.87(SD =11.33). Our sample consisted mostly of male patients (72 %). There was a heterogeneity of the sample in terms of duration of illness. The majority of the sample was illiterate 53%, and 7% of them have education level to grade 6 , and 6% have education grade 7,8,9,10 and 12 and 2 % had education level of grade 2,5 and 11 (Figure 1). Most of the patients were living in an urban area (69%) and 31% were rural. Most of the study sample were single 59%, 19% were divorced and 13% were married. Most of the patients were unemployed (67%) and 4% were retired (Figure 2).

In terms of clinical characteristics most of the sample had schizophrenia (61.11%) and 16.67% had schizoaffective disorder. In addition, the minimum duration of illness was 2 years and maximum was 45 years, mean 21.75 (SD =10.31) (Table 3).

There is a statistically significant difference between number of relapses before and after enrolment to community services interventions; the mean number of relapses decreased after enrolment to community services interventions (2.68 ± 2.76 Vs. 1.51 ± 2.50 ; P = 0.001) using a significance level of 0.05. The mean days of hospital admission/per relapse after enrolling in the program CMHS were less than the mean days before enrolling in the program (179.83 ± 471.2 Vs. 61.62± 102.14; P = 0.00), also the mean cost per admission for the patients after enrolment to the program CMHS was less than the mean cost per admission before enrolment to the program CMHS intervention (17900.83 ± 47100.2 Vs. 6100.62± 10200.14; P = 0.00), using significance level of 0.05 (Table 2) .

These results suggest number of hospital admissions decreases with CMHS. We also found that, there was a significant difference in costs of care before and after the community program. Statistically our results suggest that when psychiatry patients get community care visits, the cost of care decreases in comparison with not getting community care. The cost drooped tremendously after 2 years from adopting the CMHS to a mean 6100.62 OMR in comparison to mean OMR 17900.83 before enrolment.

And second analysis showed (Table 5) 35 (68%) of patients were diagnosed with schizophrenia and 7(13%) diagnosed with Schizoaffective disorder. 31 (57%) of the study population don't have a psychiatric condition and 41 (76%) of them don't have a medical condition. The mean duration of illness is about 21 years. 34 (65%) of participants had family support. Schizophrenia patients got benefit from the program while patients with other diagnoses didn't benefit from the program, Only patients with no medical and hypertensive condition got benefit from the program but patients who had diabetes mellitus, substance misuse, hypertension & diabetes mellitus, Hypertension & epilepsy, and HCV did not get benefit from the program. Also patients with no psychiatric disorder got benefit from the program. Patients who had a duration of illness less than 10 years got benefit from the program in terms of the duration of hospital admission/per relapse and cost per admission but they didn't get benefit in the number of relapses. Patients who had a duration

of illness greater than ten years got benefit from the program in the number of relapses, duration of hospital admission/per relapse and cost per admission. Patients with family support and those without family support got benefits from the program using a significance level of 0.05 (Table 4).

(Table 4) shows that males got benefits from the program while females didn't get benefits from the program. According to education level, only illiterate patients got benefit from the program while the differences in other education levels are not statistically significant. According to occupation, patients who were never employed and who were retired got benefits from the program while patients currently employed and housewives didn't get benefits from the program. Single and divorced patients got benefits from the program but married and widowed patients didn't get benefits from the program. Both urban and rural residents got benefit from the program, using a significance level of 0.05.

Figure 1: Distribution of Education level

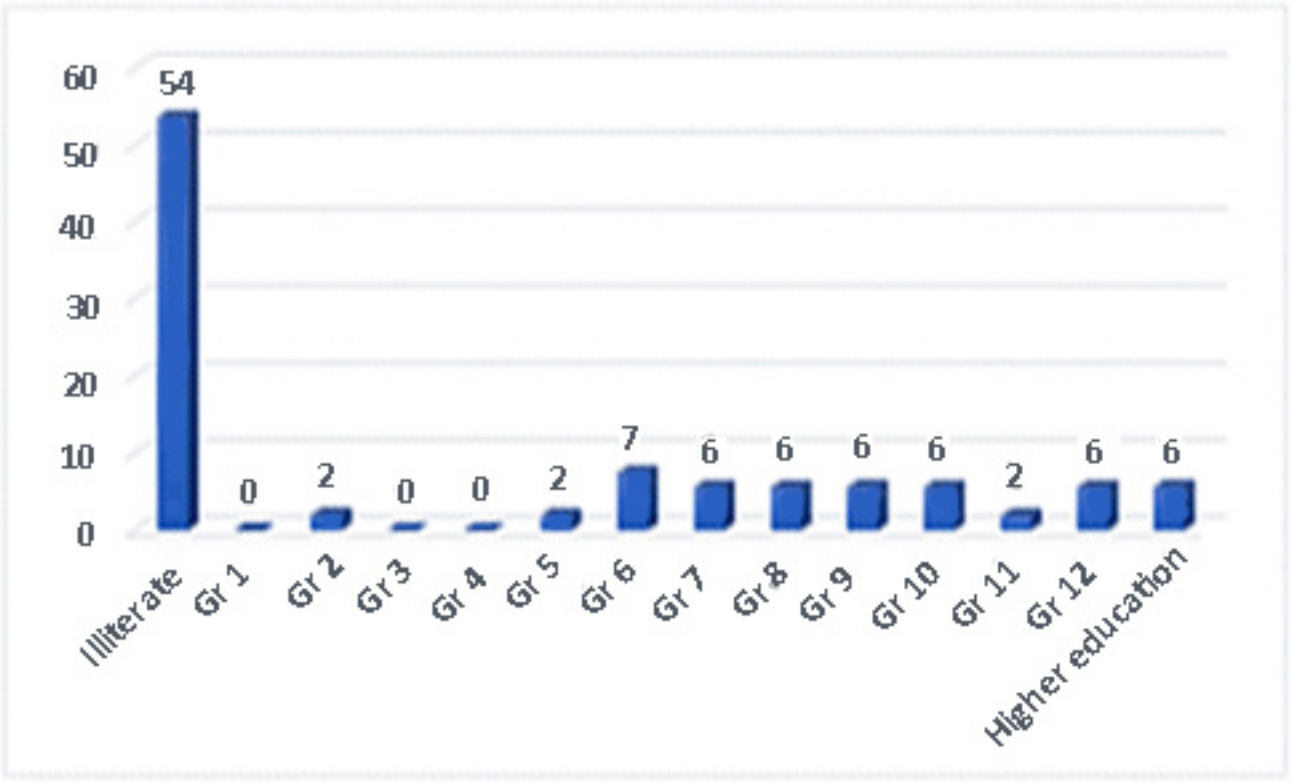

Figure 2: Distribution of occupation

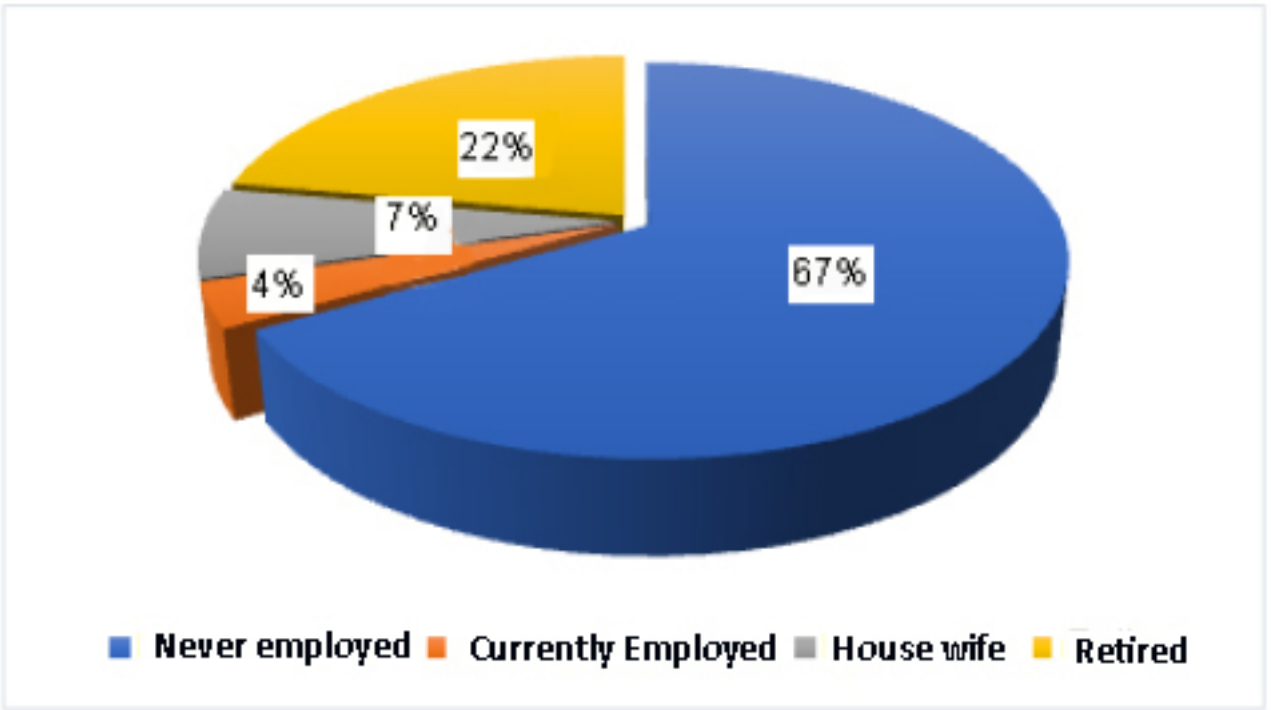

Table 1: Patients' characteristics

Variable	N	%
Sex		
Male	39	72%
Female	15	28%
Education level		
Illiterate	29	53.7%
Gr 2	1	1.9%
Gr 5	1	1.9%
Gr 6	4	7.4%
Gr 7	3	5.6%
Gr 8	3	5.6%
Gr 9	3	5.6%
Gr 10	3	5.6%
Gr 11	1	1.9%
Gr 12	3	5.6%
Higher education	3	5.6%
Occupation		
Never employed	37	67%
Currently employed	2	4%
House wife	4	7%
Retired	11	22%
Marital status		
Single	32	59%
Married	7	13%
Divorce	10	19%
Widow	5	9%
Residence		
Urban	37	69%
Rural	17	31%
Age		
Mean ± SD	47.87 ± 11.33	
Minimum	29	
Maximum	74	

Table 2: Comparison between No. of Relapses, duration of hospital admission/per relapse, and total cost per admission for the patients before and after the enrolment to the program CMHS

	Before enrolling in community services interventions (Mean ± SD)	After enrolling in community services interventions (Mean ± SD)	P-value
No of Relapses	2.68 ± 2.76	1.51 ± 2.50	0.001
Duration (Days)	179.83 ± 471.2	61.62± 102.14	0.00
Cost (RO)	17900.83 ± 47100.2	6100.62± 10200.14	0.00

Table 3: Clinical characteristics

Diagnosis	Mean (SD	Frequency & Percentage (N, %)
Mental Retardation		2 (3.7)
Schizophrenia		33 (61.1)
Schizo Affective Disorder		9 (16.7)
Frontotemporal Dementia		1 (1.9)
Bipolar Affective Disorder		6 (11.1)
Delusional Disorder		3 (5.6)
Duration of Illness	21.75 (10.31)	

Table 4: Comparison between the number of relapses, duration of hospital admission/per relapse, and cost per admission for the patients before and after enrolling in the program according to demographic variables

Variable	No of Relapses		P	Duration (Days)		Cost (RO)		P
	Before	After		Before	After	Before	After	
Sex								
Male	2.58 ±2.32	1.30±2.00	**0.002**	144±152	53±89	14400±15200	5300±8900	**0.00**
Female	2.93 ±3.76	2.00±3.05	0.145	336±865	81±131	33600±86500	8100±13100	0.162
Education Level								
H	1.33 ±0.57	0.66±1.15	0.414	55 ± 59	14 ± 24	5500 ± 5900	1400± 2400	0.109
Illiterate	2.82 ±3.27	1.53±2.04	**0.010**	271±642	65±101	27100±64200	6500±10100	**0.00**
Gr 2	10 ± -	1 ± -	-	434± -	17± -	43400± -	1700± -	-
Gr 5	1.00 ± -	13.0 ± -	-	147± -	397± -	14700± -	39700± -	-
Gr 6	3.00 ±2.00	00 ±00	0.059	78 ± 54	00 ±00	7800 ± 5400	00 ±00	0.063
Gr 7	3.33 ±0.57	4.00±3.6	0.785	127±23	161±154	12700±2300	16100±15400	0.593
Gr 8	2.33 ±1.15	1 ±0	0.175	86 ±63	49 ±7	8600±6300	4900 ±700	0.285
Gr 9	2.33 ±1.15	2.00±1.14	0.99	83 ±33	87 ±53	8300 ±3300	8700 ±5300	0.665
Gr 10	0.33 ±0.57	0 ±00	0.317	115±200	00 ±00	11500±20000	00 ±00	0.317
Gr 11	3.00 ±0.41	4 ±-	-	233±185	233±185	23300±18500	23300±18500	-
Gr 12	2.66 ±2.51	00 ±00	0.180	99 ± 88	00 ±00	9900 ± 8800	00 ±00	0.180
Occupation								
Never employed	2.63 ±2.55	1.60±2.79	**0.006**	257 ±591	71 ±114	25700 ±59100	7100 ±11400	**0.001**
Currently Employed	1.50 ±2.12	0.00 ±	-	83 ±118	0.00 ± -	8300 ±11800	0.00 ± -	-
House wife	5.25 ±4.92	3.00±2.44	0.273	135±131	109±150	13500±13100	10900±15000	0.518
Retired	2.41 ±2.64	0.58±0.66	**0.015**	108 ±124	18 ±21	10800 ±12400	1800 ±2100	**0.008**
Marital Status								
Single	2.56 ±2.04	1.87±2.95	**0.038**	166 ±173	81 ±115	16600 ±17300	8100 ±11500	**0.003**
Married	2.57 ±3.55	0.28±0.48	0.072	106 ±168	4 ±7	10600 ±16800	400 ± 700	0.075
Divorced	4.20 ±4.13	1.70±1.88	**0.016**	455 ±1044	65 ± 99	45500 ±104400	6500 ± 9900	**0.028**
Widow	0.6 ±0.51	0.60±1.34	0.98	32 ±45	8 ± 19	3200 ±4500	800 ± 1900	0.285
Residence								
Urban	2.62 ±2.70	1.56±2.68	**0.011**	154 ±169	67 ±110	15400 ±16900	6700 ±11000	**0.002**
Rural	2.82 ±2.98	1.41±2.12	**0.018**	292 ±810	48 ±81	29200 ±81000	4800 ±8100	**0.002**

Variable	N (%)	No of Relapses		P	Duration (Days)		Cost (RO)		P
		Before	After		Before	After	Before	After	
Diagnosis									
Schizophrenia	35 (65)	2.62±2.4	1.71±2.28	**0.005**	1.55±172	70±109	1.5500±17200	700±10900	**0.001**
Schizoaffective disorder	7 (13)	1.57±1.2	1.00±1.82	0.391	63.14±63.21	48±114	6300.14±6300	4800±11400	0.499
Frontotemporal dementia	1 (2)	11.00 ± -	3.00 ± -	-	3409.0± -	112± -	340900.0± -	11200± -	-
Bipolar affective disorder	5 (9)	2.80±4.0	0.8±1.30	0.375	118.00 ±181	12±1	11800 ±18100	1200±100	0.144
Delusional disorder	4 (7)	3.25±4.0	1.25±1.50	0.285	110.0±79.76	25±30	11000±7900.76	2500±3000	
Mental retardation	2 (3)	2.0±1.41	1.50±2.21	0.655	179.00±148	120±169	17900±14800	12000±16900	0.180
Comorbid Condition : Medical									
No	31 (57.0)	2.70±2.6	1.87 ±2.88	**0.022**	129 ±134	80 ±120	12900 ±13400	800 ±12000	**0.001**
Substance misuse	1 (1.9)	3.00 ± -	0 ± -	-	126 ± -	0 ± -	12600 ± -	0 ± -	-
Hypertensive	7 (13)	3.14±3.8	1.14 ±1.87	**0.047**	1262±477	41 ± 69	126200±47700	4100 ± 6900	**0.028**
Diabetes mellitus	4 (7.4)	1.75±1.7	0.5 ±1.0	0.285	102 ±1	10 ±21	10200 ±100	1000 ±2100	0.109
HCV	1 (1.9)	4.00 ± -	7.00 ± -	-	0 ±0	177±-	0 ±0	17700±-	-
Hypertensive / Diabetes mellitus	9 (16.4)	2.33±3.3	0.33 ±0.5	0.051	0 ±0	12 ±21	0 ±0	1200 ±2100	0.063
Hypertensive / Epilepsy	1 (1.9)	4.00 ± -	4.00 ± -	-	0 ±0	219 ±-	0 ±0	21900 ±-	-
Comorbid Condition : Psychiatric									
No	41 (76.0)	2.63±2.7	1.14 ±1.83	**0.00**	221 ±536	51 ± 91	22100 ±53600	5100 ± 9100	**0.00**
Substance misuse	4 (16.6)	3.22±2.9	3.33 ±2.44	0.672	148 ±133	86 ±106	14800 ±13300	8600 ±10600	0.374
Mental retardation	2 (7.4)	2.0±2.70	3.50 ±6.30	0.854	68 ±70	112 ±191	6800 ±7000	11200 ±19100	0.715
Duration of Illness / Year									
0 – 10 years	7 (13)	1.57±1.2	0.42 ±0.78	0.113	86 ± 66	13 ± 23	8600 ± 6600	1300 ± 2300	**0.046**
11 – 20 years	21 (39)	3.±2.56	2.064 ±2.26	**0.050**	143 ±161	81 ± 94	14300 ±16100	8100 ± 9400	**0.008**
> 20 year	26 (48)	2.73±3.1	1.38 ±2.89	**0.022**	271 ±661	58 ±118	27100 ±66100	5800 ±11800	**0.006**
Family Support									
Yes	35 (64.8)	2.14±2.4	0.85 ±1.51	**0.005**	103 ±133	35 ±67	10300 ±13300	3500 ±6700	**0.00**
No	19 (35.2)	3.68±3.1	2.73 ±1.41	**0.049**	371 ±755	109 ±135	37100 ±7500	10900 ±13500	**0.024**

Table 5 shows that just Schizophrenia patients got benefit from the program while patients with other diagnoses didn't get benefit from the program and Patients with family support and those without family support got benefits from the program using significance level of 0.05

Discussion

This retrospective pilot study showing the effectiveness and superiority of Community Mental Health Service (CMHS) implemented at AMH, Oman, (Saleha Al-Jaddi et al 2015) concerns the relapse rate, duration and total hospital cost per admission for the patients enrolled to CMHS. CMHS, includes home based services such as outreach team, early interventions, crisis response, recovery team and rehabilitation services adding to the usual after care services (Saleha Al-Jadidi, 2016).

A Retrospective analysis was done of the data collected between January 2015 to January 2020 on A'Shifa system of community mental health service and community mental health documents before A'Shifa system implementation for all patients. A total of 54 patients were enrolled in the study representing ages between 29-74 years; 39(72%) were male and 15(28%) were female and most of the them were singles with various residency, occupation and educational level. Unit cost per day was estimated using ordinary least regression model developed by WHO-CHOICE. Al Masarra hospital is considered a tertiary level psychiatry hospital so the unit cost is considered to be high compared to the other medical health facilities. On average every inpatient cost 148.2 OMR per day during their stay with approximately 75% of the cost providing curative care and other cost provided medications, other medical goals and diagnostic services.

To our knowledge, this is the first retrospective pilot study of the evidence that supports CMHS outreach service models using standardized inclusion and evaluation criteria in Oman.

We found that there was a significant decrease in number of admissions among patients enrolled on CMHS from (M 2.68 SD 2.76) to (M 1.51 SD 2.5) with P value 0.001. We also found that duration of stay also decreased from (179.83 SD 471.2 per day) to (61.62 SD 102.14 per day) with P value approximately 0.00 indicating high statistical significance, which is reflected also in the cost of care which dropped from (17900.83 SD 47100.2 OMR) to (6100.62 SD 10200.14 OMR). This result is congruent with our hypothesis reflecting on decreased relapse rate, length of stay and the financial impact of relapse of the service provided. Our results are in agreement with results of Heussein et al, 2009 who compared patients who are diagnosed with Schizophrenia enrolled to Community Psychiatry Service – Home Visit Treatment [CPS-HVT] vs outpatient treatment in Bahrain and concluded that CPS-HVT is superior and reduces the number and duration of admissions. Van Citters and Bartels, 2004 concluded that outreach services may provide an essential bridge that connects effective pharmacologic and psychosocial interventions with individuals however they also stated that limited data supported the effectiveness of outreach services in identifying isolated older adults with mental illness and recommended that we need more rigorous methods evaluating the efficacy of case identification models and subsequent treatment for older persons with a variety of psychiatric diagnoses. Simmond et al 2001 stated that Community mental health service is superior to standard care in promoting acceptance of treatment, and may reduce hospital admission and they recommended after a systematic review that this model of care is effective and deserves encouragement. Gillis, Koch and Jovi, 1990 investigated the cost effectiveness of the home visiting program for psychiatric patients at Valkenberg Hospital, Cape Town. Their results showed that readmissions were reduced by 31.5% over 1 year and duration of days in hospital by 55.6%. Moreover attendance at outpatient clinics also improved by 39%. The cost-effectiveness was clearly demonstrated. The same was found by T Burns, et al.

There is evidence that visiting patients in their home regularly and taking responsibility for both health and social care each reduces days in hospital. We believe that factors behind successful CMHS are multiple and overlap with each other and depends on service providers and consumers of the service. Poor compliance and difficulties in reaching/obtaining the service is the main goal behind CMHS as one of the feasible goals of aftercare protocols. Patient related and disease related factors could strongly influence medication compliance which reflects directly on readmission rate and cost effectiveness which could be easily overridden by delivering the service to the patient in certain circumstances and with certain criteria.

Therefore, another deeper analysis of the result was conducted to investigate the effectiveness of patient related (demographical factors) on CMHS and then the factor related to the disease itself. We compared the number of relapses, duration of hospital admission/per relapse, and cost per admission for the patients before and after enrolling into CMHS according to demographic variables. The results show that males got more benefits from CMHS, and illiterate patients got benefit while the differences at education levels are not statistically significant; patients who had never been employed and who were retired were got more benefits from CMHS compared witth those who were currently employed and housewives; single and divorced patients got benefits compared to married and widowed and both urban and rural got benefit from the program, using a significance level of 0.05. We believe that those results are multifactorial and possible interaction between all demographical factors rather than single implemented factors. At that level of study, we were not able to investigate each demographic factor alone and it was difficult to neutralize other demographics at the same time however, we found that our primary results may give the chance for later deeper investigation on a larger community sample. We also believe that those findings will help mental health policies makers to design the future community mental health program based on the characteristics of the population (Demographic variables) in order to reduce untreated patients and optimize resources. Our aim and results are in disagreement with the study conducted in different population (Korea) and different target sample for Park et al 2014 who investigated Sociodemographic factors associated with the use of mental health services

in depressed adults. He found that employed patients and educational level got more benefit from the service. Different communities may explain the difference in results. We also compared the number of relapses, duration of hospital admission/per relapse, and cost per admission for the patients before and after enrolling to CMHS according to the disease related factors and the results show that Schizophrenia patients, patients who had a duration of illness less than 10 years and patients with family support got more benefits from the program using a significance level of 0.05. Our results are in concordance with Piat et al, 2011, who investigated the importance of families for persons with serious mental illness living in structured community housing and they found that families supported recovery by providing affection and belonging, and offering emotional and instrumental support.

We conclude that CMHS is very crucial and superiorly effective to standardized after care plans which patients obtained before enrolling to CMHS and in decreased readmission rate, length of stay, and overall cost of the service, in Oman. Adding to that we observed that illiterate, never been employed and retired, single and divorced patients got more benefits. We also observed that Schizophrenia patients, patients who had a duration of illness less than 10 years and patients with family support got more benefits from CMHS.

This study has several important limitations. First, the small sample size was enrolled to study however we tried to enrol most of the patient enrolled to CMHS during the mentioned study time. Adding to that the CMHS was affected by the COVID 19 pandemic. Second, the lack of heterogeneity of sample residency which affects the ability to generalize the results. Therefore we recommend further studies on CMHS in Oman and further analysis of the result is needed.

Recommendations to higher authorities include: expanding the community mental health service to all levels of health care facilities, training health care providers, allocating a budget and focus on community mental health services rather than increasing beds at the hospitals and funding of future research.

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Proton Pump Inhibitors Awareness among Physicians and Pharmacists in Primary Healthcare Centres in Abha, Saudi Arabia

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Abstract

Background: Proton pump inhibitors (PPIs) effectively suppress acid secretion and play an important role in peptic ulcer disease and gastroesophageal reflux disease. Physicians and pharmacists' awareness and perception toward PPIs have a crucial role in regulating the use of PPI and preventing any adverse event, drug-drug interaction, or inappropriate use PPIs.

Aim: The current study aims to assess proton pump inhibitors awareness level among physicians and pharmacists and its detriments in PHCCs, Aseer region, Saudi Arabia.

Methods: An analytical cross-sectional study was applied to answer the main research question. The study targeted all physicians and pharmacists in primary healthcare centres in Abha who will be accessible during the study period from 23 May to 27 July. Data were collected from eligible participants using pre-structured online questionnaire. The questionnaire was developed by the researchers based on intensive literature review and expert's consultation. The questionnaire covered participants' personal data including age and gender, job title, and awareness items regarding PPI types, uses, side effects, and types.

Results: A total of 178 participants completed the study questionnaire. 97 (54.5%) participants were pharmacists, 45 (25.3%) were clinical pharmacists, and 36 (20.2%) were physicians. Participants ages ranged from 20-40 years with mean age of 25.4 ± 9.7 years. 78.7% of the participants reported that PPIs are the 1st line pharmacological treatment for peptic ulcer which was insignificantly higher among clinical pharmacists (84.4%; P=.077). Omeprazole as the most prescribed PPI was known by 75.8% of the participants. As for Long-term use of PPI adverse reactions, 22.5% reported osteoporosis, 20.2% selected vitamin B12 deficiency, 2.2% reported pneumonia, while 55.1% selected all options, especially pharmacists and clinical pharmacists (60.8% and 60%, respectively; P=.017).

Conclusion and Recommendations: In conclusion, the current study showed that medical staff in the primary healthcare centres had moderately low knowledge regarding PPI and its indications. The lowest awareness was mainly among physicians relative to pharmacists especially clinical pharmacists.

Key words: Proton pump inhibitors, awareness, practice, medical staff, pharmacist, physician, knowledge

Background

Proton-pump inhibitors (PPIs) are group of medications they act mainly through a complete and protracted reduction of stomach acid production. Among all known categories, there is no apparent proof that one agent works better than another [1-3]. PPIs are extensively prescribed for the prophylaxis and treatment of upper gastrointestinal tract diseases including gastric ulcers, gastroesophageal reflux disease (GERD), and their complications, Helicobacter pylori eradication treatment, indigestion, ulcers due to nonsteroidal anti-inflammatory drugs, stress ulcers, and other disorders due to hypersecretory status [4]. Omeprazole was the first launched PPI in 1989, then other drugs were introduced such as pantoprazole, lansoprazole, rabeprazole, esomeprazole, and ilaprazole. Recently, with more life stress, there is an upward and substantial increase in ordering of PPIs [5].

PPIs still one of the most prescribed medications worldwide. In the United States, PPIs were prescribed in 4% of outpatients in 2002 and 9.2% in 2009. Moreover, sales of PPIs accounted for about 10 billion dollars in 2007 and 13.9 billion dollars with 113 million prescriptions filled annually in 2010 [6]. The global spending on PPIs was 7 billion USD by 2006, while between April 2013 and March 2014, the PPI esomeprazole (Nexium®) was the third order-selling drug in the USA with 19.3 million prescriptions and profits of about 6.3 billion USD [7, 8]. The high increase in PPI prescribing rate during the last several years initiated a main question regarding the appropriate utilization of these drug category [9].

The construction of regulatory guidelines regarding the prescription of PPIs had a significant role in reducing inpatient use of PPIs prescriptions, only among those not receiving PPIs at the time of hospital admission. Many reported prescriptions were dispensed to outpatient clients, and hence, were dispensed mainly through community pharmacists [10]. The awareness and perception of both physicians and pharmacists towards PPIs have a crucial role in regulating the use of these drugs and preventing any adverse event, drug-drug interaction, as well as inappropriate PPIs use [11]. The current study aimed to assess proton pump inhibitors awareness level among physicians and pharmacists and its detriments in PHCCs, Aseer region, Saudi Arabia.

Methods

An analytical cross-sectional study was applied to answer the main research question. The study targeted all physicians and pharmacists in primary healthcare centres in Abha, Aseer region, southern of Saudi Arabia who will be accessible during the study period from 23 May to 27 July. Residency in Aseer region (for at least 6 months), physician and pharmacist at primary healthcare centre in Abha for at least 6 months, being in direct contact with patient or provide direct service and accepted to participate in the study were the inclusion criteria. Physicians and pharmacists who were at administrative positions or living outside Aseer region were excluded. A consecutive sampling method was applied where all eligible population who are fulfilling the inclusion criteria were invited to participate in the study during the study period.

Data were collected from eligible participants using pre-structured online questionnaire. The questionnaire was developed by the researchers based on intensive literature review and expert's consultation. A panel of 3 experts independently reviewed the study questionnaire to assess content validity and relevance. Any discordance regarding any item was solved by discussion and consensus or voting if there were no consensus. A pilot of 15 participants was conducted and assessed tool applicability and reliability (α- Cronbach's) of 0.75. The questionnaire covered participants' personal data including age and gender, job title, and awareness items regarding PPI types, uses, side effects and types. For awareness items, each correct answer was scored one point and total summation of the discrete scores of the different items was calculated. A patient with score less than 60% (12 points) of the maximum score was considered to have poor awareness while good awareness was considered if he had score of 60% or more (13 points or more) of the maximum score.

Data Analysis

After data were extracted, it was revised, coded, and fed to statistical software IBM SPSS version 22 (SPSS, Inc. Chicago, IL). All statistical analysis were done using two tailed tests. P value less than 0.05 was considered statistically significant. Descriptive analysis based on frequency and percent distribution was done for all variables including participants age, gender, job title, PPIs awareness items and participants opinion regarded categories in need to carry out large scale education on rational use of PPI. Crosstabulation was used to assess distribution of awareness level according to participants' personal data and job title. Relations were tested using Pearson chi-square test and exact probability test for small frequency distributions.

Results

A total of 178 participants completed the study questionnaire. 97 (54.5%) participants were pharmacists, 45 (25.3%) were clinical pharmacists, and 36 (20.2%) were physicians. Participants ages ranged from 20-40 years with mean age of 25.4 ± 9.7 years. Also, most of participants were males (61.8%; 110) (Table 1).

Tables 2, and 3 show distribution of awareness regarding PPI among physicians and pharmacists in primary healthcare centres in Abha, Saudi Arabia. 78.7% of the participants know that PPIs are the 1st line pharmacological treatment for peptic ulcer which was insignificantly higher among clinical pharmacists (84.4%; P=.077). Only 25.8% of the study participants know that PPI is inactive prodrug, with highest knowledge among clinical pharmacists (31.1%; P=.001).

Table 1: Personal data of physicians and pharmacists in primary health care centres, Abha, Saudi Arabia

Personal data	No	%
Age in years		
20-30	162	91.0%
31-40	16	9.0%
Gender		
Male	110	61.8%
Female	68	38.2%
Job title		
Physician	36	20.2%
Pharmacist	97	54.5%
Clinical pharmacist	45	25.3%

Table 2. Awareness regarding PPI among physicians and pharmacists in primary health care centres, Abha, Saudi Arabia

Awareness items		Total		Job title						p-value
				Physician		Pharmacist		Clinical pharmacist		
		No	%	No	%	No	%	No	%	
What is the 1st line pharmacological treatment for peptic ulcer?	PPI	140	78.7%	28	77.8%	74	76.3%	38	84.4%	.077
	H2 blockers	9	5.1%	2	5.6%	5	5.2%	2	4.4%	
	Both	20	11.2%	1	2.8%	15	15.5%	4	8.9%	
	Don't know	9	5.1%	5	13.9%	3	3.1%	1	2.2%	
Is PPI inactive prodrug?	Yes	46	25.8%	4	11.1%	28	28.9%	14	31.1%	.001*
	No	66	37.1%	7	19.4%	39	40.2%	20	44.4%	
	Don't know	66	37.1%	25	69.4%	30	30.9%	11	24.4%	
Which of the following PPI is most commonly used?	Omeprazole	139	78.1%	29	80.6%	74	76.3%	36	80.0%	.197#
	Pantoprazole	29	16.3%	3	8.3%	19	19.6%	7	15.6%	
	Lansoprazole	2	1.1%	0	0.0%	2	2.1%	0	0.0%	
	Don't know	8	4.5%	4	11.1%	2	2.1%	2	4.4%	
Can PPI be used to prevent stress ulcer?	Yes	127	71.3%	26	72.2%	70	72.2%	31	68.9%	.473
	No	30	16.9%	5	13.9%	19	19.6%	6	13.3%	
	Don't know	21	11.8%	5	13.9%	8	8.2%	8	17.8%	
Can PPI be used to treat acute pancreatitis?	Yes	40	22.5%	5	13.9%	29	29.9%	6	13.3%	.085
	No	88	49.4%	21	58.3%	40	41.2%	27	60.0%	
	Don't know	50	28.1%	10	27.8%	28	28.9%	12	26.7%	
Which of the following (1) is most commonly prescribed?	Omeprazole	135	75.8%	26	72.2%	74	76.3%	35	77.8%	.105#
	Pantoprazole	33	18.5%	5	13.9%	20	20.6%	8	17.8%	
	Lansoprazole	2	1.1%	0	0.0%	1	1.0%	1	2.2%	
	Don't know	8	4.5%	5	13.9%	2	2.1%	1	2.2%	
Does omeprazole have the largest interaction compared with other PPIs?	Yes	71	39.9%	8	22.2%	44	45.4%	19	42.2%	.001*
	No	58	32.6%	3	8.3%	40	41.2%	15	33.3%	
	Don't know	49	27.5%	25	69.4%	13	13.4%	11	24.4%	
Should omeprazole be selected for paediatric patients?	Yes	73	41.0%	13	36.1%	42	43.3%	18	40.0%	.001*
	No	73	41.0%	8	22.2%	44	45.4%	21	46.7%	
	Don't know	32	18.0%	15	41.7%	11	11.3%	6	13.3%	
Under which category is esomeprazole selected in pregnancy?	A	28	15.7%	11	30.6%	15	15.5%	2	4.4%	.029*#
	B	82	46.1%	14	38.9%	44	45.4%	24	53.3%	
	C	60	33.7%	11	30.6%	31	32.0%	18	40.0%	
	D	8	4.5%	0	0.0%	7	7.2%	1	2.2%	
Do you think that the newer PPI will produce better and safer effects?	Yes	113	63.5%	24	66.7%	65	67.0%	24	53.3%	.382
	No	16	9.0%	2	5.6%	10	10.3%	4	8.9%	
	Don't know	49	27.5%	10	27.8%	22	22.7%	17	37.8%	

P: Pearson X2 test #: Exact probability test * P < 0.05 (significant)

Table 3: Awareness regarding PPI among physicians and pharmacists in primary health care centres, Abha, Saudi Arabia

Awareness items, continued		Total		Job title						p-value
				Physician		Pharmacist		Clinical pharmacist		
		No	%	No	%	No	%	No	%	
In which formula is PPI usually available?	Tablet	76	42.7%	20	55.6%	35	36.1%	21	46.7%	.036*
	Capsule	22	12.4%	8	22.2%	12	12.4%	2	4.4%	
	Injection	2	1.1%	0	0.0%	1	1.0%	1	2.2%	
	All	78	43.8%	8	22.2%	49	50.5%	21	46.7%	
PPI is usually prescribed	Before meals	157	88.2%	30	83.3%	88	90.7%	39	86.7%	.234
	After meals	9	5.1%	1	2.8%	4	4.1%	4	8.9%	
	It does not differ	12	6.7%	5	13.9%	5	5.2%	2	4.4%	
Should PPI be swallowed as a whole piece?	Yes	143	80.3%	29	80.6%	78	80.4%	36	80.0%	.088
	No	17	9.6%	2	5.6%	7	7.2%	8	17.8%	
	Don't know	18	10.1%	5	13.9%	12	12.4%	1	2.2%	
Is it advisable to increase the dose frequency rather than a single dose to improve effect?	Yes	68	38.2%	12	33.3%	36	37.1%	20	44.4%	.020*
	No	63	35.4%	7	19.4%	39	40.2%	17	37.8%	
	Don't know	47	26.4%	17	47.2%	22	22.7%	8	17.8%	
At least, the recommended duration to prescribed PPI for Helicobacter pylori eradication is?	1 week	9	5.1%	1	2.8%	4	4.1%	4	8.9%	.053
	2 weeks	83	46.6%	9	25.0%	52	53.6%	22	48.9%	
	4 weeks	68	38.2%	21	58.3%	31	32.0%	16	35.6%	
	Don't know	18	10.1%	5	13.9%	10	10.3%	3	6.7%	
Does PPI treatment of gastric ulcer take 2 to 3 weeks only?	Yes	83	46.6%	9	25.0%	52	53.6%	22	48.9%	.004*
	No	44	24.7%	10	27.8%	18	18.6%	16	35.6%	
	Don't know	51	28.7%	17	47.2%	27	27.8%	7	15.6%	
Long-term use of PPI can cause adverse reactions such as	Vitamin B12 deficiency	36	20.2%	7	19.4%	21	21.6%	8	17.8%	.017*
	Osteoporosis	40	22.5%	16	44.4%	16	16.5%	8	17.8%	
	Pneumonia	4	2.2%	1	2.8%	1	1.0%	2	4.4%	
	All of them	98	55.1%	12	33.3%	59	60.8%	27	60.0%	

P: Pearson X2 test

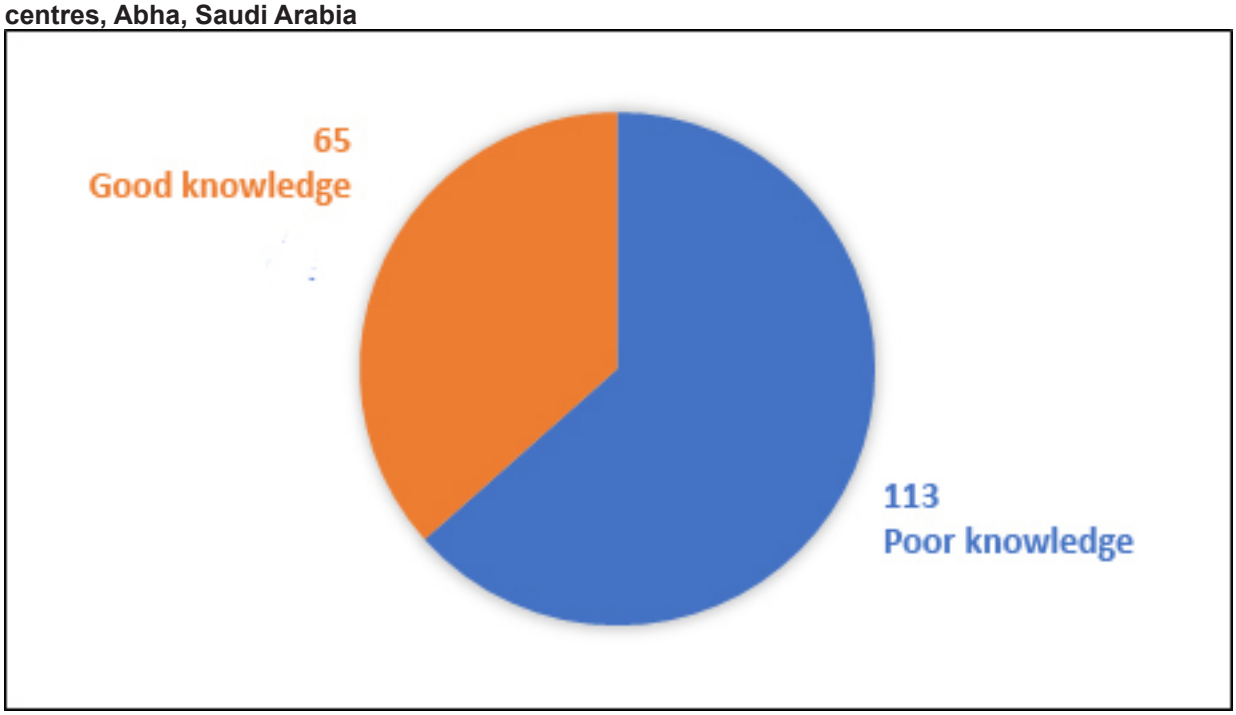
* P < 0.05 (significant)

Table 4: Distribution of overall awareness level regarding PPI by participants' personal data

Personal data	Overall knowledge level				p-value
	Poor		Good		
	No	%	No	%	
Age in years					
20-30	105	64.8%	57	35.2%	.240
31-40	7	50.0%	8	50.0%	
Gender					
Male	69	62.7%	41	37.3%	.790
Female	44	64.7%	24	35.3%	
Job title					
Physician	33	91.7%	3	8.3%	.001*
Pharmacist	55	56.7%	42	43.3%	
Clinical pharmacist	25	55.6%	20	44.4%	

P: Pearson X2 test * P < 0.05 (significant)

Figure 1: Overall awareness level regarding PPI among physicians and pharmacists in primary health care centres, Abha, Saudi Arabia



Discussion

The current study aimed to assess awareness level of physicians and pharmacists about PPIs and its detriments in PHCCs, Aseer region Saudi Arabia. The use of PPIs injections considerably increased over the past few years especially at the tertiary hospitals [12, 13]. Recently, studies showed that 86% of patients who received PPIs had no proper indications in the general medical ward of a tertiary Jordanian hospital [14]. Another study revealed that about 25% of the patients hospitalized in an internal medicine department of a tertiary Greek hospital received PPIs, with no significant indication among 81% of them [15].

Other studies showed that all patients undergoing elective surgeries were prescribed PPIs, but 82.4% of them had abandoned indication. Besides, 35.6% of inpatients were prescribed PPIs, of which 57% had no indications [12, 16]. This explains the importance of improving the knowledge of PPIs among the medical staff which is essential for improving the rationality of PPI application.

The current study revealed that only one third of the study participants were knowledgeable regarding PPIs and its applications. The highest awareness was mainly for its role in peptic ulcers as first line, types of prescribed PPIs, its role in stress ulcers, time of having PPI (before meals), and route of having PPIs. Its clear that more than three quarters of the study participants correctly reported the previously mentioned awareness issues. On the other hand, lower awareness was detected for PPI pharmacological nature, role in treating acute pancreatitis, interaction with other drugs, safety for paediatric prescription and during pregnancy, believe of newer PPIs safety, and duration of prescribing PPI for peptic ulcers and Helicobacter pylori eradication.

Our study also showed that higher awareness was detected among clinical pharmacists and community pharmacists than physicians who had very poor level of awareness (less than 10% were knowledgeable). Considering adverse reactions, the current study showed that more than half of the participants correctly know about osteoporosis, vitamin B12 deficiency, and pneumonia, while sporadic adverse reactions were reported by the other half especially vitamin B12 deficiency and osteoporosis. This match reported adverse events in the literature [17-19].

The current study findings were concordant with those findings reported by Luo et al [20], who reported that the awareness score related to PPI of medical staff was low (59.47 ± 15.75). Also, the level of awareness of pharmacist was significantly higher than that of doctors and nurses ($P < 0.01$), which was related to gender, age, occupation, educational level, professional title, hospital nature, and hospital grade. Another study in India estimated low level of awareness regarding PPI uses and adverse events among emergency care residents [21]. The later study showed that 30% of the residents prescribed acid suppressive drugs for majority of their patients, while 12% prescribed them to almost all patients they attended.

Locally, a study carried out in Jeddah, Saudi Arabia by Alnabulsi et al [22], who reported low level of physician's knowledge on PPI adverse effects and drug–drug interactions as only 20% of physicians reliably advised patients about the possible adverse effects. Also, 33% reported that they discontinued PPIs after reassessment. Gastroesophageal reflux disease and peptic ulcer disease were the most common indications for PPI use. On the other hand, Asdaq SM et al [23], assessed the knowledge, attitude, and behaviour of health care professionals of Riyadh region of Saudi Arabia on the use of PPIs. Authors reported high knowledge among both physicians and pharmacist (68.5% and 66%, respectively) and good attitude towards PPI use compared to nurses. This estimated knowledge level is higher than the current study estimates.

Lack of awareness of these healthcare staff regarding the relevant knowledge of PPI, such as drug characteristics, pharmacological action, mechanism, indication, administration time, administration method, duration, drug interaction and adverse reaction, it is easy to cause overuse of PPIs, decrease efficiency and increase adverse reactions. But only few studies focused on the awareness of PPI topics in medical staff. Consequently, reference to the current situation and possible causes of PPI overutilization in Saudi Arabia [24].

Conclusions and Recommendations

In conclusion, the current study showed that medical staff in the primary healthcare centres had moderately low knowledge regarding PPIs and their indications. The lowest awareness was mainly among physicians when compared to pharmacists, especially clinical pharmacists. Awareness was high regarding PPI types, indications, and adverse events. However, the awareness regarding drug-drug interaction, duration of prescribing the drugs, and drug safety for some categories issue needs improvement. Improving medical staff level of knowledge and minimizing their dependence on PPIs are recommended. To reduce the extensive misuse of PPI, recurrent professional development programs and trainings for healthcare professionals are required. Furthermore, prescribing guidelines must be developed for PPI reassessment and step-down strategies to ensure good practice.

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Knowledge, Attitude and Practice of Non-Psychiatric Physicians about Addiction

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Abstract

Objective: To evaluate non-psychiatric physicians' knowledge, attitude and practices regarding management of cases with addiction.

Subjects and Methods: Following a cross-sectional study, 126 non-psychiatric physicians in Aseer Region were interviewed. A study questionnaire was used for data collection. It included socio-demographic data; general attitudes and interest toward addictions, addiction psychiatry; knowledge about addictions, addictive disorders, including treatment, and practice about addictions, addictive disorders, and treatment. The survey was anonymously self-administered and participant physicians were asked to provide their written informed consent to participate in this study. Data were collected through direct interviews with physicians.

Results: Age of participants ranged from 26 to 66 years (Mean±SD: 37.1±9.1 years). Most participants (81%) were males. Only 9.5% attended a training course or a conference on management of addiction, while 12.7% attended training or a course on palliative care. Generally, participants had very low knowledge regarding management of addiction, especially maintenance daily doses of Buprenorphine and Methadone and their overdose (4.8%, 12.7% and 7.9%, respectively). Regarding positive attitude statements, the least agreed upon were "illicit drugs addicts are easy patients"; and "being at ease in working with persons with heroin addiction" (11.1%, and 14.3%, respectively), while the highest agreed upon negative statements were "deficient resources to treat drug-dependent patients"; and "need to have more training on addiction management" (82.5% and 69.8%, respectively). Acute or chronic pain crises were the most common addiction-related conditions managed by participant physicians (39.7% and 31.7%, respectively). Cases of substance-induced psychosis were managed by 12.7% of participant physicians. The most commonly prescribed drugs for patients with addiction-related conditions were morphine, fentanyl, tramadol and pregabalin (44.4%, 19% 19%, and 17.5% respectively).

Conclusions: Non-psychiatric physicians in Aseer Region have insufficient knowledge, negative attitude and poor practice about psychoactive substance use disorders. Continuing medical education and training is necessary to promote physicians' knowledge and practices related to prevention and treatment strategies for addiction diseases.

Key Words: Addiction, psychoactive substance use disorders, knowledge, attitude, practice, non-psychiatric physicians

Introduction

There is a compelling need for treatment of psychoactive substance use disorders. However, physicians appear poorly or neither trained, nor especially eager to accept/tolerate patients with psychoactive substance use disorders (1-2). In general, physicians, including psychiatrists do not feel competent/confident in treating addiction disorders, do not like working with patients affected with psychoactive substance use disorders and do not find rewarding treating patients with psychoactive substance use disorders (3).

The current Diagnostic and Statistical Manual-5th edition (DSM-5) (4) amalgamated the abuse and dependence under a single category named "Substance Use Disorder". The lack of experience and/or inadequate (theoretical and practical) training in addiction psychiatry may indeed result in an endless loop of incompetence and neglect regarding the addiction psychiatry, amongst mental health care professionals. However, despite the evidence demonstrating the need to improve addiction medicine's training not only amongst psychiatry trainees but also amongst all physician trainees, most medical students generally receive an inadequate (practical and theoretical) training in the field of addiction medicine/psychiatry (5).

Moreover, most physicians generally display lacking core clinical and therapeutic competences, as required for working with patients with psychoactive substance use disorders. Although formal addiction training within the medical field has been closely tied to psychiatry, psychiatric training generally provides a poor improvement and a limited level of knowledge over medical school, regarding addictions (6).

There are several inequalities and heterogeneous training levels in addiction psychiatry. Furthermore, most physicians reported to be less skilled in the addiction field, compared to other fields of psychiatry. Interestingly, there are not statistically significant differences between physicians regarding this finding. This appears particularly relevant if we consider that physicians should possess a comprehensive experience including behavioral, psychosocial and addiction problems (7).

Psychiatrists and non-psychiatry physicians' attitudes toward patients with psychoactive substance use disorders largely differ across different cultures. People with psychoactive substance use disorders are generally more exposed to health professionals' negative attitudes/perception as well as stigmatizing behaviors, and language (1).

Stigmatizing behaviors and attitudes displayed by physicians may lead to inadequate and inhomogeneous physical, mental healthcare and treatment, including prescribing non-evidence-based pharmacological/non pharmacological treatments, prescribing an inadequate/insufficient posology and duration of therapy. Moreover, use of potentially stigmatizing language may lead mental health professionals to poor/inadequate communication with their patients, displaying an overall judgmental and non-empathetic attitude, and other problematic and potentially stigmatizing behaviors (8-10).

Therefore, the present study aimed to evaluate non-psychiatric physicians' knowledge, attitude and practices regarding management of cases with addiction.

Subjects and Methods

Following a cross-sectional study design, the present study included a sample of 126 non-psychiatric physicians in Aseer Region. A study questionnaire adapted from the study of Orsolini et al. (4) was used for data collection. It includes the following parts:

- General socio-demographic variables;
- Knowledge about addictions, addictive disorders, including treatment;
- General attitudes and interest toward addictions, addiction psychiatry; and
- Practice about addictions, addictive disorders, and treatment

The ethical approval for this study was granted by the General Health Directorate Ethics Committee in Aseer Region. The survey was anonymously self-administered and participant physicians were asked to provide their written informed consent to participate in this study.

Data were collected through online Google Forms that were emailed to non-psychiatric physicians within Aseer Region. Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 25, IBM Corp, Armonk NY). Variables were presented as frequency and percentages.

Results

Table (1) shows that age of participants ranged from 26 to 66 years, with age of 20.6% being less than 30 years, while age of 61.9% was 30-39 years, and their mean±SD was 37.1±9.1 years. Most participants (81%) were males. About one-third of physicians (34.9%) were MBBS qualified, while 49.2% were Doctorate/Fellowship qualified. More than half of participants (55.6%) were graduated since less than 10 years. Most participants were family physicians (39.7%), or general surgeons (28.7%). Only 9.5% attended a training course or a conference on management of addiction, while 12.7% attended training or a course on palliative care.

Table (2) shows that participant physicians had very low correct responses regarding maintenance daily doses of Buprenorphine and Methadone and their overdose (4.8%, 12.7% and 7.9%, respectively), group psychotherapy (6.3%), Cannabis use (12.7%), contraindications for opioid substitution treatment and Disulfiram-like reaction (14.3% for both).

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Table (3) shows that regarding positive attitude statements, the least agreed upon were that “illicit drugs addicts are easy patients”; “being at ease in working with persons with heroin addiction”; “working in management of addiction”; and “being prepared to deal with addicts” (11.1%, 14.3%, 33.3% and 33.3%, respectively). On the other hand, the highest agreed upon negative statements were “deficient resources to treat drug-dependent patients”; “need to have more training on addiction management”; “having bad experiences with addicts is common”; “the need for training in addiction” and “it is frustrating to work with drug addicted patients” (82.5%, 69.8%, 65.1%, 63.5%, and 60.3%, respectively).

Table (4) shows that acute or chronic pain crises were the most common addiction-related conditions managed by participant physicians (39.7% and 31.7%, respectively). Cases of substance-induced psychosis were managed by 12.7% of participant physicians. The most commonly prescribed drugs for patients with addiction-related conditions were morphine, fentanyl, tramadol and pregabalin (44.4%, 19%,19%, and 17.5% respectively).

Table 1: Personal characteristics of participant physicians

Personal characteristics	No.	%
Age groups		
• <30 years	26	20.6
• 30-39 years	78	61.9
• ≥40 years	22	17.5
• Range	26-66 years	
• Mean±SD	37.1±9.1 years	
Gender		
• Male	102	81.0
• Female	24	19.0
Qualification		
• MBBS	44	34.9
• Diploma	2	1.6
• Master	16	12.7
• Doctorate/Fellowship	62	49.2
• Others	2	1.6
Years since graduation		
• <10 years	70	55.6
• 10-19 years	40	31.7
• 20+ years	16	12.7
Specialty		
• Family medicine	50	39.7
• General surgery	36	28.7
• Internal medicine	12	9.6
• Orthopedic Surgery	8	6.4
• Diabetology	4	3.2
• Obstetrics & gynecology	4	3.2
• Dermatology	4	3.2
• General practice	2	1.6
• Radiology	2	1.6
• Others	4	3.2
Attending a training course/conference on management of addiction	12	9.5
Attending a training course/conference on palliative care	16	12.7

Table 2: Correct responses of non-psychiatric physicians regarding their knowledge about addiction

Knowledge statements	No.	%
Drug dependence patients are at high risk for medical disorders	104	82.5
Patients with drug dependence tend to be poly-abusers	100	79.4
Psychosocial interventions can be considered when handling addiction patients	100	79.4
Cannabis use is associated with increased risk for psychosis	98	77.8
Indication for treatment with Naloxone	88	69.8
Patients with drug dependence may have other mental disorders	86	68.3
Males have more addiction problems than females	78	61.9
Opioid withdrawal syndrome can be fatal	74	58.7
Delirium tremens is a potentially fatal condition	72	57.1
Injection rooms are necessary in a harm reduction program	68	54.0
Buprenorphine is essential for opioid withdrawal and maintenance treatment	60	47.6
Methadone is essential medicine for opioid withdrawal/maintenance treatment	52	41.3
Opioid agonist maintenance therapy reduces the risk of contracting HIV	50	39.7
Treatment of addiction is based on empirical evidence	46	36.5
Indications for treatment with flumazenil	38	30.2
Frequency of Methadone administration	34	27.0
Frequency of Buprenorphine administration	24	19.0
Opioid agonist maintenance therapy does not reduce drug use	20	15.9
Contraindications for opioid substitution treatment	18	14.3
Disulfiram-like reaction	18	14.3
Cannabis use is associated with increased risk for deaths	16	12.7
Overdose of Buprenorphine and Methadone	16	12.7
Maintenance daily dose of Methadone	10	7.9
Group psychotherapy is preferred in treating addiction	8	6.3
Average maintenance daily dose of Buprenorphine	6	4.8

Table 3: attitude of participants regarding management of substance use

Attitude statements	Disagree		Neutral		Agree	
	No.	%	No.	%	No.	%
Positive attitude statements:						
It is important to have knowledge about use of substances	4	3.2	20	15.9	102	81.0
The problem of addiction is an important issue	4	3.2	22	17.5	100	79.4
I want to have knowledge about harm reduction programs	0	0.0	30	23.8	96	76.2
Addictions must be treated in health systems	6	4.8	26	20.6	94	74.6
Treatment of substance abuse worth the effort	8	6.3	24	19.0	90	71.4
I often ask my patients about their toxicological history	12	9.5	36	28.6	78	61.9
I am prepared to deal with addicted patients	28	22.2	56	44.4	42	33.3
I like to work in management of addiction	44	34.9	40	31.7	42	33.3
I am at ease in working with persons with heroin addiction	64	50.8	44	34.9	18	14.3
Illicit drugs addicts are easy patients	80	63.5	32	25.4	14	11.1
Negative attitude statements:						
I think that people with drug addiction cannot recover	90	71.4	18	14.3	18	14.3
Licit drugs addicted are bad people	76	60.3	26	20.6	24	19.0
I am afraid to work with persons with drug abuse	50	39.7	28	22.2	48	38.1
I am not confident with my skills to work in addiction	30	23.8	42	33.3	54	42.9
It is frustrating to work with drug addicted patients	14	11.1	56	44.4	56	44.4
I avoid addiction patients and I always refer them	20	15.9	30	23.8	76	60.3
I need training in addiction for my clinical practice	12	9.5	34	27.0	80	63.5
It is common to have bad experiences with addicts	8	6.3	36	28.6	82	65.1
I would like more training on addiction management	10	7.9	28	22.2	88	69.8
I lack the resources to treat drug-dependent patients	4	3.2	18	14.3	104	82.5

Table 4: Addiction-related managed cases and prescribed drugs during the last year by non-psychiatric physicians in Aseer Region, Saudi Arabia

Practices	No.	%
Addiction-related conditions managed during last year:		
• Acute pain crisis	50	39.7
• Chronic pain crisis	40	31.7
• Substance-induced psychosis	16	12.7
• Alcohol	10	7.9
• Opioid withdrawal syndrome	8	6.3
• Delirium tremens	6	4.8
Prescribed drugs to addicts during last year:		
• Morphine	56	44.4
• Fentanyl	24	19.0
• Tramadol	24	19.0
• Pregabalin	22	17.5
• Methadone	10	7.9
• Naltrexone	8	6.3
• Buprenorphine	2	1.6

Discussion

Historically, psychoactive substance use disorders have been perceived as personal, family, social, moral, or criminal issues rather than a health condition. Therefore, it has been assumed that subjects with psychoactive substance use disorders can be better managed at the individual, family or justice level (4).

Findings of this study revealed several points of knowledge deficiency among participant physicians' regarding management of addiction, especially contraindications for opioid substitution treatment, daily doses and overdoses of drugs for treatment of opioids, especially those of Buprenorphine and Methadone, knowing about group psychotherapy, Cannabis use and Disulfiram-like reaction.

Insufficient knowledge of physicians about management of addiction may be explained by that only 9.5% of participants attended a training course or a conference on management of addiction, and only 12.7% of them attended a course or a conference on palliative care.

Although health problems related to substance use disorders are a source of frequent consultation for physicians in daily clinical practice (11), their knowledge about its diagnosis and management remains largely inadequate (12). Several studies demonstrated the need for postgraduate continuing medical education to improve addiction medicine's training amongst all physicians, since most undergraduate medical students and trainees generally receive inadequate (theoretical and practical) training in the fields of psychiatry and addiction medicine. Moreover, it has been reported that just 1% of the typical medical school curricula are devoted to this subject (5-6). Therefore, physician's training programs should be developed to promote their knowledge about diagnosis and management of psychoactive substance use disorders (11).

The present study showed low positive attitude and high negative attitude among participants toward management of addict patients.

Patients with psychoactive substance use disorders tend to be stigmatized due to their use of drugs and drug-seeking behaviors. Moreover, psychoactive substance use disorders-related risky behaviors, e.g, speeding/dangerous driving, violence, aggressiveness, and impulse dysregulation, are seen as part of a complex disorder. Therefore, patients with psychoactive substance use disorders are usually rejected by the society due to the supposed moral valence of these behaviors. These patients may also be seen as a burden for the healthcare system, by indeed increasing the disparities of care, and the risk of not adequately providing evidence-based and effective treatments (10-13).

Previous studies have shown highly negative attitudes among physicians' and medical students' toward dealing with addiction cases in several settings (such as primary care centers, general medicine or specialized clinics) (9). Van Boekel et al. (1) reported on the experienced stigma toward patients with addiction problems among health professionals, in which they underscore the negative consequences of these attitudes. However, Karam-Hage et al. (14) reported that residents acquired positive attitudes with perceived responsibility and improved satisfaction regarding addiction treatment after an educational conference had been carried out.

Our study revealed poor practice among non-psychiatric physicians regarding management of psychoactive substance use disorders. During the past year, only 12.7% of participant physicians managed substance-induced psychosis cases. The most commonly prescribed drugs for those patients were morphine, fentanyl, tramadol and pregabalin.

Surveys of physicians also consistently show that most fail to screen for alcohol or drug addiction. Many believe that medical interventions are inappropriate and ineffective. Those who do see addiction as a medical problem tend to treat it as an acute, instead of chronic, disorder. However, Miller and Sheppard (15) emphasized that the role of physicians in the prevention and treatment of addictive disorders is growing in importance and magnitude. The public and managed care organizations are increasingly looking to physicians for leadership and advocacy for patients who have drug and alcohol addiction. The political climate and enormous need combine to make the physicians' practices essential within prevention and treatment strategies for addiction diseases.

Conclusions

Non-psychiatric physicians in Aseer Region have insufficient knowledge, negative attitude and poor practice about psychoactive substance use disorders. Continuing medical education and training is necessary to promote physicians' knowledge and practices related to prevention and treatment strategies for addiction diseases.

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Risk Factors for Diabetic Ketoacidosis among Type 1 Diabetic Children Registered at "Heraa Diabetes Center" in Makkah Al-Mokarramah City, Saudi Arabia

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Abstract

Aim of Study: To assess risk factors associated with DKA among T1DM children registered at "Heraa Diabetes Center", Makkah Al-Mokarramah City, Saudi Arabia.

Patients and Methods: A retrospective hospital-based, case-control research design was followed and included 375 diabetic patients aged less than 15 years. The "Study Group" included 125 children who had a past history of diabetic ketoacidosis (DKA Group), while the "Control Group" comprised 250 diabetic children who did not have past history of DKA. A data collection sheet was designed by the researchers.

Results: There was significantly more positive family history in the DKA group than the control group (78.4% and 68%, respectively, p=0.036). The mothers were the main person who injects the child. Differences between both study groups according to the person who injects the child was statistically significant (p=0.029). DKA occurred more than once in 59.2% of diabetic children, and in 46.4% of children with over-activity. The main presenting symptoms of DKA were polyuria, thirst and vomiting. The main causes and triggering factors were eating too many sweets (65.6%), missing blood sugar monitoring (57.6%), omitting the insulin dose (22.4%), or infection (12.8%). Children in the control group were significantly more compliant than those in the DKA group regarding daily measurement of blood sugar (82.8% and 71.2%, respectively, p=0.009), timely receiving treatment (96% and 82.4%, respectively, p<0.001), following a healthy diet (79.6% and 65.6%, respectively, p=0.003), and receiving health education (95.2% and 88%, respectively, p=0.011).

Conclusions: Risk factors for DKA include positive family history of diabetes, and less educated or employed mothers, but its incidence is lower among children of parents with health-related jobs. It can be triggered by over-activity. It is caused by eating too many sweets, missing blood sugar monitoring, omitting the insulin dose, or infection. Noncompliance is associated with higher incidence of DKA.
Recommendations: All parents of diabetic children should receive health education and be trained about management of diabetes, compliance to diabetes management, continuous monitoring of glucose levels, and early manifestations of DKA.

Key Words: Diabetic ketoacidosis, Type 1 diabetes, Children, Risk factors, Compliance, Saudi Arabia.

Introduction

Type 1 diabetes mellitus (T1DM) is the most common endocrine-metabolic disorder during childhood and adolescence (1), with increasing prevalence worldwide (2). One of its serious acute complications, ketoacidosis (DKA) accounts for most hospitalizations in cases of severe insulin deficiency (3). It comprises the biochemical triad of ketonemia, hyperglycemia and acidemia (4).

Although major advances have been achieved in the fields of care for diabetic patients, the incidence of DKA is still increasing (5), and it continues as a significant cause for morbidity and mortality (6). Frequently, it is the main presenting symptom for new-onset cases in 25-30% of T1DM cases (7).

Several risk factors for DKA have been reported. In Al-Baha, Saudi Arabia, Satti et al. (1) noted that the 74% of their admitted children with DKA had positive family history of diabetes. Vakharia et al. (8) noted that awareness that a positive family history of DM is associated with a higher risk for recurrence of DKA among diabetic children will allow for improved identification of patients who may be at risk for DKA recurrence and the education of their parents to prevent complications of DKA.

Pulungan et al. (9) emphasized that lack of parental knowledge on management of type 1 diabetes is significantly associated with non-compliance, and causes omission of insulin and failure of insulin dose adjustment. Acute infections, especially pneumonia and urinary tract infections, constitute the most common precipitating factor for DKA (10). In Jeddah, Saudi Arabia, Qari (11) showed that poor compliance was the most common precipitating factor for DKA (54.4%), followed by infections (28%).

Generally, clinical presentations of DKA develop rapidly, usually within a period of less than 24 hours. A few days before its development, certain symptoms may develop, such as polydipsia, polyuria, and rapid loss of weight. Moreover, abdominal pain and severe vomiting may occur (12).

Physical examination of a patient with DKA shows signs of dehydration, e.g., loss of skin turgor, dry mucous membranes, tachycardia, and hypotension. Mental status can vary from full alertness to loss of consciousness. Most patients are normothermic or even hypothermic at presentation. However, fever may be associated with infections. Acetone on breath and labored Kussmaul respiration may also be present on admission, particularly in patients with severe metabolic acidosis (13).

Although the diagnosis of DKA can be suspected on clinical grounds, confirmation is usually based on laboratory tests. The most widely used diagnostic criteria for DKA were blood glucose levels more than 250 mg/dL, a moderate degree of ketonemia, serum bicarbonate less than 15 mEq/l, arterial pH less than 7.3, and an increased anion gap metabolic acidosis (13). The assessment of ketonemia is usually performed by the nitroprusside reaction. Direct measurement of β-hydroxybutyrate is currently available by finger stick method, which is a more accurate indicator of DKA (14).

The primary fatal complication of DKA is cerebral edema. Moreover, vascular, musculoskeletal, pulmonary, gastrointestinal, and cognitive complications of DKA may rarely occur, but can result in acute and long-term morbidity (15).

The prevention of DKA can be successfully done by better access to medical care, proper health education, and effective communication with a health care provider during an intercurrent illness. Involvement of family members should be encouraged. They need to be educated on insulin regimen and how to perform measurements of blood glucose. Also, a written care plan should be provided to the patient and/or caregiver, as this enhances understanding and emphasizes the importance of self-management of diabetes (16). Moreover, advances in technology have provided more efficient means of monitoring and maintaining glycemic control in an outpatient setting (17-18).

Study rationale

DKA is the most severe health problem among diabetic children (19). It is typically caused by treatment non-compliance, (e.g., shortage of insulin), and may be precipitated by other factors, (e.g., infections). Although it can be a life-threatening event for T1DM children, it is a preventable condition (20). Despite the severity of DKA, research examining this event is still limited in the empirical literature (21). Therefore, the identification of magnitude of DKA and its associated risk factors is a pressing necessity.

Aim of Study

To assess risk factors associated with DKA among T1DM children registered at “Heraa Diabetes Center”, Makkah Al-Mokarramah City, Saudi Arabia.

Study Objectives

- To identify the pattern of DKA among T1DM children registered at Heraa Diabetes Center, Makkah Al-Mokarramah City, Saudi Arabia.
- To assess risk factors associated with DKA among T1DM children registered at Heraa Diabetes Center, Makkah Al-Mokarramah City, Saudi Arabia.
- To explore the association between compliance of T1DM children with occurrence of DKA.

Patients and Methods

A retrospective hospital-based, case-control research design was followed at "Heraa Diabetes Center", Makkah Al-Mokarramah City, Saudi Arabia. The study population included children with T1DM (ICD-10: E10.9), aged less than 15 years, who were registered at the study setting.

Based on patients' records, the "Study Group" (i.e., DKA Group) comprised T1DM patients who had past history of being hospitalized at least once for DKA, while the "Control Group" comprised T1DM patients who have not been previously hospitalized for DKA.

The minimum sample size for this study was decided according to Dahiru et al. (22), as follows:

$$n = \frac{Z\alpha^2 \text{ X } P \text{ X } Q}{D^2}$$

where:

- n: Calculated sample size
- $Z\alpha$: The z-value for the selected level of confidence $(1-\alpha) = 1.96$.

P: The estimated proportion of T1DM children with a history of DKA (assumed to be 0.3).

- Q: (1 – P), i.e., 0.7.
- D: The maximum acceptable error = 0.05.

$$n = \frac{(1.96)^2 \text{ X } 0.3 \text{ X } 0.7}{(0.05)^2} = 323$$

Therefore, the calculated minimum sample size was 323 T1DM children. However, the study sample included a total of 375 T1DM children, 125 in the "DKA Group" and 250 in the "Control Group", i.e., 1:2 ratio.

Study tool

Based on relevant literature, a data collection sheet was designed by the researchers. It included the following parts:

• Parent's personal data (independent variables): Age, educational level, occupation, family monthly income, and family history of diabetes.

• Diabetic child's data (independent variables): Age, gender, nationality, duration of diabetes, daily blood sugar monitoring, compliance to diet, treatment and healthcare visits, and receiving health education.

• Risk factors for DKA and previous hospitalization data (dependent variables): Frequency of hospitalization, precipitating and risk factors for DKA, symptoms of DKA, and home management of DKA.

The face validity of the data collection tool was verified by two Family Medicine consultants and one Diabetology consultant. Construct and content were validated using statistical analysis of the pilot study results (using Principal Components Analysis).

Pilot study

A pilot was conducted on data from files of 30 T1DM children at the study setting. The objective of the pilot study was to test the availability of the independent and dependent variables within the patients' record files. Internal consistency of the study questionnaire was assessed by Cronbach's alpha coefficient (α=0.79). Data collected within the pilot study was not included in the main study.

Data collection

During the period from January to April 2021, the researchers paid daily visits to Heraa Diabetes Center. Patients' files of T1DM children were consecutively reviewed by the researchers. All relevant data were recorded into the data collection sheet. The data of the most recent 125 T1DM children with previous history of DKA were included in the "DKA group". For each T1DM child with past history of DKA included in the DKA Group, two control children (with no history of DKA) were included in the "Control Group". Therefore, the total study sample included 375 children with T1DM, 125 with a past history of DKA and 250 with no past history of DKA.

Statistical analysis

Collected data were verified prior to computerized data entry and analysis using the Statistical Package for Social Sciences (IBM, SPSS version 25). Descriptive statistics were applied (frequency and percentage). The $\chi 2$-test was to compare the study groups and to identify potential risk factors for DKA. P-values less than 0.05 were considered as statistically significant.

Ethical and administrative considerations

All necessary official approvals were secured by the researchers prior to data collection. Collected data were kept confidential.

Funding and Budget

This study was completely self-funded.

Results

Table (1) shows that most type 1 diabetic children in the control and DKA groups were aged 5-10 years (58.4% and 60.8%, respectively). There was no significant difference between both study groups according to their age. Females were significantly more among the cases group than the control group (58.4% and 47.2%, respectively, p=0.041). The educational level of about half of fathers of type 1 diabetic children in the control and DKA groups was university level (44% and 53.6%, respectively). There was no significant difference between both study groups according to their father's education. The educational level of mothers in the control group was higher than the DKA group with more university educated mothers in the control group than the DKA group (52% and 39.2%, respectively, p=0.023). There were significantly more fathers with health-related jobs among the control group than the DKA group (20% and 17.6%, respectively, p<0.001). Similarly, there were significantly more mothers with health-related

jobs among the control group than the DKA group (23.2% and 20.8%, respectively, p=0.014). The monthly family income of almost half of type 1 diabetic children in the control and DKA groups was <10,000 SR (47.2% and 48.8%, respectively). There was no significant difference between both study groups according to their family monthly income.

Table (2) shows that the duration of diabetes among type 1 diabetic children in both control and DKA groups, was mainly 1-5 years, (62.4% and 60%, respectively). There was no significant difference between both study groups according to their duration of diabetes. There was significantly more positive family history in the DKA group than the control group (78.4% and 68%, respectively, p=0.036). Regarding the person who injects insulin to the diabetic child, almost half of the children in the control group received insulin injection from their mothers (48.8%), compared with 39.2% in the DKA group. Moreover, 14.8% of children in the control group used to inject themselves, compared with 27.2% in the DKA group. Differences between both study groups according to the person who injects the child was statistically significant (p=0.029).

Table (3) shows that DKA occurred more than once in 59.2% of type 1 diabetic children in the DKA group. DKA occurred in almost half of children (46.4%) with over-activity (e.g., after running or playing). The main presenting symptoms associated with DKA were polyuria, thirst and vomiting (36.8%, 23.2%, and 20.8%, respectively). Before going to hospital, 24% of children with DKA received their medication, 35.2% drank much water, while 40.8% received nothing. The main causes and triggering factors for DKA were eating too many sweets (65.6%), missing blood sugar monitoring (57.6%), omitting the insulin dose (22.4%), or infection (12.8%).

Table (4) shows that children in the control group were significantly more compliant than those in the DKA group regarding daily measurement of blood sugar (82.8% and 71.2%, respectively, p=0.009), their timely receiving of treatment (96% and 82.4%, respectively, p<0.001), following a healthy diet (79.6% and 65.6%, respectively, p=0.003), and receiving health education (95.2% and 88%, respectively, p=0.011). However, there was no significant difference between both study groups regarding regular visits to the diabetes clinic.

Table 1: Demographic characteristics of diabetic children

Characteristics	Control (n=250)		DKA (n=125)		P-value
	No.	%	No.	%	
Age of child					
• <5 years	67	26.8	38	30.4	
• 5-10 years	146	58.4	76	60.8	
• >10 years	37	14.8	11	8.8	0.245
Gender					
• Male	132	52.8	52	41.6	
• Female	118	47.2	73	58.4	0.041
Nationality					
• Saudi	220	88.0	108	86.4	
• Non-Saudi	30	12.0	17	13.6	0.659
Father's education level					
• Primary/Intermediate	20	8.0	7	5.6	
• Secondary	120	48.0	51	40.8	
• University	110	44.0	67	53.6	0.198
Mother's education level					
• Primary/Intermediate	30	12.0	26	20.8	
• Secondary	90	36.0	50	40.0	
• University	130	52.0	49	39.2	0.023
Current father's job					
• Healthcare-related	50	20.0	22	17.6	
• Not healthcare-related	190	76.0	82	65.6	
• Retired	10	4.0	21	16.8	<0.001
Current mother's employment					
• Healthcare-related	58	23.2	26	20.8	
• Not healthcare-related	71	28.4	54	43.2	
• Housewife	121	48.4	45	36.0	0.014
Family monthly income					
• <10,000 SR	118	47.2	61	48.8	
• 10,000-20,000 SAR	102	40.8	54	43.2	
• >20,000 SAR	30	12.0	10	8.0	0.173

Table 2: Clinical characteristics of patients in the control and DKA groups

Characteristics	Control (n=250)		DKA (n=125)		P value
	No.	%	No.	%	
Duration of diabetes					
• < One year	21	8.4	13	10.4	
• 1-5 year	73	62.4	75	60.0	
• >5 years	73	29.2	37	29.6	0.798
Family history of diabetes					
• Yes	170	68.0	98	78.4	
• No	80	32.0	27	21.6	0.036
Who injects insulin to the child‡					
• The mother	122	48.8	49	39.2	
• The father	68	27.2	30	24.0	
• The diabetic child	37	14.8	34	27.2	
• Someone else	38	15.2	16	12.8	0.029

‡ More than one person can be stated

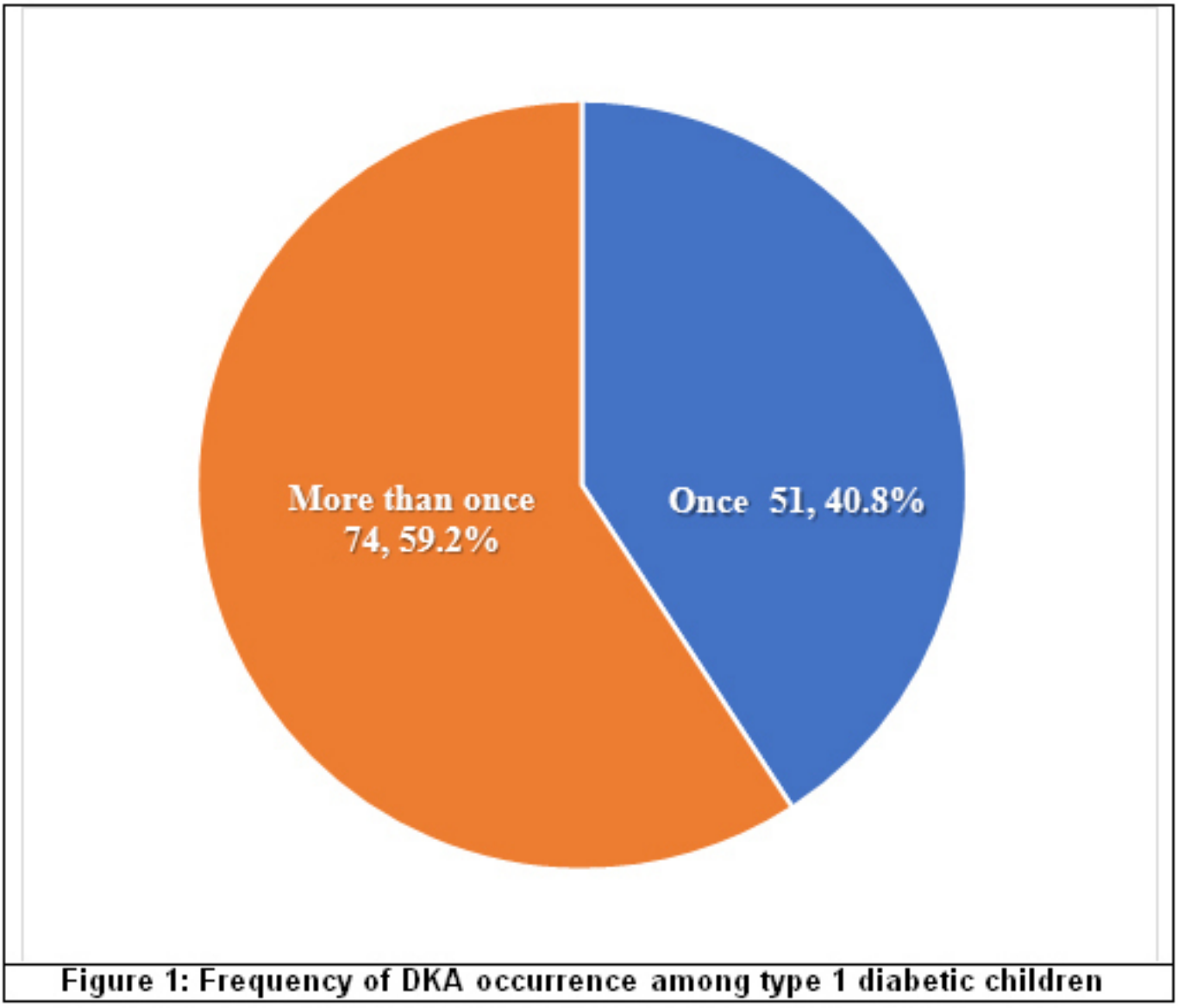

Figure 1: Frequency of DKA occurrence among type 1 diabetic children

Table 3: Characteristics of ketoacidosis among DKA group (n=125)

Characteristics	No.	%
First presentation of diabetes	13	10.4
Frequency of DKA episodes		
• Once	51	40.8
• More than once	74	59.2
Child's level of activity before DKA		
• Sleeping	33	26.4
• Sitting	34	27.2
• Overactivity (e.g., Running/Playing)	58	46.4
Main presenting symptoms associated with DKA		
• Polyuria	46	36.8
• Excessive thirst	29	23.2
• Persistent vomiting	26	20.8
• Colic	16	12.8
• Fever	16	12.8
• Others	13	10.4
Pre-hospital home management		
• Giving medications	30	24.0
• Drinking much water	44	35.2
• Nothing	51	40.8
Causes and triggering factors for DKA		
• Receiving sweets	82	65.6
• Missing blood sugar daily monitoring	72	57.6
• Omission of insulin injection	28	22.4
• Infection	16	12.8

Table 4: Compliance of type 1 diabetic children in the control and DKA groups

Characteristics	Control (n=250)		DKA (n=125)		P-value
	No.	%	No.	%	
Daily measurement of blood sugar					
• Yes	207	82.8	89	71.2	
• No	43	17.2	36	28.8	0.009
Timely receiving treatment					
• Yes	240	96.0	103	82.4	
• No	10	4.0	22	17.6	<0.001
Regular visits to diabetes clinic					
• Yes	220	88.0	102	81.6	
• No	30	12.0	23	18.4	0.094
Following a healthy diet					
• Yes	199	79.6	82	65.6	
• No	51	20.4	43	34.4	0.003
Receiving health education					
• Yes	238	95.2	110	88.0	
• No	12	4.8	15	12.0	0.011

Discussion

Findings of the present study revealed that in the DKA Group, DKA was the first presentation of their diabetes in 10.4% of children. In addition, more than half of children (59.2%) experienced several DKA episodes.

Incidence of a DKA episode as the first presentation of T1DM in our study is less than that reported by Szypowska et al. (23) in Poland, and Jefferies et al. (24), in New Zealand, who found that about one-quarter of T1DM children presented with DKA at their first diagnosis. A much higher incidence of DKA episodes was reported by Onyiriuka and Ifebi (25) in Nigeria, where about three-quarterss of diabetics presented with DKA.

Differences in reported incidence of DKA as the first presentation of T1DM may reflect variable awareness levels among parents and primary care physicians about early monitory symptoms for recognition of T1DM. Therefore, a higher incidence of DKA at first diagnosis of T1DM reflects poorer awareness and less consciousness about early diagnosis of T1DM among children.

In agreement with our findings, Al-Hayek et al. (26) reported that 45.6% of T1DM Saudi adolescents in Riyadh City had several DKA episodes. Fazeli Farsani et al. (27) noted that worldwide incidence of DKA ranges from 8 to 51.3 cases/1000 patient-years. However, Li et al. (28) in China, reported a higher incidence rate (i.e., 263/1,000 patient-years).

The variation in incidence rates of DKA has been explained by differences in national health care systems, with limited access to routine health care for T1DM and the infrequent self-monitoring of blood glucose (27). Several epidemiological studies have reported that hospitalization for DKA has increased worldwide (29), probably due to increased admissions for mild DKA cases (30).

Therefore, in order to minimize the incidence of DKA, it is important to raise parents' awareness regarding premonitory symptoms and signs for diabetes and DKA and the pressing need to facilitate prompt access to health care.

Our study revealed that significant risk factors for DKA among T1DM children included being a girl, in addition to mothers' lower educational level, an employed mother and a positive family history of diabetes. On the other hand, having a parent with a healthcare-related job and the mother being the one who injects insulin to her child proved to be a prophylactic factor.

In agreement with our findings, Neu et al. (31), in Germany, reported that DKA is frequently higher among girls than boys. In Saudi Arabia, several studies reported similar results. In Al-Madina Region, Hamed (32), reported a higher incidence of DKA among females than males (58.7% and 41.3%, respectively). Satti et al. (1), in Al-Baha, reported a female:male ratio of 1.22:1. Also Zahib et al. (33), in Abha City, reported higher DKA incidence among females than males, but the difference was not statistically significant.

In Korea, Lee et al. (34) reported that low parental education is a significant factor for DKA severity. Similarly, in Iraq, Al-Obaidi et al. (35) noted that higher educational levels of parents were associated with lower frequency of DKA among their children with T1DM.

Parents' educational status, especially that of the mother, seems to be positively associated with having better awareness regarding diabetes and its complications among their children. This can be reflected in earlier diagnosis and management of T1DM and better watchful, preventive and nursing care, e.g., timely injecting of insulin. This may explain why children of busy employed mothers have higher incidence of DKA¸ and T1DM children of parents with jobs related to healthcare have less incidence of DKA.

In agreement with our findings, several studies confirmed the significant association between occurrence of DKA and the positive family history of diabetes. Alhomood et al. (36), in Abha, Saudi Arabia, reported that 18.7% of T1DM children had a diabetic relative. Similarly, in Finland, Parkkola et al. (37) reported that 12.2% of the children with newly diagnosed T1DM had at least one affected first-degree relative. Also Sipetić et al. (38), in Bilgrade, Serbia, reported that risk of T1DM is significantly associated with a positive family history.

Gender difference in DKA has been explained by several factors. The first one is attributed to puberty-associated hormonal changes, especially the raising in the serum levels of some counter-regulatory hormones, e.g., estrogen, which is, by far, higher in girls than boys at puberty. The second factor is related to body-image psychiatric problems, including eating problems, since adolescent diabetic girls often miss insulin injections for the sake of losing weight. Moreover, girls with DKA may have more behavioral problems, lower social competence, and higher levels of family struggle (25; 39).

Our study demonstrated that DKA was triggered among T1DM overactive children (e.g., after running or playing), while the main causes for DKA were excessive eating of sweets, omitting the insulin dose, missing the daily blood sugar monitoring, or infection. Moreover, the most common symptoms associated with DKA were polyuria, thirst, vomiting, colic and fever.

In Karachi, Pakistan, Shahid et al. (40) reported that the most common clinical symptoms for DKA among diabetic patients were nausea and vomiting (57.7%), colic (42.2%) and polyuria (28.1%). Various precipitating factors of DKA were reported, especially missed insulin dose and an ongoing infection.

Children in the DKA Group were significantly more non-compliant than those in the Control Group regarding daily measurement of blood sugar, timely receiving insulin, following a healthy diet, and receiving health education.

Moreover, home management of children with DKA included receiving medication and hydration, but mostly children received nothing before going to hospital.

Therefore, for management of T1DM and prevention of DKA, it has been recommended to use recent technological advances to obtain continuous and efficient diabetes monitoring and to maintain glycemia at home. Real-time continuous glucose monitoring can significantly control hemoglobin A1c, and provides warning for early detection of glucose abnormalities and prompt intervention (17-18).

Wallace and Matthews (41) stressed that, at-home use of ketone meters that detect blood β-hydroxybutyrate has shown to aid in early detection and management of ketosis, which may decrease the need for specialized care. Short-acting insulin can be administered with fluids early on to prevent DKA. Atkilt et al. (42) added that the odds of developing DKA in newly diagnosed T1DM children is 49% lower for children whose parents knew its signs and symptoms than parents' who did not know, since parents who know its signs and symptoms can seek health care very early before their children develop DKA.

Precipitating factors for DKA are particularly important, as both infection and non-compliance are common in diabetic patients. The greater incidence of infection in diabetic patients is due to several factors including damage to neutrophil function, impairment of humoral immune system, and neuropathies (43). In Pakistan, Shams et al. (44) reported that 62% of diabetics are non-compliant to their treatment regime.

Conclusions

Results of the present study indicated that DKA may be the first presentation of T1DM, with higher incidence among girls than boys, and high tendency for recurrent episodes. Risk factors for DKA include positive family history of diabetes, less educated or employed mothers, but its incidence is lower among children of parents with health-related jobs. DKA can be triggered by child's over-activity. Its main presenting symptoms include polyuria, thirst and vomiting, while it is caused by eating many sweets, missing blood sugar monitoring, omitting the insulin dose or infection. Non-compliance regarding "daily measurement of blood sugar, timely receiving treatment, following a healthy diet or receiving health education" is associated with higher incidence of DKA.

Recommendations

All parents of T1DM children should receive health education and to be trained about management of diabetes, compliance to diabetes management, continuous monitoring of glucose level, and early manifestations of DKA.

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Physicians' Perspectives of Barriers to Insulin Initiation for Adults with Type 2 Diabetes Mellitus in Primary Health Care Centers (PHCCs), Tabouk Province - Kingdom of Saudi Arabia (KSA)

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Abstract

Aim: The goal of this study is to explore the family physicians' perspectives of the barriers in initiating insulin for adult patients with Type 2 diabetes mellitus (T2DM) in their primary health care settings.

Background: Insulin therapy often becomes necessary when oral anti-hyperglycemic agents are not enough, no longer effective or even as an initial choice. Timely insulin initiation was noticed to be a clinical problem among people with type 2 diabetes mellitus (T2DM) registered in primary health care centers (PHCCs) of Tabouk Province, KSA. Tackling this inertia or insulinophobia is a challenge in order to delay or prevent serious complications of uncontrolled diabetes. Our study and many other studies indicated that this therapeutic inertia is inappropriately due to many patient, system and physician-related factors. The present study aimed to investigate physicians' perspectives of barriers to insulin initiation for adults with T2DM registered in PHCCs, Tabouk Province - KSA and to identify opportunities for better outcomes.

Materials and Methods: This is a cross sectional study where 102 primary health care physicians (PHCPs) (58 females and 44 males) from multi PHCCs in Tabouk Health Province – Kingdom of Saudi Arabia (KSA), responded correctly to online reliable self-administered questionnaire (Cronbach alpha of 0.77344) to address their perspectives of barriers to insulin initiation for adult patients with T2DM. All participants were physicians attending PHCCs with well-equipped diabetes care clinics. Data were collected during a period from 6th – 17th June 2021. Participants included 11 (10.8%) family medicine consultants, 14 (13.7%) family medicine specialists and 77 (75.5%) general physicians.

Results: 68.6 of the study participants had barriers in initiating insulin for their patients with T2DM. A significant statistical disproportional correlation was found between the level of specialty and the rate of reporting barriers to insulin initiation (P<0.001). The top 10 listed barriers included the following: patients' refusal to initiate insulin (71.4%), physicians' fear of hypoglycemia (51.4%), inability of patients to perform home blood glucose monitoring (HMGM) (50%), physicians have no access to second opinion (44.3%), insufficient educational courses for physicians (37.1%), no family support for patients (34.3%), no clear MOH circular to support physicians' initiation of insulin at PHCCs (28.6%) , insufficient hypoglycemic medications at PHCCs (25,7%), inability of patients to manage hypoglycemia (24.3%), and patients' noncompliance to insulin regimen (24.3%).

Conclusion: Despite the free of cost availability of all types of insulin, including the safest and peak less ultra-long (degludec) and long (Glargine), the availability of free of cost glucometers for all people with diabetes, the presence of a well-equipped diabetes clinic at every PHCC, the long list of guidelines and educational courses as well as an appointment system with electronic health information system (HIS), insulin inertia is a common problem among PHCPs working in Tabouk Health Region.

Key words: Barriers, insulin initiation, insulin, primary health care, type 2 diabetes mellitus.

Introduction

Globally, diabetes mellitus is a leading cause of mortality and reduced life expectancy with growing prevalence especially in the Middle East. In 2017, global incidence, prevalence, death, and disability-adjusted life-years (DALYs) associated with diabetes were 22.9 million, 476.0 million, 1.37 million, and 67.9 million, with a projection to 26.6 million, 570.9 million, 1.59 million, and 79.3 million in 2025, respectively. Estimated years of life lost (YLL) due to diabetes is 109,707 years, while estimated quality adjusted life years loss (QALY) is 133,054 years with overall economic burden that reaches 842 million $ including direct and indirect costs (1).

The World Health Organization (WHO) has reported that Saudi Arabia ranks the second highest in the Middle East, and is seventh in the world for the prevalence of diabetes. It is estimated that around 7 million of the population are diabetic (13.4% of individuals aged 15 years and above) and almost around 3 million have pre-diabetes (2).

In 2014, the health care budget in KSA was 180 billion (Saudi Riyal) of which 25 billion was spent on the entire Saudi diabetic population. This implies that the direct expense of diabetes is costing Saudi Arabia around 13.9% of the total health expenditure (3).

The UKPDS Post Trial Monitoring Study, comprising 5102 patients, showed that intensive control of glycated hemoglobin (HbA1c) from the time of diagnosis can reduce the risk of myocardial infarction, and mortality in general (4). These data are also supported by the results of the ADVANCE and VADT studies in which patients on intensive treatment who reached lower HbA1c values had lower risk of developing both micro and macro vascular complications (5-7) .

Despite increase in the availability and safety of insulin and evidence-based treatment guidelines, worldwide over the past decade, a significant proportion of people with type 2 diabetes (T2DM) fail to achieve glycemic goals. For example, in the USA, the proportion of patients who achieved the American Diabetes Association (ADA) recommended target of glycated hemoglobin A1c below 7.0% declined from 52.2% between 2007 and 2010 to 50.9% between 2011 and 2014 (8).

Similarly, a further study performed in 2018 in Spain showed that therapeutic inertia was seen in 26.2% of patients with HbA1c>7% and 18.1% of those with HbA1c>8%, with issues of non-intensification occurring after a median follow up of 4.2 years (9). In KSA only one third of patients with T2DM have optimum glycemic control (8).

Insulin treatment often becomes necessary due to the progressive nature of type 2 diabetes, when oral anti-hyperglycemic agents are not enough, or even as an initial choice. This problem of uncontrolled T2DM is partly due to inappropriate or delay in timely initiation of insulin. In our study and many other worldwide studies this therapeutic inertia or insulinophobia is shown to be multifactorial and mainly due to patient, physician, and system-related factors (10).

This therapeutic inertia was noticed among many uncontrolled people with T2DM registered in PHCCs in Tabouk, KSA. Tackling this therapeutic inertia is a challenge in order to generate appropriate policy initiatives to improve the effectiveness of PHCPs in timely controlling diabetes and reducing the individual, social and economic burden of this serious disease.

Material and Methods

Type of study: qualitative cross sectional study
Study population: PHCPs working in MOH, Tabouk Province
Sample size and selection:
275 PHCPs are working in Tabouk Health Province. Using a confidence level of 95% and a marginal error of 5%, sample size was estimated by online sample size calculator to be 147 PHCPs(11). Questionnaires were distributed to all PHCPs working in PHCCs in Tabouk Province, Saudi Arabia to avoid any expected low response due to summer annual vacations. After 2 weeks 150 physicians returned their answers giving a response rate of 54.5%. Only 102 questionnaires were included in data analysis after exclusion of physicians with less than one year experience in PHCCs and physicians who filled in the questionnaire incorrectly. The questionnaire encompassed data as regards physicians' demographic details, years of experience, job classification according to Saudi Commission for Health Services (SCFHS), and types of barriers to the initiation of insulin (physicians', patients' and system's related barriers). The inclusion criteria were all physicians who are working in PHCC with diabetes clinics for at least one year.

Measurement tool:
A self-administered questionnaire was used among 102 PHCPs to explore physicians' perspectives of barriers in initiating insulin for adults with T2DM. The questionnaire was adapted from the PAINT questionnaire of the Japanese DAWN study (12) and was reviewed by 4 consultant family physicians and a clinical research expert working in Tabouk. A pilot study of 20 PHC physicians was done to assess the reliability of this questionnaire in our community. The internal consistency of the 20 responses collected was found to be good, with Cronbach alpha of (0.77344).

Sources of bias:
-Interpreter bias: To overcome this bias, an explanatory covering letter was attached to questionnaires and respondents were requested to call back the researchers if they have any ambiguities.

-Missing values: any missing value was excluded from data analysis.

Ethical issues considerations:
The cover letter of the questionnaire clarified the objectives of the study and the assurance of confidentiality. Study protocol was approved by the Institutional Review Board, Regional Directorate of Health Affairs, Tabouk Region, Saudi Arabia (Registration No. H-07-TU-077). Verbal informed consent was received from each participant before the study.

Statistical Analysis

Recorded data were analyzed using the Statistical Package for Social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Appropriate statistical analytical techniques were performed. Frequency distribution tables were constructed with mean and standard deviation. Significant level was set at less than 0.05 throughout the study. Independent t-test, Pearson correlation coefficient and Chi-square were used to examine the association between each independent variable and each outcome measure.

Results

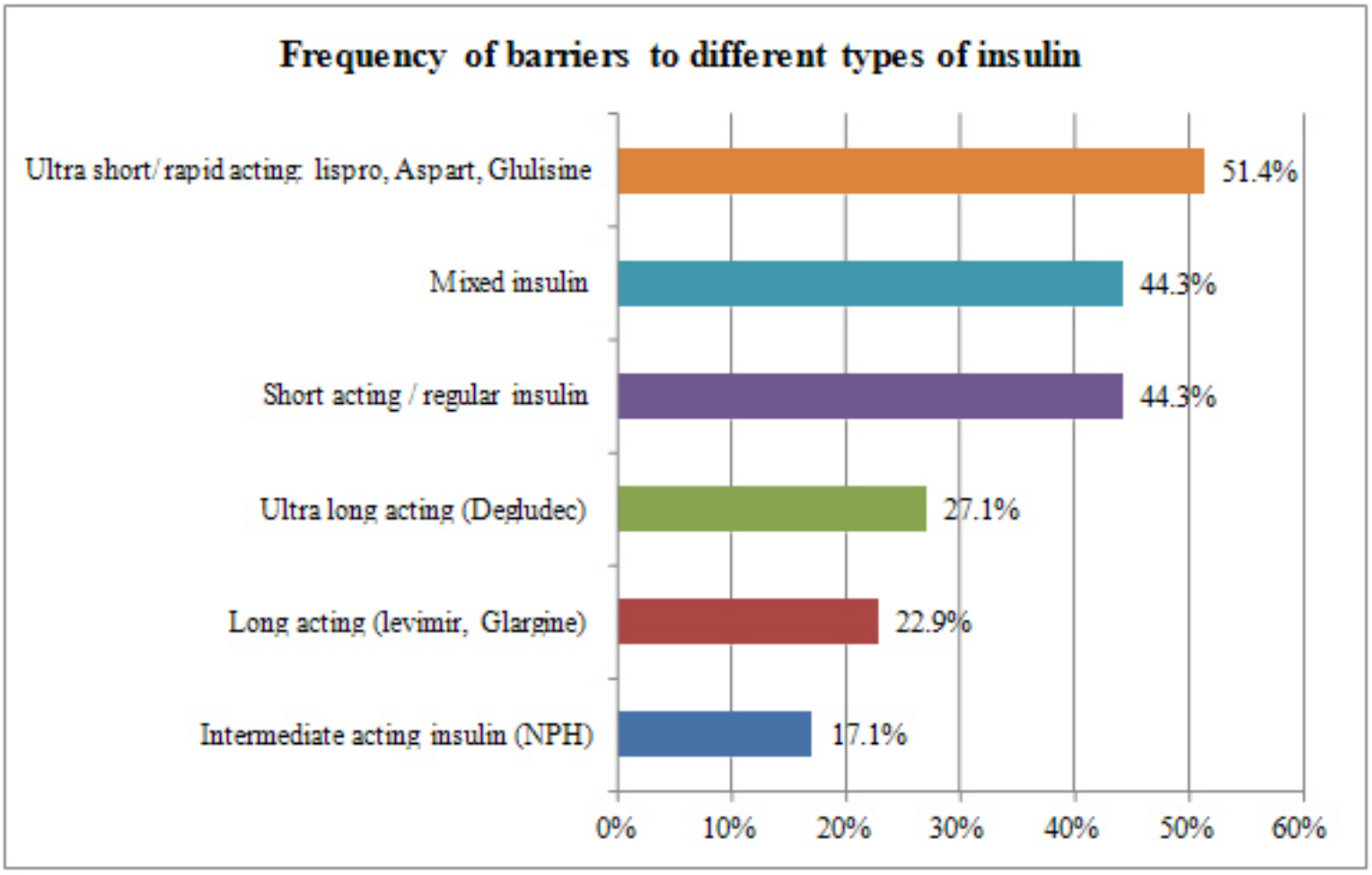
Table 1: Demographic and individual characteristics of participants

Demographic data	No.	%
Age (Group)		
<30 years	8	7.8%
30-<40 years	63	61.8%
40-<50 years	24	23.5%
50-60 years	7	6.9%
Sex		
Male	44	43.1%
Female	58	56.9%
Job title		
General physician	77	75.5%
Specialist	14	13.7%
Consultant	11	10.8%
Years of experience in PHC of MOH (KSA)		
<2 years	30	29.4%
2-5 years	18	17.6%
5-10 years	37	36.3%
≥10 years	17	16.7%
Nationality		
Saudi	5	4.9%
Non-Saudi	97	95.1%
Name of the PHC center/health sector		
Urban	79	77.5%
Rural	23	22.5%

The present study included 102 participants (43.1 % male and 56.9% female).

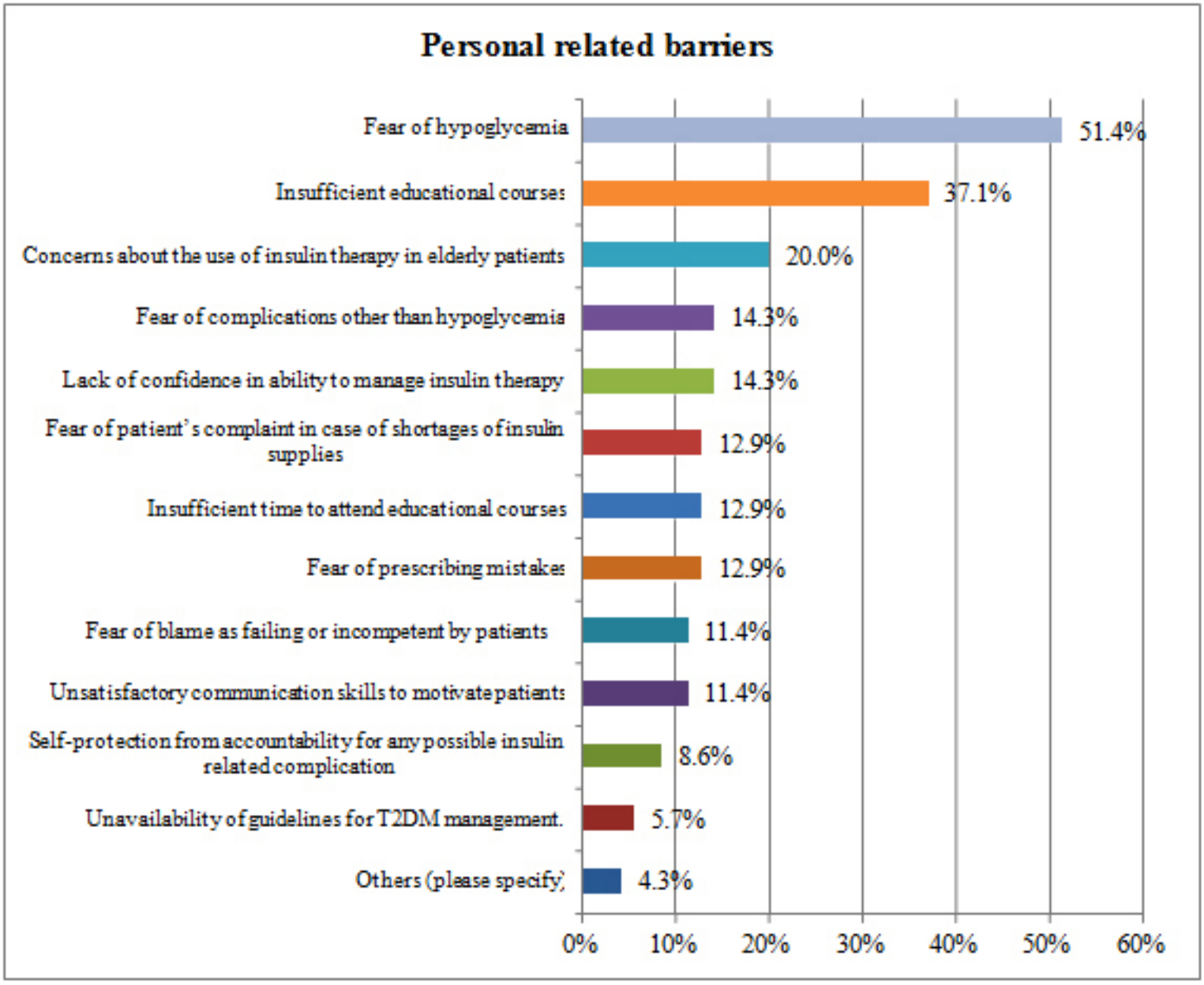
4.9% of physicians were Saudi and 95.1% non-Saudi. The majority of participants were general physicians (75.5 %), while specialists and consultants were 13.7 % and 10.8 % respectively. 70.6% of these participants have a cumulative experience of more than 2 years in providing family health care in KSA.

Figure 1: Barriers to specific types of insulin



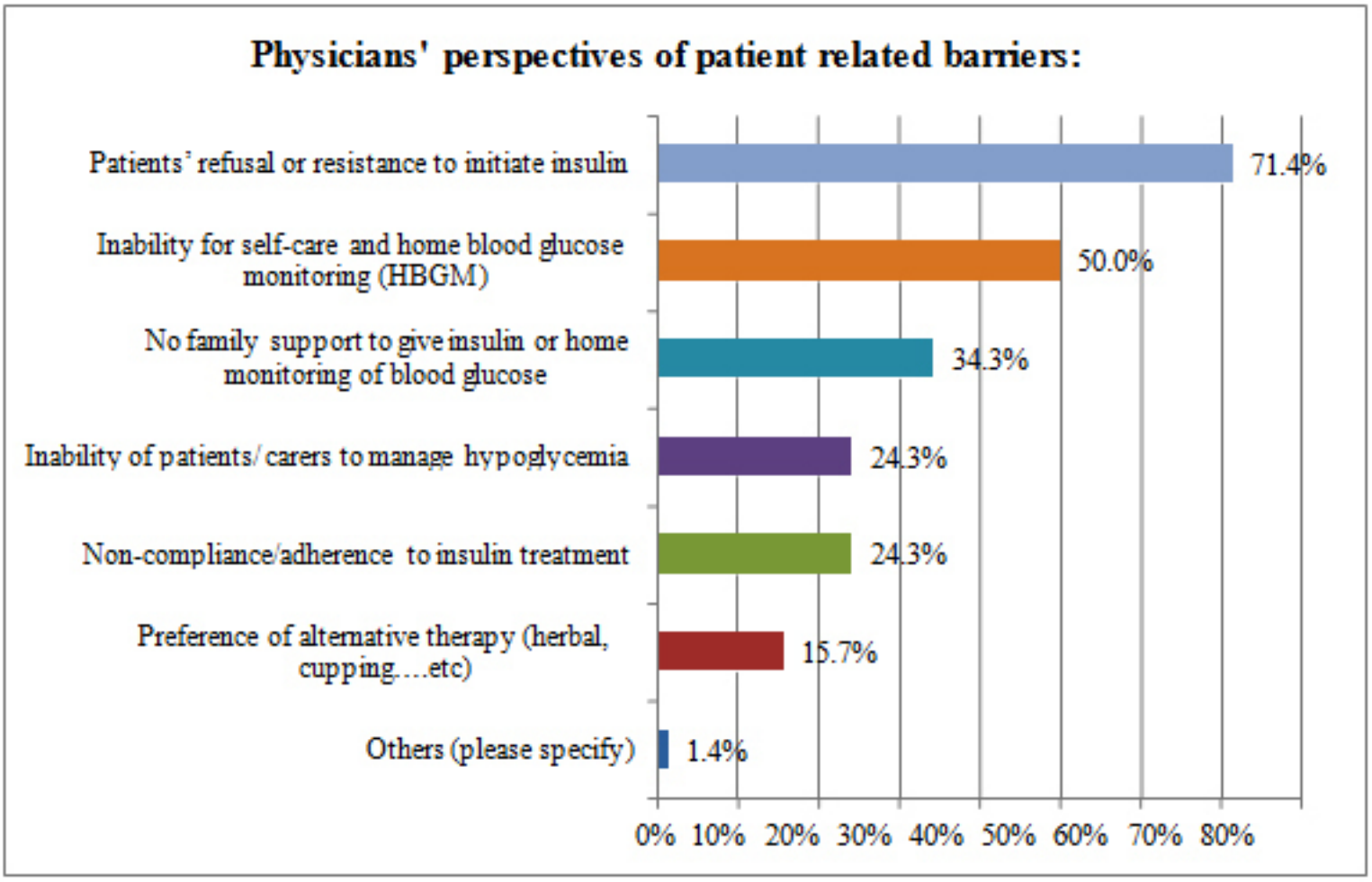
51.4 % and 44.3% of participants expressed barriers to initiate ultra-short and rapidly acting insulin respectively, followed by mixed insulin (44%), ultra-long (27%), long acting (22%) and 17% for NPH insulin.

Figure 2: Physician related barriers to the initiation of insulin



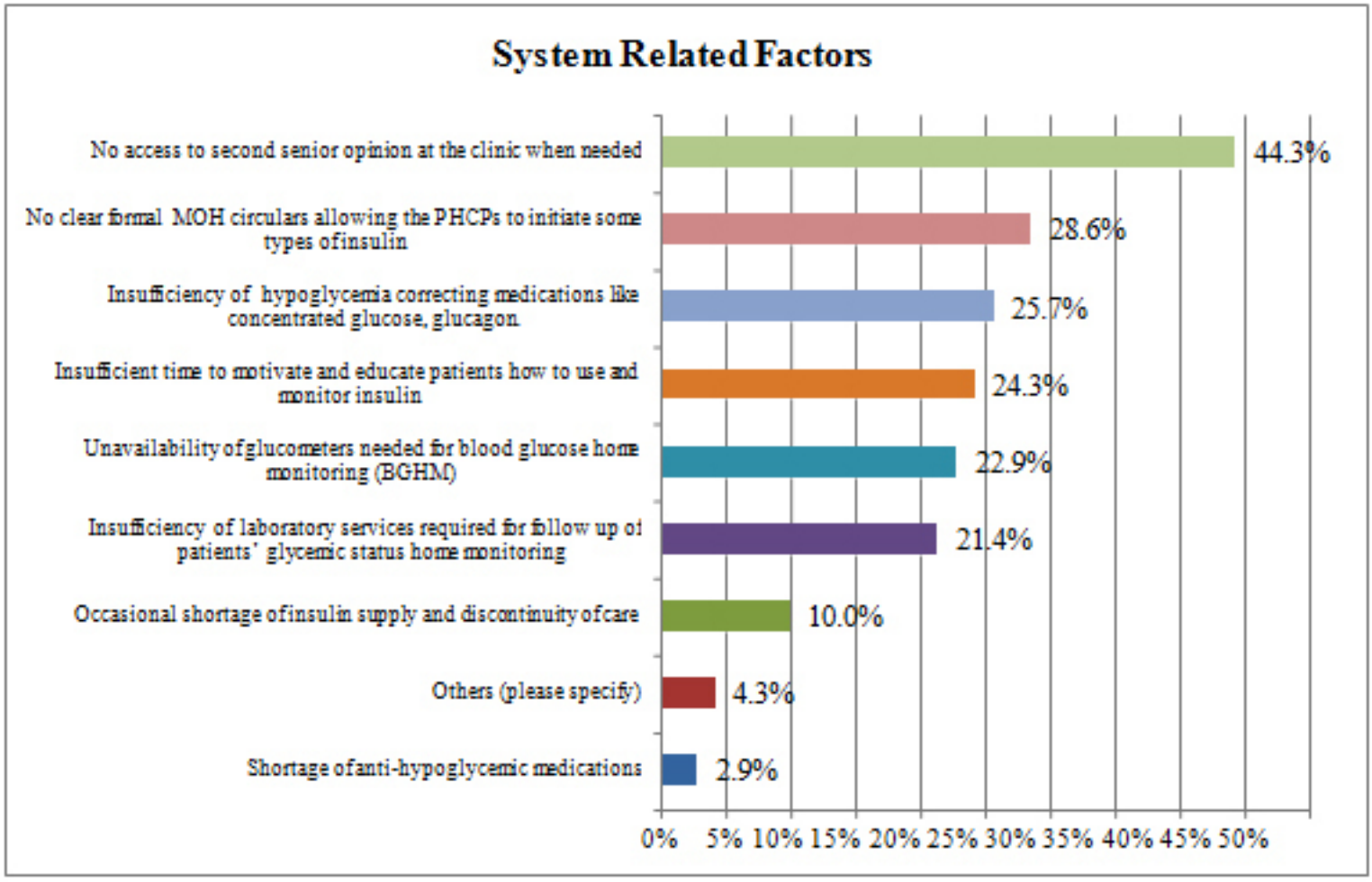
68.6% of participants reported barriers in initiating insulin. The most frequently reported personal barriers were fear of hypoglycemia (51.4 %) followed by insufficient educational courses (37.1 %), and use of insulin in elderly people (20 %). The list of personal barriers also included fear of complications other than hypoglycemia (14.3%), insufficient confidence in initiating insulin (14.3%), fear of patients' complaints in case of insulin supply shortage (12.9%), insufficient time to attend educational courses (12.9%), fear of prescribing mistakes (12.9%), fear of patients blaming them in case of failure (11.4%), unsatisfactory communication skills to motivate patients (11.4%) and only 5% expressed concerns regarding diabetes management guidelines.

Figure 3: Patient related barriers



The most frequently reported patient related barrier was patients' refusal or resistance to initiate insulin (71.4 %) followed by inability of self-care and home blood glucose monitoring (50%) and no family support in giving insulin or monitoring of home blood glucose (34.4 %). Other patient related barriers included fear from inability of the patient or family to manage hypoglycemia (24.3%), noncompliance to insulin regimen (24.3%) and preference of alternative medicines and procedures like herbal and cupping (15.7%).

Figure 4: Health system related barriers



The most frequently reported system barrier was no access to second senior opinion at the health center (44.3 %) followed by no clear MOH circular to allow physicians to initiate some types of insulin (28.6%) and insufficiency of anti-hypoglycemic medications (25.7%). Other system related barriers included insufficient time to motivate patients (24.3%), unavailable glucometers for HBGM ((22.9%), insufficient laboratory services required for follow up of patients (21.4%) and discontinuity of care due to occasional interruptions of insulin supply (12.9%).

Table 2: Correlation between barriers to initiate insulin and some personal characteristics

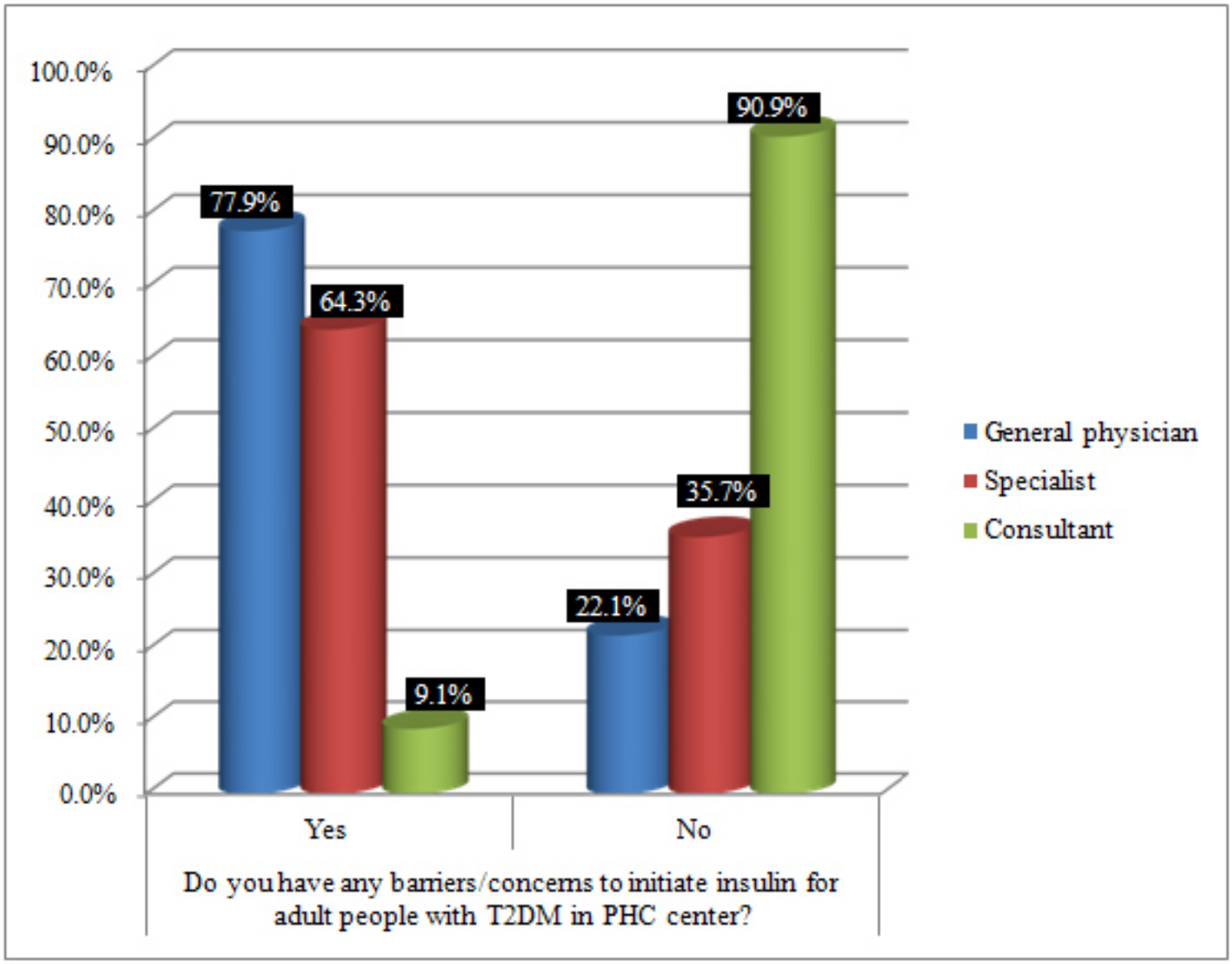
Demographic data	Do you have any barriers/concerns to initiate insulin for adult people with T2DM in PHC center?				Total	Chi-square test	
	Yes (n=70)		No (n=32)				
	No.	%	No.	%	No.	x2	p-value
Age (Group)							
<30 years	6	75.0%	2	25.0%	8		
30-<40 years	47	74.6%	16	25.4%	63	FE	0.165
40-<50 years	12	50.0%	12	50.0%	24		
50-60 years	5	71.4%	2	28.6%	7		
Sex							
Male	33	75.0%	11	25.0%	44	1.459	0.227
Female	37	63.8%	21	36.2%	58		
Job title							
General physician	60	77.9%	17	22.1%	77		
Specialist	9	64.3%	5	35.7%	14	FE	<0.001**
Consultant	1	9.1%	10	90.9%	11		
Years of experience in PHC of MOH (KSA)							
<2 years	24	34.3%	6	18.75%	30		
2-<5 years	14	20%	4	12.5%	18	5.163	0.16
5-10 years	23	32.9%	14	43.75%	37		
≥10 years	9	12.9.9%	8	25%	17		
Nationality							
Saudi	4	80.0%	1	20.0%	5	FE	0.574
Non-Saudi	66	68.0%	31	32.0%	97		
Type of the PHC center							
Urban	53	67.1%	26	32.9%	79	0.385	0.535
Rural	17	73.9%	6	26.1%	23		

Using: Chi-square test & Fisher's Exact test

Table (1) presented that, there were only significant disproportional relations between barriers to initiate insulin and the job title at (p-value <0.001).

There was no significant statistical correlation between having barriers to initiate insulin and years of experience in providing family health care in KSA, sex, age or whether the participant works in rural or urban family health center. Only 9.1% of consultants expressed barriers to insulin initiation, which was statistically significant (P<0.001) lower than both specialist and general physicians (64.3% and 77.9 % respectively).

Figure. 5: Relation between barriers to initiate insulin to job title



Discussion

Diabetes mellitus is a common chronic disease characterized by high incidence of micro and macro vascular complications with social, economic and health burden. Numerous studies have shown that optimizing metabolic control may reduce these risks, but unfortunately glycemic control in diabetic patients is often inadequate mainly due to the phenomenon of insulin inertia or insulinophobia which has been studied for almost 20 years (10).

Insulin inertia was noticed among patients with T2DM registered in PHCCs of Tabouk Province, KSA. Overcoming this problem is a key step in improving long-term care for people with T2DM. This requires an understanding of provider, patient, and healthcare system barriers that need to be addressed together, rather than as separate entities (10,13).

To the best of our knowledge, the present study is the first cross section study that has addressed insulin inertia among PHC physicians in KSA with its unique feature of involving more FM specialists and consultants (24.5% of total participants) in addition to general physicians (75.4%) who work in PHCCs with diabetes clinics. Also most of the participants in the present study were non Saudi (95%) which reflects the reality of manpower of physicians working in PHCCs in Tabouk Province. This is in contrast to a similar Saudi study where Saudi physicians were (88,2%) and most of them were general practitioners (86.3%), specialists were (10 %) and consultants were only (3,8%)).

(14). Another similar Saudi study involved mainly Saudi citizens and only 19.1% of them had postgraduate qualifications (15). We claim that these differences gave our study more reliability in exploring PHC physicians' perspectives of barriers to insulin initiation for patients with T2DM.

In our study 150 PHCPs timely answered and returned the questionnaires with 54.5% response rate. This is in contrast with another two similar Saudi studies (14,15) , where the overall response rate was 100% and 84% respectively. The low response rate in our study might be due to the time of distribution of questionnaires coincides with summer annual vacation of many physicians. In spite of this low response rate we reached the estimated sample size.

In our study 70.6% of physicians have cumulative experience of more than 2 years in PHCCs. This finding is consistent with two other similar studies: the Japanese study (DAWN) where most physicians had experience with insulin therapy and a similar Saudi study where 59.7% of physicians had experience from 0-5 years (14). But counter to these findings, in another Saudi study, half of the physicians reported that they have no experience with the initiation of insulin (15).

In the present study and as reported by many other studies, clinical inertia is multifactorial, with a range of contributing factors from patients, clinicians, and the healthcare delivery system (14-17). Almost all authors agree on the clinician's greater responsibility as a cause of inertia (18).

68.6% of physicians in our study addressed barriers to insulin initiation. This finding is higher than the global figure of insulin inertia that affects approximately one-third of patients with T2DM, but consistent with what has been stated by Lakkis et al where 73.6% of family physicians had insulin therapeutic inertia (16). In another study 29.6% of general physicians reported that insulin may not be needed for patients with T2DM initially irrespective of their blood glucose level (17). In a similar Saudi study, about 63.5% of physicians were neutral to barriers related to physicians, while 14,2% agreed and 22,3,% disagreed to presence of barriers (14).

Furthermore, 95.7 % and 44% of participants in our study addressed insulin inertia for short or rapidly acting insulin and premixed insulin respectively, but unexpectedly 27% and 22% of physicians expressed barriers to initiate the safest and peakless types of insulin, namely, ultra- long (like Deglutec) and long (like Glargine) respectively. We claim that this inertia might be partially improved if second specialist opinion is accessible especially for the initiation of short and rapid acting types of insulin. This claim is based on the findings that 44.3% of physicians in our study addressed the inaccessibility of a second specialist opinion as a barrier for insulin initiation. This explanation is supported by another study where 37% of general physicians expressed their need for a second opinion to initiate insulin for patients with T2DM (17).

The present study also revealed a highly significant disproportional correlation between the qualification level and the presence of insulin therapeutic inertia ($P<0.001$). This is in concordance with the findings of the Japanese study (DAWN) where initiation of insulin was higher among PHC physicians with family medicine postgraduate qualifications (JDS-certified specialists and non JDS-affiliated physicians) (12). Another study in France found that early (versus late) initiation of insulin therapy was 9.9 times more likely to be prescribed by specialists than by a primary care physician ($P < 0.0001$) (19). Other Saudi studies reported similar findings (14,15). Accordingly health care policy makers in Tabouk, KSA need to recruit more family medicine specialists and consultants where they do not exceed 8% of the current PHC physician's work force. On the other hand our study did not state any correlation between insulin inertia and factors like physician's age, sex, nationality, years of experience or whether the place of work is urban or rural. Counter to these findings, a similar study conducted in Jeddah, KSA by Randa et al. reported significant correlation between physician barriers and their age and years of experience (14). Absence of these logic correlations in our study needs further analysis.

In our study, in spite of the availability of safe and peakless types of insulin, the most frequently reported physician barriers to insulin initiation was fear of hypoglycemia (51.4 %) or fear of inability of the patient or family to manage hypoglycemia at home (24.3%). These findings are consistent with another Saudi study where 71.2% of physicians were worried about hypoglycemia when they initiate insulin (15). Moreover, the most commonly cited barriers to insulin initiation for physicians included hypoglycemia (20).

In our study insufficient home blood glucose monitoring (HBGM) due to lack of family support (34.4%) or unavailable glucometers (22.9%) were reported by 50% of physicians as a barrier to insulin initiation. In a similar Saudi study 45.0 % of physicians agreed that Lack of family support is a barrier to start insulin (14). We claim that unavailability of home glucometers were recently fixed with free access for all patients with diabetes in Tabouk Province. We believe some other reasons behind our physicians' concerns with the barrier of insufficient HBGM might include time constraints for health education and motivation of patients a barrier that has been reported 24.3% of physicians. Time constraints were commonly cited as a source of clinical inertia (14),

It is necessary for physicians to recognize that time spent to educate patients to avoid clinical inertia will ultimately save time, costs, and resources by reducing complications (18,21,22).

In this context we also believe that the National Health System should promote and facilitate chronicity management methods in line with technological advances, making use of telemedicine systems capable of guaranteeing the exchange of data and information between the healthcare facility and the patient (23).

In our study insufficient educational courses of diabetes was reported by 37.1 % of participants, but only 5% expressed concerns regarding updated diabetes management guidelines as barriers for insulin initiation. Although evidence-based target guidelines are generally seen as "enablers" for primary care practitioners, their potential for improving clinical inertia is limited (24,25). Similar findings have been reported in another study where physicians expressed lack of knowledge, lack of experience with and use of guidelines related to insulin therapy as a barrier to the initiation of insulin (14,26,27,28). Several studies refer the condition of "non-adherence" of the clinicians to the guidelines as a behavioral problem, because making therapeutic decisions is a complex task that involves a variety of cognitive processes (29).

Andreozzi addressed that with adequate training, clinicians can evaluate their own performances, identify critical areas and adopt suitable strategies to overcome their barriers (10). An effective approach would be to provide HCPs with a concise and readily accessible central resource, e.g., the "Wise List" in Sweden, which summarizes the recommended core medicines that should be used in the treatment of common diseases such as diabetes (30). Several studies have documented that monitoring of physician's prescribing behavior with active feedback is very effective in improving insulin inertia (31).

37.2% of physician related insulin inertia to barriers like blaming of insulin shortage, prescribing mistakes and failure to control diabetes. We claim that this behavior is a defense of some physicians who try to avoid any intervention that may threaten their existence in a job especially as most participants are non-Saudi. This assumption needs further analytical research.

Both lack of communication skills and non-confidence were reported by 14.3% and 11.4% of our participants respectively as barriers to initiate insulin for patients with T2DM. These levels are much lower than what has been reported in another Saudi study where they were barriers for about a third of physicians(14).

20% of physicians in our study expressed barriers to initiate insulin for senior people. This is in contrast to the findings of a Canadian study which reported old age (60-69 years) as a factor strongly associated with early initiation of insulin (32).

In our study, the most frequent patient related barrier stated by physicians was refusal or resistance to initiate insulin (71.4 %). In contrast with another Saudi study where one quarter (24.4%) of the diabetic patients refused insulin. This study also showed different causes for their refusal including: fear of injection, pain, insulin injection needs help from others, fear of hypoglycaemia and embarrassment (33).

A literature review done by Jennifer et al. revealed that physicians often overestimate patient resistance to insulin initiation (33). We agree with the conclusion of this review and claim that our participants overestimated the barrier of patient resistance.

In Arab countries, 73% of PCPs prefer to delay insulin therapy until it is "absolutely essential (34). The reasons behind these assumptions were not analyzed in our study but we claim that patients' preference of alternative medicines like herbal and cupping (15.7%) failure of HBGM (50%) insufficient family support (34.3%) and fear of non-compliance of patients to insulin regimens (24.3%) may partially explain this assumption among our participants. Patients' preference of herbal medicine is reported by another Saudi study (15). Many other studies stated that expecting a new method of diabetes treatment (54.7%), fear of needles and requiring someone else to administer the injection (19.2%) are the main reasons behind patient refusal or resistance to start insulin therapy (14,18,34).
In our study, the most frequently reported system related barriers were: no access to second senior opinion at the health center when needed (44.3 %) followed by no clear MOH circular to allow physicians to initiate insulin (28.6%), insufficiency of anti-hypoglycemic medications at family health centers (25.7%), insufficiency of laboratory services required for follow up of DM (21.4%) and discontinuity of care due to occasional interruptions of insulin supply (12.9%). In Tabouk, we claim that this situation appears to have changed and many of these barriers are already fixed. Saudi MOH Wasfaty initiative now allows all patients to collect their medication from private pharmacies, all health centers have been equipped with HbA1C measuring devices, glucometers are available free of cost for all people with DM, a system of referral to both hospital laboratory and central PHC laboratory services are now available. All these system related facilities make most of these barriers illogical, but we agree with their barriers related to clear MOH circular that supports insulin initiation by PHCPs and quick access to a second specialist opinion. System related barriers reported in another similar Saudi study included: excessive workload, lack of insulin, few number of diabetes educators and lack of continuity of care (14). The most cited system related barriers include: no clinical guidelines, no disease register, bureaucratic difficulties with new drugs, resource constraints, no decision support, no team approach to care, poor communication between physicians and staff and no structured education activity (10).

Limitations

- This study addresses barriers to insulin initiation from only PHC physicians' perspectives and did not include patient's perspectives.
- Time of the study coincides with summer annual vacation of many physicians, with low response rate.

Recommendations

It is important that provider, patient, and healthcare system level barriers are considered together rather than as separate entities. Overall, the lesson from this study is to focus on the methods of education for both patients and physicians to approximate the gap between the existing ways of ineffective teaching to another evidence based learning method that improves clinical performance including insulin inertia. Clinical trials reinforce the need for a combination of good education and support, clear concise treatment strategies, involvement of all diabetes team especially nurses and pharmacists in patient education, recruit more family medicine specialists and consultants to PHC centers to reduce insulin inertia.

Conclusions

Despite the availability of all types of insulin, including the safest and peakless ultra-long (degludec) and long (Glargine) and their availability along with glucometers free of cost for all people with diabetes, the presence of well-equipped diabetes clinics in every PHCC and a long list of guidelines and educational courses, insulin inertia is a common problem among PHCPs working in Tabouk Health Region. PHCPs related their barriers to personal, patient and system factors. Recruitment of more family

medicine specialists and consultants along with shift from the traditional methods of teaching to more practice performance monitoring, review of physician's insulin prescribing behavior and on practice dual feedback with physicians and other health team members are assumed by the researchers and supported by evidence, may help to overcome this insulin inertia.

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Covid-19 immunisation in Refugee Camps.

Our immune system is unique to each individual depending on stimuli it receives during a person's life. The immune system response to vaccination may be affected by many factors such as age medical therapy and co-morbidities. Of particular importance may be the presence at the time of vaccination of unrelated infections and infestations that can act to prevent a proper antibody response to any immunisation.

A few years ago, whilst lecturing to an International Master of Public Health course at the Hebrew University in Jerusalem. As part of my role I was asked to supervise a student project entitled " Problems with Poliomyelitis vaccinations in India". As we discussed the timing of the second injections required one member of the group a doctor from India working in Public health commented that they often give the 3 or 4th doses of vaccine before their patients get an adequate antibody response. Noting that the recipients often have a number of co-morbidities particularly infection and infestations engaging their immune system thus distracting the system from fully responding to the stimulus of the added vaccine.

This situation is particularly applicable to the many refugee camps and millions of refugees scattered throughout the Middle East the result of the current round of conflicts in Syria, Iraq and Libya affecting not only these countries but also Turkey, Jordan and Lebanon.

As the current Omicron variant has shown variants of concern will arise wherever the Covid-19 virus is allowed to run rampant. The refugee camps would appear to be ideal breeding grounds for mass infections. It should be important that a vaccinations regime should be implemented as soon as possible. At the same time the problem of inadequate antibody response must be considered and a regime of testing the antibody response must be implemented this should be done within 3 - 4 weeks following the final vaccination either the 2 jabs such as AstraZeneca or similar vaccines or the one dose vaccines such as the Johnson and Johnson. Could be major problems and spread of the virus if patients who have been fully vaccinated were allowed free movement in the community yet have low or no resistance to the virus making them dangerous super spreaders.

As well the oral vaccine developed in Israel currently being trialed in South Africa would be ideal in the camps where medical assistance is far from ideal.

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Role of SGLT2 Inhibitors and GLP-1 Analogs in Cardiovascular Risk Reduction in Type 2 Diabetes

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Abstract

The leading cause of morbidity and mortality in patients with type-2 diabetes mellitus is cardiovascular (CV) disease, which makes it an important target in management. Sodium-glucose cotransporter 2 (SGLT-2) inhibitors and glucagon-like peptide-1 receptor agonist (GLP-1 RA) are both two new antidiabetic drug classes that showed significant reduction in major cardiovascular events (MACE). With the introduction of these drugs, comprehensive CV risk reduction has been achieved in addition to glucose control. Both drugs work in different ways; the SGLT-2 Inhibitors lead to urinary excretion of 60-90 grams of glucose as well as sodium leading to osmotic diuresis. On the other hand, GLP-1 agonists affect postprandial glucose by enhancing insulin secretion in the beta cells and inhibition of glucagon secretion in the alpha cells in a glucose dependent manner. Different types of drugs are discussed in detail according to different trials such as EMPA-REG, EMPEROR REDUCED, CANVAS, CREDENCE, VERTIS-CV, DAPA-HF and DECLARE TIMI 58 for SGLT-2 Inhibitors, while for GLP-1 agonists, trials such as ELIXA, FREEDOM, EXCEL, LEADER, SUSTAIN, PIONEER 6, REWIND and HARMONY. According to U.S. Drug and Food Administration guidance in 2008, it is required that all new oral hypoglycemic agents undergo cardiovascular outcome trials to evaluate CV safety. Both the SGLT2 inhibitors and GLP-1 agonists have undergone large trials that have led to massive evidence on their cardiovascular safety and renal benefits. The decision on using which drug from both classes depends on different factors like atherosclerotic disease and chronic Kidney disease.

Key words. diabetes, cardiovascular, reduction

Introduction

Cardiovascular (CV) disease remains the leading cause of morbidity and mortality in patients with type-2 diabetes mellitus (DM) and is thus an important target for management. Sodium-glucose cotransporter 2 (SGLT-2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1 RA) are two antidiabetic drug classes that have been demonstrated to significantly reduce the risk of major adverse cardiovascular events (MACE) and with introduction of these drugs there has been a paradigm shift to ensuring comprehensive CV risk reduction in addition to the glucose control previously accorded with initial oral antidiabetic drug classes (Das et al., 2020).

Their mechanism of action is as outlined in the table below :

SGLT-2 Inhibitors	SGLT-2 is a low affinity, high capacity glucose transporter in the proximal tubules of the kidney responsible for filtering approximately 90% of glucose Inhibition of SGLT-2 leads to urinary excretion of 60-90 grams of glucose as well as sodium, leading to osmotic diuresis (Feingold, 2020)
GLP-1 RAs	GLP-1 is cleaved from the pro-glucagon molecule by pro-convertase enzymes in the gastrointestinal tract. Most of GLP-1 is stored in L-cells of the ileum and colon and is released at mealtime in response to neurohumoral signals and presence of food in the gut. GLP-1 affects postprandial glucose by enhancing insulin secretion in the beta-cells and inhibits glucagon secretion in the alpha-cells in a glucose dependent manner (Feingold, 2020)

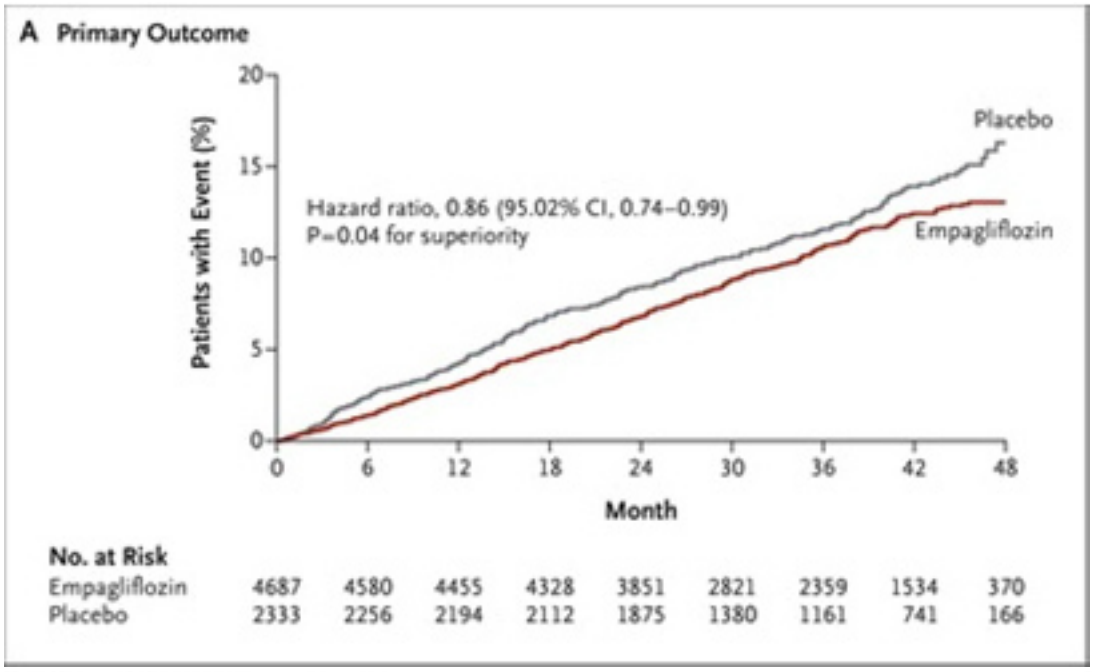
SGLT2-Inhibitors

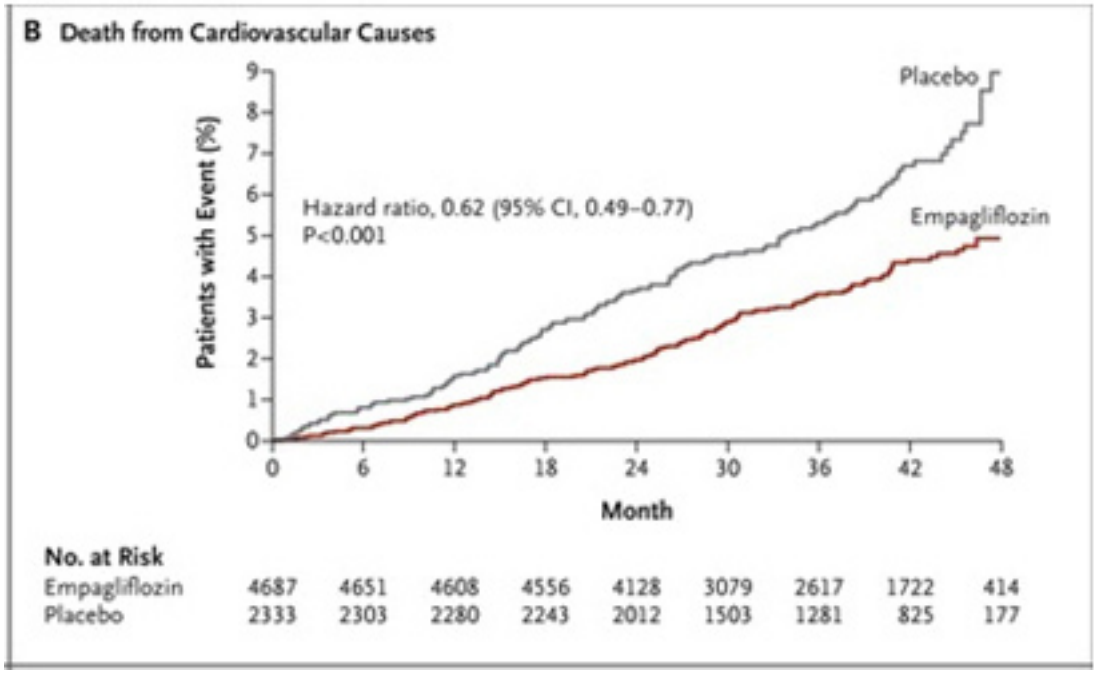
This drug class has 4 major drugs as outlined in the table below:

Year	Trial	Drug	Dosage Recommendations
SGLT-2 Inhibitors			
2015 2020	EMPA-REG EMPEROR REDUCED	Empagliflozin	10mg PO daily for CV benefit (ACC, 2020)
2017 2019	CANVAS CREDENCE	Canagliflozin	100mg PO daily for CV benefit (ACC, 2020)
2019	VERTIS -CV	Ertugliflozin	5mg PO daily, can be increased to 15mg (Feingold, 2020)
2019 2019	DAPA-HF DECLARE TIMI 58	Dapagliflozin	10mg PO daily for CV benefit (ACC, 2020)

1. Empagliflozin

Empagliflozin has been shown to have favourable effects on weight reduction, reduction in blood pressure without raising the pulse, improves markers of arterial stiffness and vascular resistance, has benefit on visceral adiposity, albuminuria, plasma urate levels and favourable effect on LDL and HDL levels. The EMPA-REG outcome trial examined the above favorable effects of empagliflozin compared to placebo. Primary outcomes evaluated included cardiovascular death, nonfatal Myocardial infarction (MI), and nonfatal stroke. Secondary outcomes included composite endpoints of the primary outcomes and hospitalization for unstable angina. The conclusions are summarized below: primary outcome was lower in the empagliflozin group (Figure A), decreased cardiovascular death (B), decreased all-cause mortality (C) and decreased hospitalization due to HF (D) (Zinman, et al., 2015).





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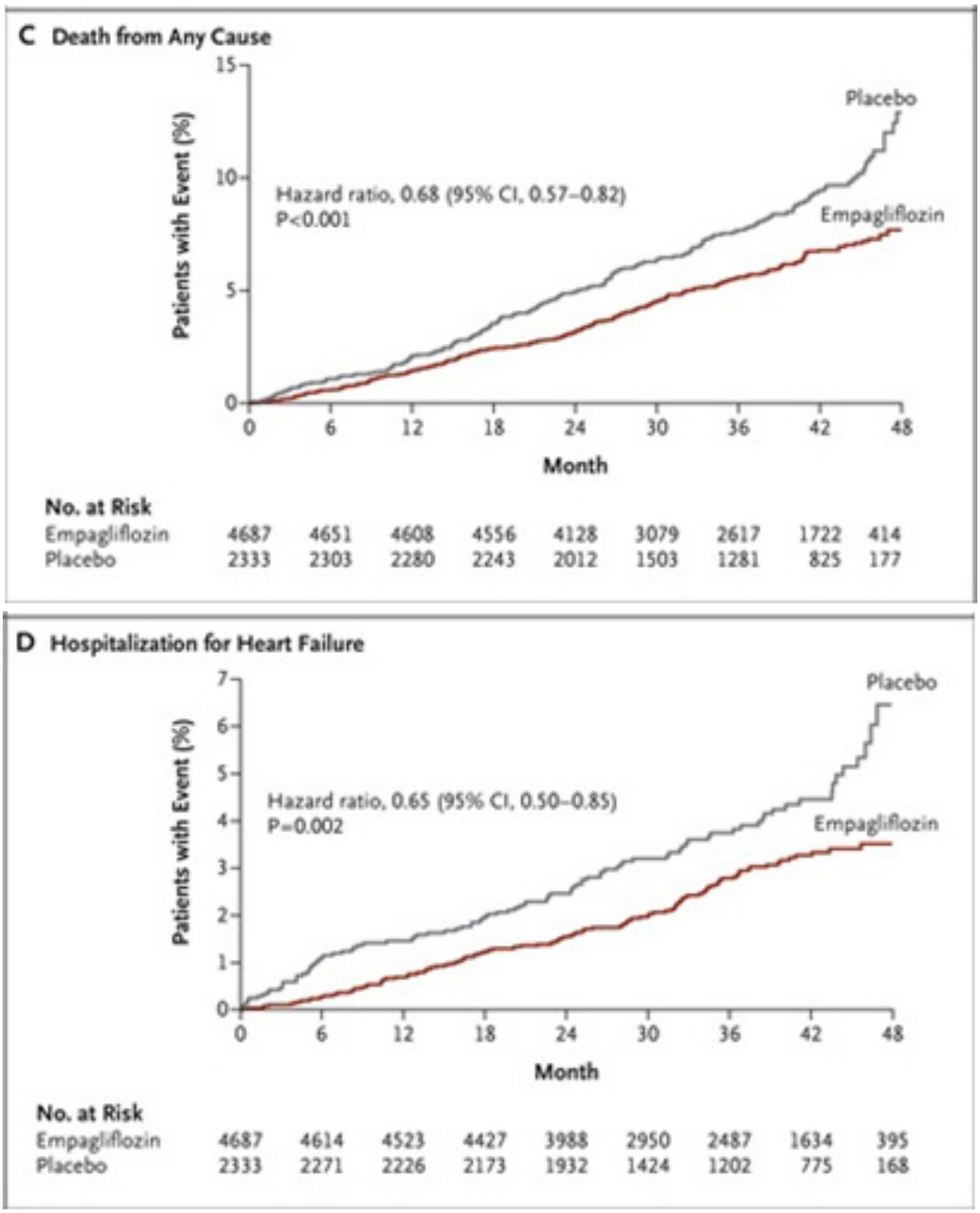


The EMPEROR-Reduced trial concluded that empagliflozin had improved outcomes in patients with heart failure with symptomatic stable ejection fractions of < 40%. This was superior to the placebo group and irrespective of whether a patient had diabetes or not (Kumbhani, et al., 2020).

2. Canagliflozin

The Canagliflozin Cardiovascular Assessment Study (CANVAS) assessed Canagliflozin at reducing risk of MACE: cardiovascular (CV) death, non-fatal stroke or non-fatal myocardial infarction (MI) (Carbone and Dixon, 2019). The study participants were 10,420 patients with HbA1c ≤ 10.5% and ≥7% as well as established CV disease or two or more risk factors of it.

The effects of Canagliflozin were as depicted in the table below:

Cardiovascular risk factor	Observed effect of canagliflozin
HbA1c	Reduced by 0.58%
Body weight	Reduced by 1.60 kg
Systolic blood pressure	Reduced by 3.93 mm Hg
Diastolic blood pressure	Reduced by 1.39 mm Hg
High-density lipoprotein (HDL) cholesterol	Increased by 2.05 mg/dL
Low-density lipoprotein (LDL) cholesterol	Increased by 4.68 mg/dL
LDL/HDL cholesterol ratio	Remained unchanged

(Carbone and Dixon, 2019)

Canagliflozin significantly reduced CV risk factors in patients followed up for a period of 3-7 years. MACE risk reduced by 14% in the control versus placebo group: with CV death outcome reducing from 12.8 to 11.6/1000 patient-years; nonfatal stroke from 8.4 to 7.1/1000 patient-years, nonfatal MI from 11.6 to 9.7/100 patient-years and statistically insignificant reduction in all-cause mortality from 19.5 to 17.3/1000 patient-years. Other benefits of canagliflozin treatment included a 33% relative risk reduction in heart failure hospitalisations, a 30% reduction in fatal HF outcomes and a 22% reduction in composite CV death or HF hospitalization (Carbone and Dixon, 2019). Of the latter, patients with previous HF, BMI ≥30 kg/m2, HbA1c ≥8%, on diuretics, and those who were not on metformin had suggested considerable benefits on canagliflozin treatment.

The Canagliflozin and Renal Events in Diabetes and Nephropathy Clinical Evaluation (CREDENCE) trial focused on renal outcomes in patients with more advanced diabetic kidney disease. The trial showed Canagliflozin to have a significant benefit in both renal and cardiovascular outcome especially in patients who had advanced diabetic kidney disease (Robin, et al., 2020).

3. Ertugliflozin

According to Feingold (2020), the VERTIS-CV RCT randomized type-2 DM patients with atherosclerotic CV disease in three groups – 5mg ertugliflozin (n=2752), 15mg ertugliflozin (n=2747) and placebo (n=2747) added to the standard of care for diabetes (Consentino, et al., 2020). It focused on the 3 point MACE of CV death, nonfatal MI or nonfatal stroke after a mean duration follow-up of 3.5 years (Feingold, 2020; Zannad and Cowle, 2020). The heart failure hospitalizations were significantly reduced in patients treated with ertugliflozin (2.5% vs. 3.6%, p=0.006) (Feingold, 2020; Constentino et al., 2020). According to Williams, et al., 2021, this trial has a CV inferiority for the 3 point MACE compared to the CV superiority trials like EMPA-REG, CANVAS, CREDENCE and DECLARE-TIMI because the participants in this trial had a higher proportion of patients with heart failure (~ 24%).

4. Dapagliflozin

The DECLARE-TIMI 58 aimed to assess if the use of Dapagliflozin in patients with type 2 diabetes and at risk for cardiovascular disease reduces the risk of MACE. The study was a randomized, double-blind, multinational, placebo-controlled, phase 3b trial conducted in 33 countries. Participants were 17,160 patients with T2DM and a history of either established ASCVD (n = 6,971) or multiple risk factors for ASCVD (n = 10,189) (Wiviott et al., 2019).
The primary safety outcome was a composite of MACE: cardiovascular death, myocardial infarction, or ischemic stroke. The primary efficacy outcomes were MACE and the composite of cardiovascular death or hospitalization for heart failure. The secondary safety outcomes were renal dysfunction and death from any cause. They showed that dapagliflozin use among patients who had or were at risk for atherosclerotic cardiovascular disease reduced hospitalization without significant effect on MACE (Wiviott et al., 2019).

Later on, The DAPA-HF trial, a double-blinded, multicentre RCT that looked at a once daily dose of dapagliflozin at 10mg against a placebo in 4,744 subjects with heart failure with reduced ejection fraction (HFrEF) with type II diabetes, pre-diabetes and without diabetes was conducted. Inclusion criteria included heart failure patients with a NYHA class II or more, an ejection fraction of 40% or less and an elevated NT-proBNP level who were receiving standard heart failure therapy (McMurray, et al., 2019) (Docherty, et al., 2020). As opposed to prior HF trials, this RCT had a wide age gap including subjects between ages of 18 and 130 years (Rich, et al., 2020).

The trial concluded use of dapagliflozin at 10mg OD was beneficial to patients with HFrEF with or without diabetes in decreasing composite outcomes of cardiovascular mortality and hospitalization associated with heart failure. As compared to the DECLARE-TIMI 58 trial which looked at the same drug, this trial had the benefit of specifically looking at subjects with HFrEF and was the initial trial that showed benefit dapagliflozin, an SGLT2 inhibitor, in use for patients with HFrEF but without diabetes (McMurray, et al., 2019) (Wivott, et al., 2019).

Lo, et al., (2020) conducted a systematic review and meta analysis of 4 major trials, EMPA-REG, CANVAS, DECLARE -TIMI 58 and CREDENCE looking at the overall cardiovascular and renal outcomes following treatment with SGLT-2 inhibitors as second line therapy addition to metformin. The trials did not have enough data on diabetics with an estimated glomerular filtration rate between 30 and 45 mL/min/1.73m2 but the meta analysis included data on those with an eGFR above and below 60 mL/min/1.73m2. Regardless of atherosclerotic cardiovascular risk the meta analysis demonstrated that overall, SGLT-2 therapy is associated with a 7% reduction in MACE (major adverse cardiovascular event), an 11% reduction in cardiovascular death, a 29% reduction in heart failure hospitalization, a 35% reduction in the progression of renal disease in those with an eGFR above and below 60 mL/min/1.73m2 and a reduction in all cause mortality (Lo, et al., 2020). The efficacy of SGLT-2 inhibitors is affected by the renal function. The evidence for cardiovascular benefit from SGLT-2 therapy was weakest in patients with an eGFR below 60 mL/mi/1.73m2 but there was clearer evidence of a lower adverse renal event in this group (Lo, et al., 2020). SGLT-2 inhibitors are reno-protective, implicating benefits for cardiovascular health. Of note, African Americans made up less than 10% of the participants in these large trials affecting the generalisability of these findings to them.

GLP -1 Receptor Agonists

This drug class can be divided into short-acting and long-acting agents:

Short-acting GLP-1 RAs			
2015	**ELIXA**	**Lixisenatide**	10ug or 0.01mg daily, after 14-days increase to 20ug or o,02 mg daily (Feingold, 2020)
2016 **2017**	**FREEDOM** **EXSCEL**	**Exenatide**	**5ug or 0.005mg twice daily and after 1 month increase to 10ug or 0.01mg twice daily (Feingold, 2020)**
Long-acting GLP-1 RAs			
2016	**LEADER**	**Liraglutide**	**0.6mg SC daily for CV benefit* (ACC, 2020)**
2016 **2018**	**SUSTAIN** **PIONEER 6**	**Semaglutide**	**0.25mg SC per week for CV benefit *(ACC, 2020)**
2018	**REWIND**	**Dulaglutide**	**0.75mg SC per week for CV benefit* (ACC, 2020)**
2018	**HARMONY**	**Albiglutide**	**30mg SC per week, can increase to 50mg (Trietley and Skef, 2017)**
** can be titrated slowly to higher doses or maximally tolerated*			

1. Lixisenatide

According to the results of the Evaluation of Lixisenatide in Acute Coronary Syndrome (ELIXA) trial, which was the first CVOT for the GLP-1 receptor agonists class following 6,068 type 2 diabetic patients with history of ACS (MI or hospitalization for unstable angina within the previous 180 days) over a period of 25 months, lixisenatide did not affect the rate of cardiovascular events (measured as composite endpoint of cardiovascular death, myocardial infarction, stroke, or hospitalization for unstable angina) compared to placebo among the patients studied, type 2 diabetics with history of ACS (Pfeffer, et al., 2015).

2. Exenatide

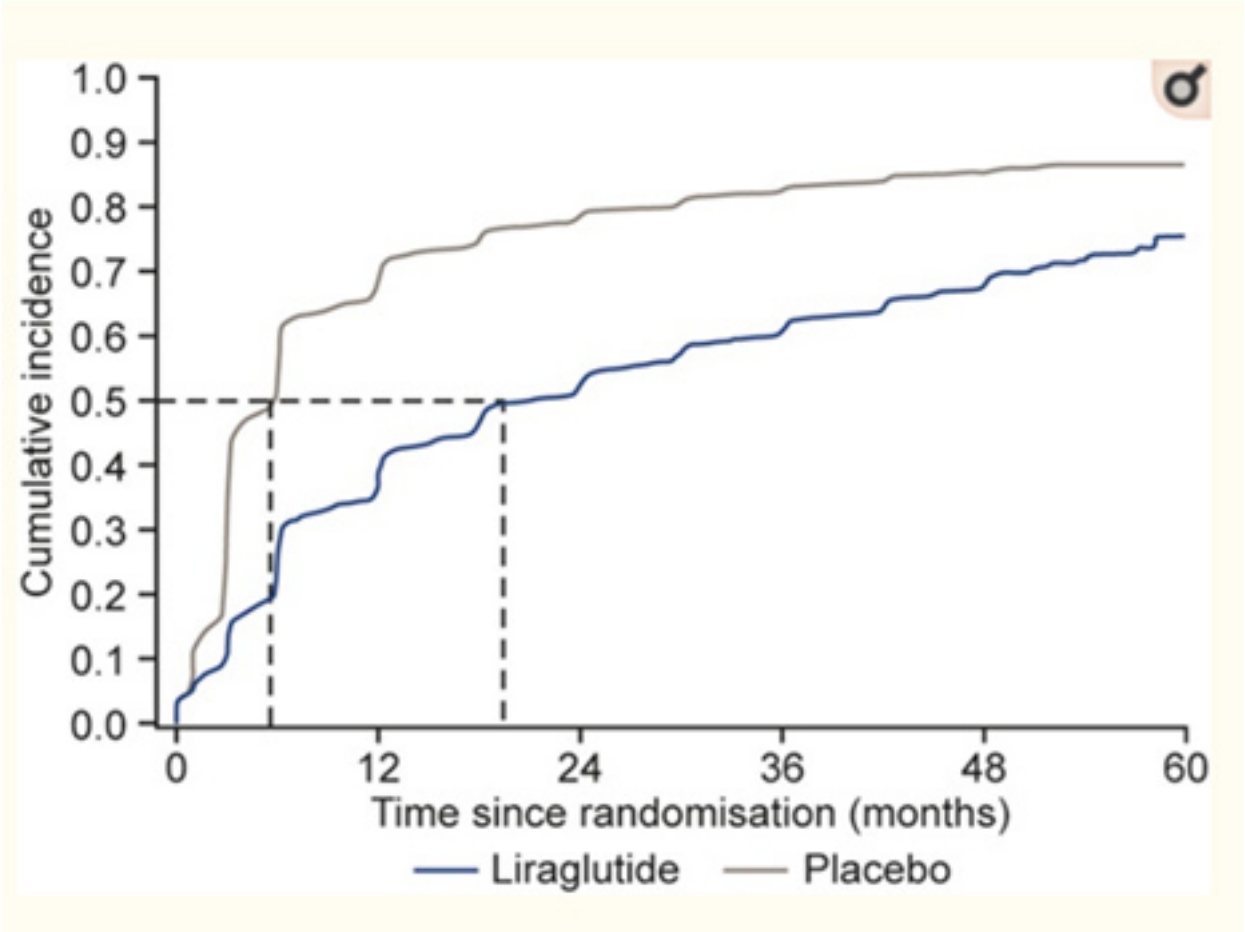
Effects of Once Weekly Exenatide on Cardiovascular Outcomes in Type 2 Diabetes (EXSCEL) trial, a randomized, double-blind, placebo-controlled trial which was conducted in 687 sites in 35 countries with a total of 14,752 patients for a median duration of 3.2 years followed up type 2 diabetic patients with HbA1c between 6.5 and 10% with (70%) or without (30%) prior cardiovascular events (coronary artery disease, ischaemic CVA, or atherosclerotic peripheral arterial disease) (Sheahan, et al., 2020). Patients were assigned 1:1 to either 2 mg of extended released exenatide or a volume-matched placebo once weekly (Holman & et al., 2017). Primary outcomes evaluated included occurrence mortality due to cardiovascular causes, nonfatal MI or nonfatal stroke. The trial concluded Exenatide use in diabetic patients with or without prior cardiovascular disease did not have any significant difference in occurrence of MACE between the study and placebo arm (Holman, et al., 2017).

3.Liraglutide

The LEADER trial, a double-blinded, placebo-controlled, event and duration based trial with a follow up of 32 to 60 months comparing use of Liraglutide (n= 4668) and a Placebo (n= 4672) found significant reduction of cardiovascular death, non-fatal MI and non-fatal stroke. Further analysis of the data was able to extrapolate the glycaemic deterioration over time. The end point was measured as HBA1C >8 or change of 0.5 % on the next visit and intensification of oral hypoglycaemics and insulin as supportive treatment (Zinman, et al., 2018) (Marso, 2016).

The study shows that liraglutide reduces the HBA1C and lessens the need for drug intensification when compared to a placebo in T2DM with High Cardiovascular risk. The trial followed the patients up over a mean period of 3.8 years and found that even though the Liraglutide lessens glycaemic deterioration, there is a convergence of HBA1C control after 5 years. This is in keeping with the natural progression of T2DM (Figure 1).

Figure 1 (Image extracted from Marso, et al., 2016)



Cumulative incidence plot of time to HbA_{1c} ≥8% and reduction <0.5% since previous visit or substantial intensification* in insulin or OAD treatment. Aalen-Johansen plot, with death as a competing risk factor.

* Substantial intensification of insulin or OAD defined as: start of new OAD; start of insulin; increase in insulin dose ≥ 10 units; or addition of mealtime bolus insulin to basal insulin or a shift from basal insulin to premixed insulin.

HbA_{1c} glycated haemoglobin, *OAD* oral antihyperglycaemic drug.

4.Semagludide

SUSTAIN-6 and PIONEER 6 studies both are noninferiority cardiovascular outcomes trials of oral semaglutide whose primary outcome measures included the first occurrence of a major CV event defined as deaths arising from cardiovascular causes, non-fatal MI or stroke) (Marso, et al., 2016) (Husain, et al., 2019).

In the SUSTAIN-6 trial, the majority of T2DM individuals' (83%) who either had chronic kidney disease, established CV disease or both, were randomized to receive semaglutide once a week (0.5mg or 1.0 mg) or placebo for a duration of 104 weeks. At the end of the study period, the risk of the primary outcome was 42% lower in the semaglutide arm, and this was significant for noninferiority. With regards to the individual components of the primary outcome, the risk of nonfatal MI was 26% lower in the treatment arm, but this was not statistically significant while the risk of mortality from CV causes was the same in both groups. The risk of nonfatal stroke was 39% lower in the active treatment group and this attained statistical significance (Marso, et al., 2016).

In the PIONEER-6 trial, subjects with T2DM who either had a high cardiovascular risk or established cardiovascular disease were randomized to receive semaglutide given as a once-daily dose or placebo (Husain et al., 2019). At the end of the study period of 15.9 months, the occurrence of MACE was reduced by 21% in the treatment arm thus demonstrating that oral semaglutide was non-inferior. In the analysis of the various primary outcome components, the treatment arm had a reduction of 51% in CV deaths, as well as a 26% and a 49% reduction in non-fatal strokes and all-cause deaths, respectively (Husain, et al., 2019).

5. Dulaglutide

The REWID trial looked at the CV safety of addition of dulaglutide to diabetic patients with HbA1c ≤ 9.5%, above the age of 50 years with established vascular disease receiving a maximum of 2 or more oral agents with or without basal insulin over a median period of 5.4 years which was the longest known for a GLP-1 RA. The trial showed dulaglutide has a safety profile comparable to the other GLP-1 RA studied in previous trials, and is superior to placebo in reducing cardiovascular events for diabetic patients with high CV risks when added on top of other oral hypoglycemic agents (Doupis, 2019).

6. Albiglutide

In 2018, the harmony outcomes trial, a randomized, double-blinded, placebo-controlled trial, with 9,463 patients in 28 countries with over 610 study sites looked into efficacy of once weekly albiglutide in type 2 diabetic patients with established cardiovascular disease and HbA1c levels of above 7% over a period of 1.6 years. Patients who received albiglutide had better improvement in their glycaemic control compared to the placebo group. The study control group also showed a major reduction in cardiovascular events and weight. Furthermore, in patients who were already receiving standard diabetic care, the inclusion of albiglutide contributed to a significant reduction in stroke, MI, cardiovascular events (22%), and hypoglycaemic episodes (Hernandez, et al. 2018).

While most trials on GLP-1 receptor agonists demonstrate beneficial effects in reducing MACE, results have been inconsistent regarding the effects of GLP-1 analogues on stroke and MI. Additionally, data on individuals with DM but without established CVD is limited though recent CVOTs have included many subjects without CVD. In a recent meta-analysis by Marsico, et al. (2020), data from 7 RCTs of GLP-1 analogues involving 56,004 patients with T2DM were analyzed. In this analysis, GLP-1 receptor agonists were associated with a significant decrease of 12% in the risk of three-point MACE. There was also a significant decrease in the risk of all-cause death (11%), CV mortality (12%), fatal and non-fatal stroke (16%), and HF hospitalization (8%) as well as a trend towards a reduction in the risk of MI. There was no significant difference in the efficacy of GLP-1 analogues between individuals with and without established CVD (Marsico, et al., 2020).

Conclusion

Following the U.S. Drug and Food Administration guidance in 2008, that required all new oral hypoglycemic agents to undergo cardiovascular outcome trials to evaluate for their cardiovascular safety (Regier, et al., 2016), the newer classes of SGLT2 inhibitors and GLP-1 RA have undergone relatively extensive large trials that have brought forth a wealth of information on their cardiovascular safety and additional renal benefits for particular drugs in those classes providing the clinician with excellent options of add-on 2nd line therapy. Keeping in mind diabetes already provides an inherent cardiovascular risk as the disease process progresses, it cannot be stressed enough that the drugs used to control hyperglycemia need to show benefit of reducing these cardiovascular risks especially in patients that already possess multiple cardiovascular risk factors or already have ongoing evidence of cardiovascular disease as can be seen in most cases in clinical practice. Ultimately, the decision to use which drug amongst the two classes depends on several factors including presence of atherosclerotic disease, and Chronic kidney disease which will guide which medication can or cannot be added, and the need to provide weight loss benefit to patients and cost and it is up to the clinician to individualize treatment.

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Diagnostic approach to eosinophilia in children

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Abstract

Hematopoiesis is the process which maintains life-long production of haemopoietic (blood) cells from bone marrow. Blood consists of three types of cells (Erythrocyte – Leukocytes - palates), and plasma. Leukocytes are divided into 2 types of granulocytes (including neutrophils, eosinophils and basophils); and agranulocytes (including lymphocytes and monocytes). Eosinophil attack and kill parasites and cancer cells, and help with allergic responses, so their role is to protect the body from bacteria and parasites. They are found in the peripheral blood and also tissue, so they are closer to where the site of infection may occur.

The eosinophil is a much-overlooked cell, more usually considered as a curious form of phagocytic leucocyte with functions similar to its more numerous cousins, the neutrophil. However, a dramatic blood and tissue eosinophilia is an important part of adaptive immunity to parasitic helminthic infections, whilst more detrimentally, the eosinophil is thought to make a major contribution to the inflammation underlying the pathogenesis of disorders such as asthma, allergic rhinitis and atopic dermatitis .[1].

Eosinophilia is a common finding in clinical practice and presented in a broad spectrum of diseases, some of them hematologic disorders and others non – hematologic (infection disease – allergic disease – medication reaction, and autoimmune disease).

Key words: eosinophilia, children, diagnostic approach

Definition

Eosinophilia is defined as an elevated absolute number of eosinophilic leukocytes in peripheral blood or tissue. The first step in elucidating the cause is to determine the absolute eosinophil count (AEC)[2], which is calculated from multiplying the percentage of eosinophils by the total white blood cell count,. using the following formula: Absolute Eosinophil Count = WBC * Eosinophils / 100

Eosinophilia is classified into three degrees:[3]
●**Eosinophilia – AEC ≥500 eosinophils/microL** in most clinical laboratories. Eosinophilia is not defined by the percentage of eosinophils (typically <5 percent in healthy individuals), because the percentage varies with the total WBC count and the proportion of other WBC lineages (eg, neutrophils, lymphocytes).

●**Hyper eosinophilia – ≥1500 eosinophils/microL** (with or without end-organ damage).

●**Hyper eosinophilic syndromes (HES)** – AEC ≥1500/microL (on two occasions ≥1 month apart) **plus** organ dysfunction attributable to eosinophilia.

THE IDIOPATHIC hyper eosinophilic syndrome (HES) is a leukoproliferative disorder, or more likely disorders, marked by a sustained overproduction of eosinophils. The distinctiveness of the syndrome, in addition to its eosinophilia, is its marked predilection to damage specific organs, including the heart. Such cardiac pathology is not unique to the idiopathic HES, because it may develop with eosinophilia associated with other diseases with identifiable etiologies. Conversely, yet enigmatically, not all patients with hyper eosinophilia develop the organ damage characteristic of the HES [4].

Tissue HE can be defined as a percentage of eosinophils that exceeds 20% of all nucleated cells in the bone marrow or tissue infiltration that is deemed extensive by a pathologist [5].

Physiology

Eosinophils are bone marrow–derived cells of the granulocyte lineage. They have an approximate half-life of 8 to 18 hours in the bloodstream, and mostly reside in tissues where they can persist for at least several weeks. Their functional roles are multifaceted and include antigen presentation; the release of lipid-derived, peptide, and cytokine mediators for acute and chronic inflammation; responses to helminth and parasite clearance through degranulation; and ongoing homeostatic immune responses. They can be part of the overall cellular milieu in malignant neoplasms and autoimmune conditions, and connective tissue disorders [6].

In normal tissue and organs, eosinophils are either absent or scattered, depending on the sites. Tissue eosinophilia is defined as increased eosinophils or signs of eosinophil degranulation in extramedullary sites such as the gastrointestinal tract, lung, thymus, spleen or lymph nodes. Eosinophils are normally controlled by cytokines interleukin (IL)-5, GM-CSF, and IL-3 produced by T-lymphocytes, mast cells, and stromal cells. Upon activation, eosinophils release their granules, such as eosinophil peroxidase, eosinophil cationic protein, major basic protein, and cytokines like TGF-β that may lead to thrombosis and tissue fibrosis and injury [7].

Eosinophils have been implicated in the pathogenesis of tissue fibrosis, thrombosis, vasculitis, and allergic inflammation. The propensity of eosinophils to cause these effects depends on a number of factors, including the number of eosinophils, their location, and degree of activation. Although these factors may be influenced by the underlying etiology of the eosinophilia, the consequences of eosinophilic inflammation can be identical despite markedly different clinical diagnoses [8].

Activated eosinophils contribute to disease pathogenesis both through direct cytotoxic effects and by recruitment and activation of other inflammatory cells. Tissue deposition of eosinophil granule proteins (major basic protein, eosinophil-derived neurotoxin, eosinophil cationic protein, and eosinophil peroxidase) contained in the characteristic secondary granules of eosinophils plays a major role in direct tissue damage. Granule proteins can be released from intact eosinophils through a process called piecemeal degranulation, whereby selective secretion of individual granule components occurs without disruption of the cell membrane, or from “cell-free” granules liberated by exocytosis or during extracellular DNA trap cell death (ETosis). In addition to the granule proteins, a wide array of cytokines and chemokines are stored preformed in the secondary granules and can be secreted in response to specific signals, leading to the recruitment and activation of other cells involved in the inflammatory response, including lymphocytes, mast cells, and fibroblasts. Eosinophil activation also leads to secretion of reactive oxygen intermediates and the formation of increased numbers of lipid bodies, the primary site of synthesis of eicosanoids, inflammatory mediators that include leukotriene C4 and 5-lipoxygenase [8].

Normal eosinophils are round to oval, 10 to 15 μm in diameter, and have a nucleus cytoplasmic ratio of 1:3; they are identified via their characteristic refractile, coarse, orange-red granules, which are typically uniform in size and generally evenly fill the cytoplasm. Eosinophils exhibit the same stages of development as neutrophils. In the most mature eosinophil form, the nucleus segments into two or more lobes connected by thin filaments with approximately 80% of segmented eosinophils containing a two-lobed nucleus with lobes of equal size and ovoid shape with dense chromatin. The remainder of segmented eosinophils will typically have three lobes, and occasionally, an eosinophil can have up to four or five lobes. Immature eosinophils are rarely seen in the blood, but can be seen in bone marrow smears, and may have fewer granules than the more mature forms. The eosinophilic

myelocyte is the earliest recognizable eosinophilic form on light microscopy. Eosinophilic myelocytes typically contain orange-red secondary granules with rare primary granules. Sometimes irregular eosinophilic cytoplasmic granulation or abnormal nuclear lobulation can alert one to a clonal eosinophilic abnormality or neoplastic process. For example, eosinophils can present with atypical/basophilic granules at any stage of maturation, but this is most often seen at the myelocyte stage. The abnormal granules resemble basophilic granules but lack myeloperoxidase and toluidine blue reactivity. These cells are referred to as harlequin cells and are associated with clonal myeloid disorders, typically a specific type of acute myeloid leukemia (AML) [9].

Causes of eosinophilia

Peripheral eosinophilia can be divided into categories of primary, secondary and idiopathic. Primary eosinophilia usually occurs in the context of hematologic malignancies and myeloproliferative disorders, including acute or chronic myeloid leukemia, and a variety of other proliferative conditions with eosinophil counts usually greater that 5000/ul. Secondary eosinophilia is associated with many other conditions. Many infectious agents can cause secondary eosinophilia that can be of moderate to severe level. In addition, a variety of diseases including most prominently allergic disorders, drug allergy, autoimmune diseases, endocrine disorders such as Addison's disease, and many different cancers can be associated with eosinophilia [10].

*Acute eosinophilia: which is associated with Allergic rhinitis – asthma – hypersensitivity reaction to drugs and foods and parasitic diseases.

*Chronic eosinophilia: Eosinophils can be inappropriately stimulated by activated T cells releasing both IL-3 and IL-5. The eosinophil granule contents irritate and deform the normal structures they come in contact with, including vascular walls, endo-cardial surfaces and mesenchymal tissues. Because of these effects, persistent eosinophilia signifies a serious parasitic infection or other serious disorders that stimulate eosinophilia through generalized T cell activation [11].

The most common cause of eosinophilia is related to socioeconomic factors. In developing world countries, the most common cause is parasitic infection, otherwise in the developed world countries it is allergy.

The causes of eosinophilia are various and can be summarized by the acronym "APLV" which refers to Allergic disorders, Parasitic infections, Leukemia/Lymphomas (and solid tumours) and Vasculitis-Immunodeficiency diseases, with allergic disorders and parasitic infections representing the most commonly identified causes. Allergic disorders are usually associated with mild eosinophilia, whereas values >20.000 cell/µl are highly suggestive for myeloproliferative disorders [12].

A Allergic disorders

Asthma: Infiltration of the bronchial mucosa by often large numbers of eosinophils is one of the consistent features of asthma. The ability of eosinophils to generate an array of pro-inflammatory mediators, in particular the cytotoxic granule proteins such as eosinophil major basic protein (MBP), has led to the hypothesis that asthma is an on-going mucosal inflammatory disease, a major component of which is the tissue damage mediated by eosinophil-derived mediators. Eosinophils are present even in mild asthma and their numbers correlate with disease severity [1].

Atopic dermatitis may produce a more significant eosinophilia if affecting a large part of the body and if associated with significant atopy. Eosinophilic esophagitis as well as other eosinophilic gastrointestinal diseases can cause a mild peripheral eosinophilia [13].

Chronic sinusitis, especially of the polypoid variety seen in aspirin-exacerbated respiratory disease, produces a more robust eosinophilic response that can be in the mild to moderate range. Often these patients start with nasal allergies and asthma, but then develop abnormal arachidonic acid metabolizing cascades and hence have a more dramatic presentation both of their disease entity and of the eosinophilia [13].

Allergic bronchopulmonary aspergillosis, related both to a fungus (Aspergillus) and to sensitization in an allergic/asthmatic host, can also produce varied and sometimes significant degrees of eosinophilia and also elevated total immunoglobulin (Ig)E [13].

Chronic eosinophilic pneumonia often starts in a sensitized, asthmatic host. Although these patients may have milder peripheral eosinophilia at disease onset, they often have more moderate range eosinophilia later in the course. They also have bronchoalveolar lavage fluid that contains at least 40% eosinophils in up to 80% of cases. This form of eosinophilic pneumonia can be premonitory to the later development of the eosinophilic vasculitis, eosinophilic granulomatosis with polyangiitis (EGPA), previously known as Churg-Strauss vasculitis [13] .

Drug allergy can cause anywhere from mild to severe eosinophilia and often waxes quickly and wanes in a slower fashion; it can take months for eosinophilia from drug allergy to clear. There is usually, although not always, an associated drug rash of the diffuse/maculopapular variety. Patients can also present with asymptomatic eosinophilia owing to drugs, especially penicillins, cephalosporins, or quinolones. Pulmonary infiltrates and peripheral eosinophilia have been associated with varied medications, including nonsteroidal anti-inflammatory drugs, sulfa drugs, and nitrofurantoin. Drug-induced diseases of other organs can also elicit tissue and blood eosinophilia (e.g. drug-induced interstitial nephritis) [6].

Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome is a life-threatening adverse drug reaction that is distinct from other drug-related reactions.

Patients with DRESS present with generalized rash, fever and internal organ involvement weeks to months after initiation of several known medications. Characteristic laboratory findings include eosinophilia and/or atypical lymphocytes, in addition to evidence of organ dysfunction. Prompt recognition of this disorder is important because the mortality is 10% but can be up to 40% if organ failure is present [14].

DRESS syndrome usually presents within 8 weeks of initiation of the causative medication. Aromatic anticonvulsants (phenytoin, phenobarbital, carbamazepine) are the most common cause of DRESS, but a variety of other drugs, such as allopurinol, minocycline, dapsone, sulfasalazine, and mexiletine, have also been associated with DRESS. The estimated occurrence of the syndrome is between 1 in 1,000 and 1 in 10,000 exposures to antiepileptic drugs. There is a 10% mortality rate from DRESS, mostly due to liver damage thought to be secondary to eosinophilic infiltration. The diagnostic criteria for DRESS syndrome include (a) widespread cutaneous eruption; (b) fever; (c) systemic involvement, including lymphadenopathy and/or 1 or more internal organ involvements (for example, interstitial nephritis, myocarditis, pericarditis, pneumonitis, hepatitis); and (d) 1 or more biologic abnormalities (for example, eosinophilia >1,500/mm3, mononucleosis-like atypical lymphocytosis) [14].

A wide variety of parasites can elicit eosinophilia, even if only relatively few of them can be responsible for such a marked increase in eosinophil levels. The pattern and degree of eosinophilia in parasitic infections result from the development, migration, and distribution of the parasite within the host, as well as from the host's immune response. Parasites tend to elicit marked eosinophilia when they or their products come into contact with immune effector cells in tissues, particularly during migration. When mechanical barriers separate the parasite from the host, or when parasites no longer invade tissues, the stimulus to eosinophilia is usually absent. Therefore, eosinophilia is highest in infections with a phase of parasite development that involves migration through tissues (eg, trichinosis, ascariasis, gnathostomiasis, strongyloidiasis, schistosomiasis, and filariasis). Detection of eggs, larvae or adult worms in faeces is necessary to make a diagnosis. However, being very difficult to obtain, a negative examination does not allow to exclude a parasitic infection with certainty. The rapid increase in eosinophil count, the potential risk of evolution to the hypereosinophilic syndrome or to organ damage, and the history suggestive of a parasite infection prompted us to undertake an albendazole-based empiric therapy [15].

A variety of infections may be associated with eosinophilia; these include helminths (worms), fungi, protozoa, bacteria, the retroviruses HIV and human T cell lymphotropic virus type 1 (HTLV-1), and scabies (a mite infestation). Most acute bacterial infections and viral infections are not associated with eosinophilia[16].

Gastrointestinal disorders: Eosinophilic gastroenteritis, ulcerative colitis and regional enteritis are often associated with blood eosinophilia. Chronic active hepatitis, milk precipitin disease, and radiation therapy for intra-abdominal neoplasia can engender blood eosinophilia[11].

Eosinophilic esophagitis (EoE) is also a common cause of HE in the pediatric age group. This diagnosis can often be missed if an appropriate history is not obtained. The primary symptoms of EoE vary with age, with younger patients presenting with feeding difficulties, frequent vomiting, food refusal/selective eating, and failure to thrive. As these children increase in age, complaints of abdominal pain and dysphagia increase, and adolescents can develop food impactions. Other primary gastrointestinal eosinophilic disorders (eosinophilic gastrointestinal disease) can also cause HE in children, although these disorders are less common than EoE. Additionally, inflammatory bowel disease can be associated with a peripheral eosinophilia[5].

Eosinophilic gastroenteritis: is a rare condition defined by eosinophilic infiltration of the intestinal wall, especially at stomach and duodenum levels. Clinical manifestations are abdominal pain and cramps, growth retardation, diarrhea, vomiting, failure to thrive, malabsorption syndrome. Diagnosis requires presence of symptoms, eosinophilic infiltration on biopsy specimens and the absence of a known cause of eosinophilia [17].

Additionally, inflammatory bowel disease can be associated with a peripheral eosinophilia.

Rheumatologic disease is the less common etiology of HE in children. Notably, eosinophilic granulomatosis with polyangiitis (EGPA, previously called Churg-Strauss syndrome) is a potentially life-threatening vasculitis rarely seen in the pediatric population and is commonly associated with moderate-to-severe peripheral blood eosinophilia, allergic rhinitis, and asthma. The most commonly involved organs include the lung and skin, although this disease can affect virtually any organ system, including the cardiovascular, gastrointestinal, renal, and central nervous systems. Other autoimmune diseases associated with HE in children include systemic lupus erythematosus, dermatomyositis, and inflammatory arthritis[5].

Approximately 10% of patients with rheumatoid arthritis will develop a mild eosinophilia.
Immune deficiency syndromes: Such as Wiskott – Aldrich syndrome, Job's Syndrome, hyperimmunoglobulin E Syndrome, Severe combined immune deficiency due to adenosine deaminase deficiency and Omenn's Syndrome.[11]

Eosinophilia is frequently present in the thrombocytopenia with absent radii (TAR) and familial reticule endotheliosis with eosinophilia syndromes. Hodgkin disease and non-Hodgkin lymphoma are frequently associated with eosinophilia. Brain tumors and myeloproliferative disorders are also associated with blood eosinophilia. Hyper eosinophilic syndrome is very rare in children. It is associated with various systemic symptoms and

a diversity of potential organ involvement. Eosinophil counts are usually > 5,000/µl. One of the most serious and more frequent complications in this disorder is cardiac disease secondary to endomyocardial thrombosis and fibrosis. Mortality is very high with a mean survival of 9 months[11].

Neoplasms: Before the recognition that most patients with hyper eosinophilia did not have a truly malignant disease, patients with HES were reported as having eosinophilia leukemia. The distinction between these disease processes, the truly malignant and the more usual nonmalignant HES, can be difficult in some patients who present with acute HES. Acute eosinophilic leukemia can be distinguished from HES when there is a marked increase in the number of immature eosinophils in the blood and/or marrow, with more than 10% blast forms in the marrow, infiltration of tissues with immature cells of predominantly eosinophilic type, and a clinical course similar to other acute leukemias. including pronounced anemia and thrombocytopenia and susceptibility to infections[5].

Lymphocytic variant HE/HES (L-HE or L-HES) is a category of disorders characterized by a clonal or aberrant lymphocyte population that produces cytokines that propagate eosinophil production and survival. Included within this category are lymphoid neoplasms, some of which are more common in children (ex. pre-B cell acute lymphoblastic leukemia [ALL]). ALL can present with HE in children, in some cases months before the underlying malignancy is detected. In these situations, eosinophils are not part of the neoplastic clone and represent a secondary response to the malignancy[5].

Adrenal insufficiency has been associated with eosinophilia, possibly due to the loss of endogenous glucocorticoids [5].

Hypoadrenalism associated with Addison disease and adrenal hemorrhage are associated with blood eosinophilia[11].

Other secondary causes of HE to consider in certain clinical situations include graft-vs.-host disease following hematopoietic stem cell transplantation, solid-organ transplant rejection, and sickle cell disease[5].

A systematic approach to the evaluation and management of eosinophilia

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History:

Clinical history is the key to identify the potential causes of eosinophilia and should first involve evaluation of the presenting complaint, followed by a systemic review.

Patients should be questioned about the following symptoms:

● Allergy: a history of fever, eczema, asthma, pruritus, urticaria, angioedema, rash and ulcers.

● History of traveling or residence in an area where parasitic infection is pandemic, or if the patient is living in a tropical region to rule out exposure to soil or freshwater which suggest parasitic disease.

● History of diet to rule out risk for ingestion of raw or undercooked meat, particularly wild game meat that can increase risk for Trichinosis. Ingestion of fruits, vegetables, or soil (i.e., a child with pica) possibly contaminated by dog or cat feces can be a risk factor for Toxocariasis.

●HIV positive patients are more likely to have disseminated parasitic or fungal infections that promote eosinophilia.

●History of medication especially non – prescription drugs or newly-given drugs (usually started 2 – 6 weeks previously) and immunosuppressive drugs. Some drugs (ex: sulfonamides, cephalosporins, penicillin, nitrofurantoin, carbamazepine, allopurinol, phenytoin or gold).

Presenting with fever, rash, lymphadenopathy and impaired liver function may indicate an adverse drug reaction.

●History of rash or lymphadenopathy is not related only to drug reaction. Leukemia, lymphoma, or systemic Masto cytosis can all cause both a rash and lymphadenopathy.

●Respiratory: Nasal/sinus symptoms, wheezing, cough, chest congestion

●Gastrointestinal: Weight loss, dysphagia (eosinophilic esophagitis), nausea, vomiting, diarrhea and abdominal pain (eosinophilic gastroenteritis), food intolerance, changes in stools

●Cardiac history: Dyspnea, chest pain, palpitations, symptoms of heart failure in a patient with marked eosinophilia, and this case considered a clinically urgent situation.

●Nervous system: Transient ischemic attack, cerebrovascular accident, behavioral changes, confusion, balance problems, memory loss, change in vision, numbness, weakness, pain

●Other: Including symptoms attributable to lymphadenopathy or hepatosplenomegaly (i.e. new abdominal or chest discomfort, early satiety), ocular findings, genitourinary complaints, myalgia, arthralgia, and anaphylaxis.

●Galich's Syndrome: rare condition of recurrent angioedema with eosinophilia and increased IgM levels.

Physical exam:

Physical examination is still the cornerstone to evaluate the presenting complaint. A careful physical exam should be completed at every visit, noting any fever, skin rashes, lymphadenopathy, nasal obstruction, abnormal or decreased lung sounds, abdominal tenderness, hepatosplenomegaly, cardiac failure, neuropathy or joint redness/swelling.

***Temperature:** should be checked and documented. Presenting with fever may indicate parasitic or fungal infection or drug reaction.

***Skin:** should be inspected for erythema, eczematous, rash, oedema, urticaria or skin infiltration.

***Vasculitis signs** should be examined to rule out a primary vasculitis condition such as eosinophilic granulomatosis with polyangiitis (Churg – Strauss Syndrome)

***Lymph node:** in case of lymphadenopathy the lymph nodes should be assessed from the size – texture looking for a possible neoplasm (EX: lymphoma – lymphoid or myeloid leukemia).

Hard – fixed and non – tender nodes are more likely to associated with malignancy.
***Bronchospasm** should be checked to rule out asthma, allergic bronchopulmonary aspergillosis or a severe drug reaction. Presenting of cough, dyspnea or wheeze may indicate a lifecycle – related pulmonary migration of parasites, a drug reaction or eosinophilic leukemia. Schistosomiasis can cause pulmonary hypertension, and eosinophilic granulomatosis with polyangiitis can cause pulmonary infiltrates.

***Hepatomegaly and splenomegaly** should be checked looking for lymphoma or eosinophilic leukemia
***Cardiomegaly,** arrhythmia or heart failure may be features of cardiac damage by eosinophilia

Eosinophils can accumulate in multiple organs, most commonly involving the heart, skin, lungs, spleen and liver. Neurological end-organ complications in hyper eosinophilic syndrome are unusual and have been established to be of three types: brain infarction, encephalopathy and sensory polyneuropathy. It is important to consider HES as an etiology for stroke and a high eosinophil count is an initial diagnostic clue[18].
Diagnostic evaluation: At the first step we should consider the severity of eosinophilia.

All children who meet diagnostic criteria for HE (i.e., blood AEC ≥1,500 cells/microL on at least 2 separate occasions [interval ≥1 month] or marked tissue eosinophilia) or moderate-to-severe eosinophilia with illness symptoms should undergo an initial diagnostic evaluation to try to determine the underlying etiology. Laboratory evaluation should include complete blood count with differential to evaluate for abnormalities in the other blood cell lines[19]. The CBC and blood film should also be used to look for the following findings: *Cytopenia, which may be found in hematological malignancy.

*Thrombocytosis which may occur secondary to infection, inflammation, hemorrhage, or malignancy as well as in certain hematological disorders (such as chronic myeloid leukemia, essential thrombocythemia, and polycythemia vera).

*Lymphocytosis which can present in many hematological neoplasms
*Malignant cells
*Filariae

Patients who present with acute eosinophilia need to be evaluated for the two most common causes, i.e. atopic and related diseases and parasitic infections. Atopic disease is the most common cause of eosinophilia in industrialized countries while parasitic disorders are more common elsewhere [10].

The first step in an evaluation of a chronic hyper eosinophilia syndrome would be to repeat the eosinophil count within at least two, and up to four weeks after initial observation in those whose eosinophilia is persistent and not easily explained. Attention needs to be paid to all of the diseases mentioned above and their potential associations with mild, moderate or severe eosinophilia. Under certain circumstances more intense evaluation, including chromosomal evaluation for the underlying disease needs to be aggressively pursued [10].

A peripheral blood smear should be reviewed to evaluate for white blood cell blasts or other blood dyscrasias that could suggest a primary hematologic disorder. If blasts are noted, LDH, uric acid and hematology/oncology consultation is indicated. Bone marrow examination (aspiration and biopsy) should be considered for any child whose initial evaluation demonstrates no clear secondary etiology and a primary hematologic cause of the eosinophilia remains possible. In addition, bone marrow examination is appropriate for any acutely ill child with specific organ involvement and no clear underlying diagnosis, children with an eosinophil count >100,000 eosinophils/microL, or children with abnormal features on their peripheral blood smear (immature or dysplastic white blood cells, thrombocytopenia, or unexplained anemia). Serum chemistries, creatinine, and urinalysis should be completed to evaluate for evidence of renal or bladder involvement. Abnormal serum chemistries could also suggest underlying adrenal insufficiency. Liver function tests (to determine hepatic involvement) and cardiac troponin levels (for evidence of subclinical myocardial disease) should also be obtained. Patients with an elevated troponin level should be further evaluated with electrocardiography and echocardiography. Serum B12 level should be obtained as a screening marker for myeloproliferative neoplasms and autoimmune lymphoproliferative syndrome (ALPS). Serum tryptase can be obtained to screen for systemic Masto cytosis. Stool testing for ova and parasites and serologic testing for endemic parasites should also be routinely completed (Strongyloides, Toxocara, Trichenella). The indication for additional parasite testing is typically determined by exposure (diet, travel). Chest radiography should be completed to evaluate pulmonary involvement. Finally, in patients with a history of recurrent infections, lymphadenopathy, and/or hepatosplenomegaly, flow cytometry to evaluate lymphocyte subsets and immunoglobulin levels can be sent to screen for lymphocyte clonality and selective lymphocyte and immunoglobulin deficiencies. Additionally, T-cell receptor rearrangement studies can be useful to provide evidence of oligoclonality in the lymphocyte compartment. Finally, depending on risk factors, HIV testing may be indicated [5]. If the patient is unwell or the count of eosinophil is markedly elevated and the cause is not obvious, further investigation is indicated. Sometimes such investigation is urgent (EX: in cardiac failure or if the eosinophil count is considerably high).

Treatment of eosinophilia :
Evaluation and treatment of pediatric patients with hyper eosinophilia is challenging, as the etiology is often difficult to discern. The differential diagnosis is broad, and work-up can ultimately be extensive and costly; thus, it is important to identify underlying conditions at which treatment can be directed rather than directing treatment at the eosinophilia itself [20].

Most cases of secondary eosinophilia are treated on the basis of their underlying causes. Allergic and connective tissue disorders may be amenable to corticosteroid treatment. Parasitic and fungal infections can be worsened or disseminated by use of steroids and should be ruled out if they are indicated by patient history[21].

In patients with primary eosinophilia without organ involvement, no treatment may be necessary. Cardiac function should be evaluated at regular intervals, however, as peripheral eosinophilia does not necessarily correlate with organ involvement. Steroid responsiveness should be evaluated, both for prognosis (steroid-responsive patients do better) and to guide treatment when needed [21].

Choices for systemic treatment of primary eosinophilia with organ involvement initially include corticosteroids, and interferon (IFN)-alpha for steroid-resistant disease. Other agents for steroid-resistant disease, which are usually given as long-term maintenance regimens to control organ involvement, include the following:

Hydroxyurea – Chlorambucil – Vincristine -Cytarabine - 2-Chlorodeoxyadenosine (2-CdA) -Etoposide Cyclosporine. [21]

Treatment decisions are determined based on suspected etiology and level of eosinophilia. The level of intervention involves the correct treatment of the underlying disorder. If an autoimmune disease is identified, appropriate treatment for the primary autoimmune disease should be undertaken. The same would hold for immunodeficiency or infection. For patients with HES with the **FIP1L1 genetic*** translocation, treatment with imatinib should be initially considered. For those without the translocation, steroids are the mainstay of therapy. Interferon alpha as well as other potential cytotoxic drugs such as hydroxyurea are necessary under some circumstances with severe hyper eosinophilia [10].

Hyper eosinophilic syndromes are a heterogeneous group of disorders that may be associated with life-threatening organ injury as a result of tissues infiltration by eosinophils. The main goal of therapy is to mitigate eosinophil-mediated organ damage. When possible, therapy should be directed at the underlying etiology. However, even in the absence of any known cause, when organ damage is present, hyper eosinophilia must be treated promptly and aggressively to reduce potential morbidity and mortality. Areas covered: Conventional therapies, including corticosteroids, hydroxyurea (hydroxycarbamide) and interferon-alpha, have shown variable efficacy and a non-negligible toxicity emphasizing the need of new therapeutic strategies based on drugs with different mechanisms of action. Expert opinion: Tyrosine kinase inhibitors have a central role among targeted therapies of hyper eosinophilic syndromes. Imatinib, initially empirically used based on its activity in chronic myeloid leukemia, achieved preliminary excellent results further confirmed in a large series of patients. Third-generation tyrosine kinase inhibitors such as ponatinib, while active in vitro and in vivo in animals, still deserve confirmation in properly designed clinical trials. In addition, clinical investigation on monoclonal antibodies against interleukin-5, interleukin-5Rα, IgE, and CD52 represents a promising area of research.[22] Finally, experimental treatment with anti-IL 5 has been considered in a variety of eosinophil associated secondary diseases including asthma, as well as in the treatment of primary hyper eosinophilia. This has resulted in significant success in terms of prevention of exacerbations of the underlying disease, as well as reduction in steroid dose required for the treatment of the primary and/or secondary cause of eosinophilia [10]. Management of medical emergencies should not be delayed by the diagnostic evaluation of eosinophilia. Patients with an acute illness due to leukocytosis or organ dysfunction from eosinophil infiltration may require urgent treatment with high dose steroids, leukapheresis, and/or cytoreduction as described separately[3].

Summary

Eosinophilia is defined as increase in peripheral blood eosinophil count Eosinophilia (≥500 eosinophils/microL) and hyper eosinophilia (≥1500 eosinophils/microL). Eosinophilia is a common finding in children. Allergic disease (eczema, allergic rhinitis, asthma) is a common cause of mild-to-moderate eosinophilia in the pediatric population and a minority of these patients can meet criteria for HE disease. Atopic disease is the most common underlying cause of eosinophilia in industrialized countries while parasitic disorders are more common elsewhere. To approach patients with eosinophilia we should follow the traditional model of clinical history, physical examination, laboratory, and other investigations, considering the likely causes in the individual patient. Ask for new exposures, including dietary changes and new medications, obtain a travel history, looking for focal symptoms, including rash, cough, shortness of breath, fever, connective tissue complaints, and GI symptoms, all may help clinically focus the evaluation.

Laboratory investigations including stool examination to rule out parasitic infections - Peripheral blood smear may help identify specific pathogens (e.g., microfilariae) or may identify an acute or chronic leukemia associated with eosinophilia. Other laboratory assessments to consider are complete blood count, serum immunoglobulins (including IgE), serum tryptase, and bone marrow biopsy. Treatment should be directed to treat underlying cause of eosinophilia rather than treat eosinophilia itself.

Corticosteroids have been used as first-line treatment. However, mucosal ulcers do not respond to corticosteroids. Other immunosuppresants and immunomodulating agents have been used as detailed in the medication section. These include hydroxyurea, vincristine, cyclophosphamide, busulfan, methotrexate, chlambucil, etoposide, cyclosproin, and alemtuzumab.

***FIP1L1 genetic: FIP1L1; factor interacting with PAPOLA and CPSF1**

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Machine Learning in Otorhinolaryngology, Head and Neck Surgery and its applications in diagnosis and management: Undergraduates Perception toward New Era

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Abstract

Background & aim: Machine learning (ML) is a growing field concerned with predicting novel situations from previous observations. The aim of this study was to determine medical students' perceptions of ML in otorhinolaryngology, head, and neck surgery and its applications in diagnosis and management. Also, to assess medical students' awareness of current challenges facing the application of ML in medical practice in the Kingdom of Saudi Arabia (KSA).

Methods: A cross-sectional survey was conducted in February–May 2021 among medical students in Saudi Arabia. The participants were provided with questionnaires of the survey using electronic forms. Validation of the questionnaire was done using exploratory factor analysis and confirmatory factor analysis. There were 8 validated items on Attitude and 6 items on Knowledge.

Results: A total of 538 students completed the questionnaire. The majority of the students were familiar with machine learning in general 308 (57.3%). However, only a few of the participants were familiar with machine learning applications in the field of otorhinolaryngology, head, and neck surgery 184 (34.2%). There was a significant difference between knowledge and attitude with the current year of study and GPA score, however, gender had no difference, yet there was a significant association between attitude among male and female medical students.

Conclusion: Medical students in the KSA demonstrated a good knowledge of ML in general, although many were not familiar with machine learning applications in the field.

Key words: Machine learning, Otorhinolaryngology, Medical student, Kingdom of Saudi Arabia

Introduction

Machine learning (ML) is a subfield of artificial intelligence (AI) constituting vast resources to combine computer science and data by utilizing statistical algorithms to help solve various medical problems. It is a growing field that is concerned with predicting novel situations from previous observations. ML has a great potential to deal with large, complex, and disparate data commonly found in the medical field. Due to its vast potential, it is considered as the future of research in the biomedical field, personalized medicine, and computer-aided diagnosis (1). The common applications of ML across a range of specialties include enhanced cancer diagnosis, adaptive clinical trial designs, and prognosis prediction by integrating clinical and genomic data (2,3). The deployment of ML models in the healthcare domain can increase the speed and accuracy of diagnosis and improve treatment planning and patient care (4). Li W et al conducted a study for a more accurate diagnosis of COVID-19 based on symptoms and results of routine tests by applying ML to reanalyze COVID-19 data from 151 published studies and they found that it was able to distinguish COVID-19 patients from influenza patients with a specificity of 97.9% and a sensitivity of 92.5% (5). Deep learning is becoming the gold standard in ML and is gradually becoming the most commonly used computational approach in ML. It has the ability to learn a large amount of information with great results (6). But to improve the diagnostic performance, we cannot rely solely on ML as it is also important to understand the role of human decisions (7). AI has the potential to deliver more precise results in clinical diagnosis. A study conducted in China developed and utilized an AI system, Med3R which became the first AI system to successfully pass the written test of the National Medical Licensing Examination in China 2017 with a total score of 456, exceeding 96.3% of human examinees. Med3R with the help of real electronic medical records has been used to provide aided clinical diagnosis services (8).

Otolaryngology-head and neck surgery is the oldest branch in medicine that carries unique opportunities to show the potential of ML (9). Recently, there has been a steep increase in the literature volume describing the vast applications of ML in the field of otolaryngology–head and neck surgery that include automatic recognition of auditory brainstem response waveforms, genomic prediction of oral squamous cell carcinoma, and acoustic voice feature classification (10-12). ML with the use of deep learning algorithms can be helpful in improving accuracy and can also improve doctors' confidence in both diagnoses and decision-making with respect to this field. Fang SH et al (13) and Fujimura S et al (14) utilized the use of ML in diagnosing a plethora of diseases of the head and neck through detection of the pathological voice using cepstrum vectors and discrimination of "hot potato voice" using a support vector machine respectively. Halicek M et al conducted a study to detect tumours of the thyroid and salivary glands using hyperspectral imaging and deep learning (15,16). Bing D et al have reported its use in predicting hearing outcomes in sudden sensorineural hearing loss (17). Formeister EJ et al predicted the postoperative complications in head and neck microvascular free tissue transfer (18).

The medical schools should be aware of the perception of medical students about ML to enhance the students' knowledge about this science and its importance in diagnosing as well as treating diseases with accuracy along with fewer side effects. Therefore, knowing the perceptions of medical students in this field will be beneficial for medical schools and the students to develop their understanding of ML. Given the importance of computer science in medical practice and advancement in ML, otolaryngologists and head and neck surgeons are tasked with how ML can identify the statistical patterns of data generated by tens of thousands of physicians and billions of patients by training computers to perform specific tasks with sometimes superhuman ability (19). This study examines the medical students' perceptions of ML in otorhinolaryngology, head, and neck surgery, and its importance in the medical field.

Methods

A questionnaire-based cross-sectional survey was conducted in February 2021 among medical students in Saudi Arabia. The study was approved by the Institutional Review Board of the Medical Research Unit, College of medicine, Imam Mohammad Ibn Saud Islamic University. The study was conducted using questionnaires through an electronic form which was distributed among medical students. Validation of the questionnaire was done using exploratory factor analysis (EFA) and confirmatory factor analysis (CFA). There were 8 validated items on Attitude and 6 items on Knowledge. The questionnaire addressed demographic information, knowledge of ML in otorhinolaryngology, head and neck surgery, sources of information, and the level of awareness of its applications in diagnosis, and management. Students' consent to participate in the survey was done.

The questionnaire was completed by 538 respondents. Medical Students were asked about their gender, age, year of study, and their Grade Point Average (GPA) scores. Further questions addressed whether they were familiar with ML use in otorhinolaryngology, head and neck surgery to assess the extent to which the universities and college of medicine in Riyadh informed the students of ENT about ML and its importance in the diagnosis and treatment of a variety of diseases, as well as, its benefits in decreasing the time it takes to reach a diagnosis and offer treatment in some diseases in otorhinolaryngology, head, and neck surgery. The survey asked if medical students in Riyadh agreed that they knew the importance of ML or not or whether the ENT curriculum or even any curriculum in the colleges introduced ML. Students were asked if they thought this information would be offered in advanced-level courses in medical school and if the students preferred to know it during the residency in otorhinolaryngology, head, and neck surgery, for example.

Statistical analysis: Statistical analysis was performed using SPSS 28.0 (IBM, Armonk-USA. Counts and percentages were used to summarize categorical variables. The mean ± standard deviation was used to summarize the distribution of continuous variables. Chi-square test of independence was used to assess the association between categorical variables. The association of attitude and knowledge was analyzed using the Chi-square test. EFA and CFA were carried out to explore the factors associated with machine learning in otorhinolaryngology and also for validation of the instrument using SAS 9.4

Results

The questionnaire was completed by 538 respondents (70.6% males and 29.4% females). Respondents aged 18–20 years and 21–23 years represented 12.6% and 40.7% of the study sample, respectively, while respondents aged 24–26 years represented 44.6% of the study sample. Interns represented 13.1% of the study sample. Approximately half of the respondents were in the 5th year of study (48.3%). Respondents in the pre-clinical years (1st, 2nd, and 3rd years) and clinical years (4th year, 5th years, and interns) represented 27.1% and 72.8% of the study sample, respectively. Half of the respondents (45.7%) reported a GPA of 3.75–4.49, and one-third (30.3%) reported a GPA of 4.5–5 (Table 1).

Table 1: Descriptive statistics of the study sample (n=538)

Variables	n (%)
Gender	
Male	380(70.6)
Female	158(29.4)
Age in Years	
18-20	68(12.6)
21-23	219(40.7)
24-26	240(44.6)
>26	11(2.0)
Current year of Study	
First year	61(11.3)
Second year	37(6.9)
Third year	48(8.9)
Fourth year	62(11.5)
Fifth year	260(48.3)
Intern	70(13.0)
GPA	
2-2.74	18(3.3)
2.75-3.74	86(16.0)
3.75-4.49	246(45.7)
4.50-5	163(30.3)
Prefer not to answer	25(4.7)

Table 2 showed that three main challenges faced the application of ML: unfamiliarity with ML (35.1%), machine errors that compromise patient care (29.2%), and affordability (28.2%). One-third of the respondents thought applying ML in otorhinolaryngology was important due to the anatomical complexity (35.1%). Others (30.7%) thought that it was important to improve physician's decision-making skills and less than one-quarter (1.9%) thought that it was important to reduce diagnostic errors. Suggested options to overcome these challenges included: exposing medical students to the concept of ML in their curriculum (32.9%), advertising ML applications among physicians (26.0%), promoting research importance in ML (24.9%), and increasing the affordability of ML applications (14.3%).

Table 2: Challenges and suggestions for overcoming the application of ML

Variable	n (%)
Q10. In your opinion what is the most important challenge that faces the application of machine learning in medical practice	
Affordability	151(28.1)
Machine errors may compromise patient care	157(29.2)
Unfamiliarity with machine learning	189(35.1)
Data security	35(6.5)
I don't know	06 (1.1)
Q11. In your opinion why is the application of machine learning in otorhinolaryngology, Head and Neck surgery important?	
Not important	51(9.5)
The anatomical complexity	189(35.1)
Decrease diagnostic errors	118(21.9)
To improve physician's decision making skills	165(30.7)
I don't know	15(2.8)
Q12. In your opinion what can be done to overcome the challenges that face machine learning application in otorhinolaryngology, Head and Neck surgery	
Expose medical students to the concept of machine learning in their curriculum	177(32.9)
Advertise machine learning applications among physicians	140(26.0)
Promote research importance in machine learning	134(24.9)
Increase the affordability of machine learning applications	77(14.3)
I don't know	10 (1.9)

Table 3 depicts the percentage of attitude and knowledge in ML. The majority of the participants 308(57.3%) were familiar with ML. About 235(69.2%) considered that ML was important in health practice. But only 173(32.1%) had it covered in the ENT curriculum. Most of the students 343(54.8%) felt that there was a great future for ML in ENT in KSA. Only a few students felt that 162(30.1%) ML was not important to learn in the curriculum of ENT. The students were also open-minded in responding to the not necessary instrument in ML in the field of ENT 166(30.9%). Only 297(55.2%) felt that ML in ENT should be taught after graduation.

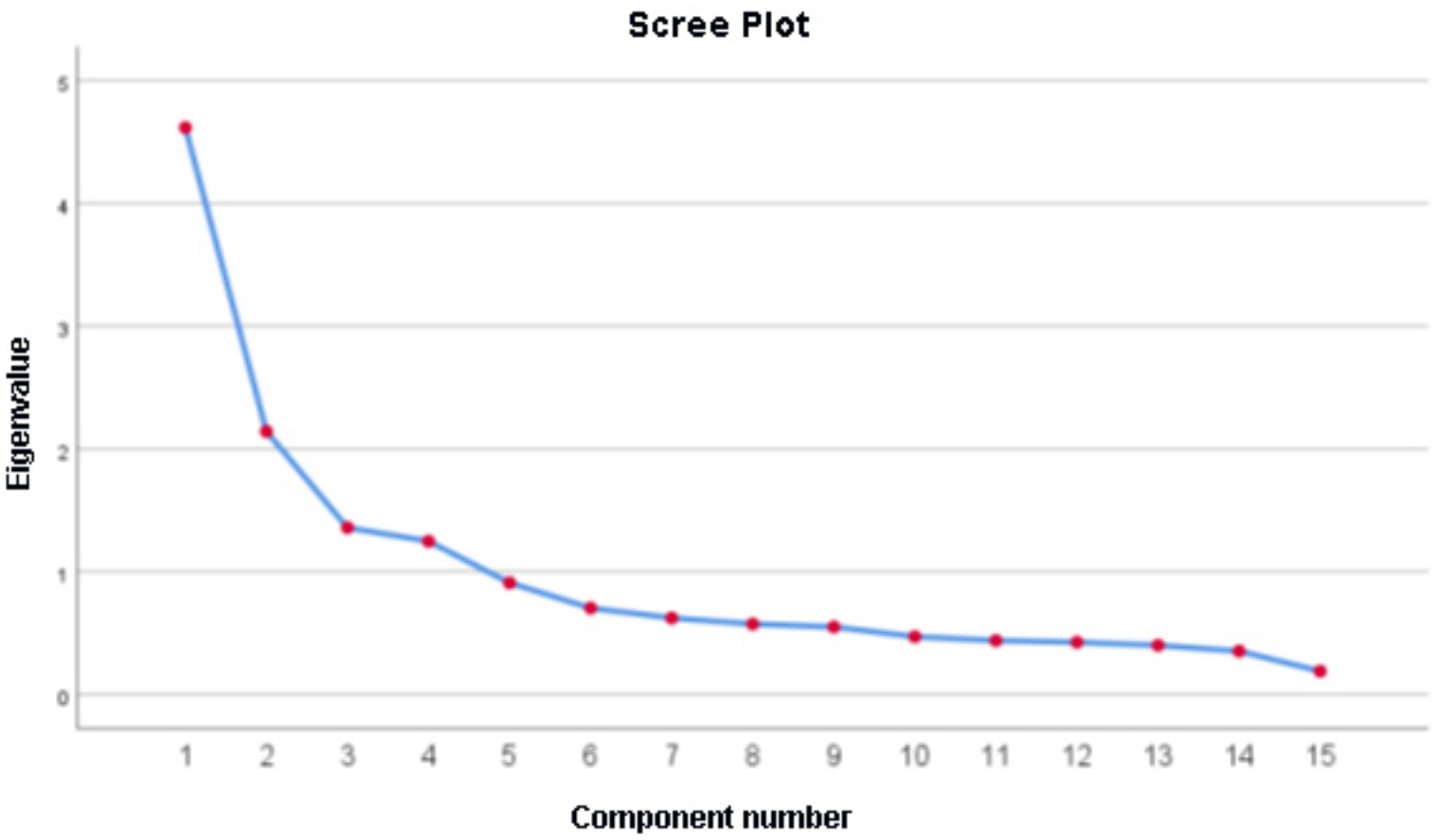
Table 3: Distribution of the Machine Learning questionnaire in Otolaryngology.

Items in Machine Learning Questionnaire	SA	A	U	D
Q6. Are you familiar with "machine learning"?	101 (18.8)	207 (38.5)	136 (25.3)	94 (17.5)
Q7. Are you familiar with "machine learning" applications in medical practice?	71 (13.2)	226 (42.0)	124 (23.0)	117 (21.7)
Q8. Are you familiar with "machine learning" applications in the field of Otolaryngology-Head and Neck surgery?	47 (8.7)	137 (25.5)	177 (32.9)	177 (32.9)
Q9. In your opinion is "machine learning" important in health practice:	152 (28.3)	220 (40.9)	140 (26.0)	26 (4.8)
Q13. Do you think that the ENT curriculum has been covered Machine Learning very well	42 (7.8)	131 (24.3)	218 (40.5)	147 (27.3)
Q14. Do you think that Machine Learning in ENT has a great future especially in the Kingdom of Saudi Arabia?	108 (20.1)	235 (43.7)	173 (32.2)	22 (4.1)
Q15. Do you think that the benefits and negatives of Machine Learning have been excellently demonstrated in ENT specialty?	63 (11.7)	165 (30.7)	237 (44.1)	73 (13.6)
Q16. Do you think that the Machine learning will be a reason for a qualitative shift in the ENT surgeries?	126 (23.4)	190 (35.3)	184 (34.2)	38 (7.1)
Q17. Do you prefer to go more deeply into Machine Learning in the ENT specialty, because it is considered a step forward in the development of the health system?	150 (27.9)	210 (39.0)	138 (25.7)	40 (7.4)
Q18. Do you think that Machine Learning in ENT surgeries will have a positive effect in terms of reducing the duration of operations?	135 (25.1)	246 (45.7)	130 (24.2)	27 (5.0)
Q19. Do you think that Machine Learning in ENT surgeries will have a positive effect in terms of reducing the complications of surgery?	106 (19.7)	257 (47.8)	142 (26.4)	33 (6.1)
Q20. Do you think that machine learning is not important to learn in ENT curriculum	41 (7.6)	121 (22.5)	152 (28.3)	224 (41.6)
Q21. Do you think that machine learning in ENT had an impact on you for considering this specialty in the future?	108 (20.1)	170 (31.6)	168 (31.2)	92 (17.1)
Q22. In ENT curriculum; there are certain instruments that I don't need to know?	57 (10.6)	109 (20.3)	197 (36.6)	175 (32.5)
Q23. I think that machine learning in ENT should be after graduation when choosing this specialty	142 (26.4)	155 (28.8)	136 (25.3)	105 (19.5)

*SA: Strongly Agree , A: Agree, U: Unsure , D: Disagree, SD: Strongly disagree- nobody strongly disagreed.

Figure 1 represents the Scree plot of the exploratory factor analysis with Eigenvalue in the y-axis and the component (Questions) in the x-axis. This is a pictorial representation of deciding the number of factors to enter into the final rotation. As per the previous literature, it is wise to fix our Eigenvalue at 1.5 which gives us two factors namely one with an Eigenvalue at 4.618 and another at 2.143 namely attitude and knowledge, respectively.

Figure 1: Showing Scree plot of the EFA with Eigen value in the y axis and the component (Questions) in the x axis



Exploratory Factor analysis (EFA) and Confirmatory factor analysis (CFA): An EFA was done on the ML-survey questionnaire with an Eigenvalue restricted at 1.5 or above which had given two factors with 30.78% and 14.29% variation explained respectively. The Kaiser Mayer-Olkin (KMO) (20) which is a measure of sampling adequacy was found to be 0.815. Bartlett's test of Sphericity was found to be highly significant with a P-value <0.001. The factor analysis was performed based on the Principal component analysis with including factor loading only 0.5 and above was considered further, which is indicated as bold and italic in Table 4. Factor loading less than the specification was not included in the further modeling. Table 4 explains the factor loading for each item. A Promax rotation with Kappa= 4 was chosen. This resulted in 10+6 items into two factors which were named as Attitude (first factor) with 10 items and Knowledge for the second domain with 6 items. Question 23 "I think that machine learning in ENT should be after graduation when choosing this specialty" was removed from the model as it had the least factor loading which was not included in either of the factors. Question 20 "Do you think that machine learning is not important to learn in ENT curriculum" had a negative factor loading for the factor Attitude but it had a higher and positive factor loading in Knowledge factor so it was considered into the second factor. Negative factor loadings indicated that the scoring has to be given in reverse order. CFA with the above 16 items was carried out where the Chi-square statistics had a P-value of <0.0001 with an RMSEA (21) of 0.14, despite a Bentler's CFI of 0.67 (21,22) which was considered to be low. However, the fitted factor's Cronbach's alpha (23) was considerably higher with 0.827 for Attitude and 0.737 for Knowledge.

Table 4: Factor loading after Promax rotation with Kappa=4 in exploratory factor analysis:

Items in Machine Learning Questionnaire	Attitude Eigen values=4.618 Cronbach's α=0.827	Knowledge Eigen values=2.143 Cronbach's α=0.737
17. Do you prefer to go deeper in the Machine Learning in ENT specialty, because it is a considered step forward in the development of the health system?	*0.746*	0.068
19. Do you think that the Machine Learning in ENT surgeries will have a positive effect in terms of reducing the complications of surgery?	*0.732*	0.169
18. Do you think that the Machine Learning in ENT surgeries will have a positive effect in terms of reducing the duration of operations?	*0.694*	0.094
16. Do you think that the Machine learning will be a reason for a qualitative shift in the ENT surgeries?	*0.684*	0.086
6. Are you familiar with "machine learning"?	*0.657*	0.505
9. In your opinion is "machine learning" important in health practice:	*0.631*	0.218
14. Do you think that Machine Learning in ENT has a great future especially in the Kingdom Of Saudi Arabia?	*0.612*	0.257
21. Do you think that machine learning in ENT had an impact on you for considering this specialty in the future?	*0.572*	0.225
23. I think that machine learning in ENT should be after graduation when choosing this specialty	0.347*	*0.251*
20. Do you think that machine learning is not important to learn in ENT curriculum	-0.47	*0.672*
22. In ENT curriculum; there are certain instruments that I don't need to know.	0.032	*0.669*
13. Do you think that the ENT curriculum has covered Machine Learning very well	0.189	*0.664*
8. Are you familiar with "machine learning" applications in the field of Otolaryngology-Head and Neck surgery?	0.383	*0.635*
15. Do you think that the benefits and negatives of Machine Learning have been excellently demonstrated in ENT specialty?	0.334	*0.634*
7. Are you familiar with "machine learning" applications in medical practice?	0.587	**0.621**

Bold values indicate item retained in the scale. *q23 I think that machine learning in ENT should be after graduation when choosing this specialty had a least factor loading.

A path diagram in Figure 2 based on the principal component analysis was drawn which is displayed with the respective factor loading according to the factors and items within the subscales.

Figure 2: Path diagram showing the respective factor loading according to the factors and items within the sub scales

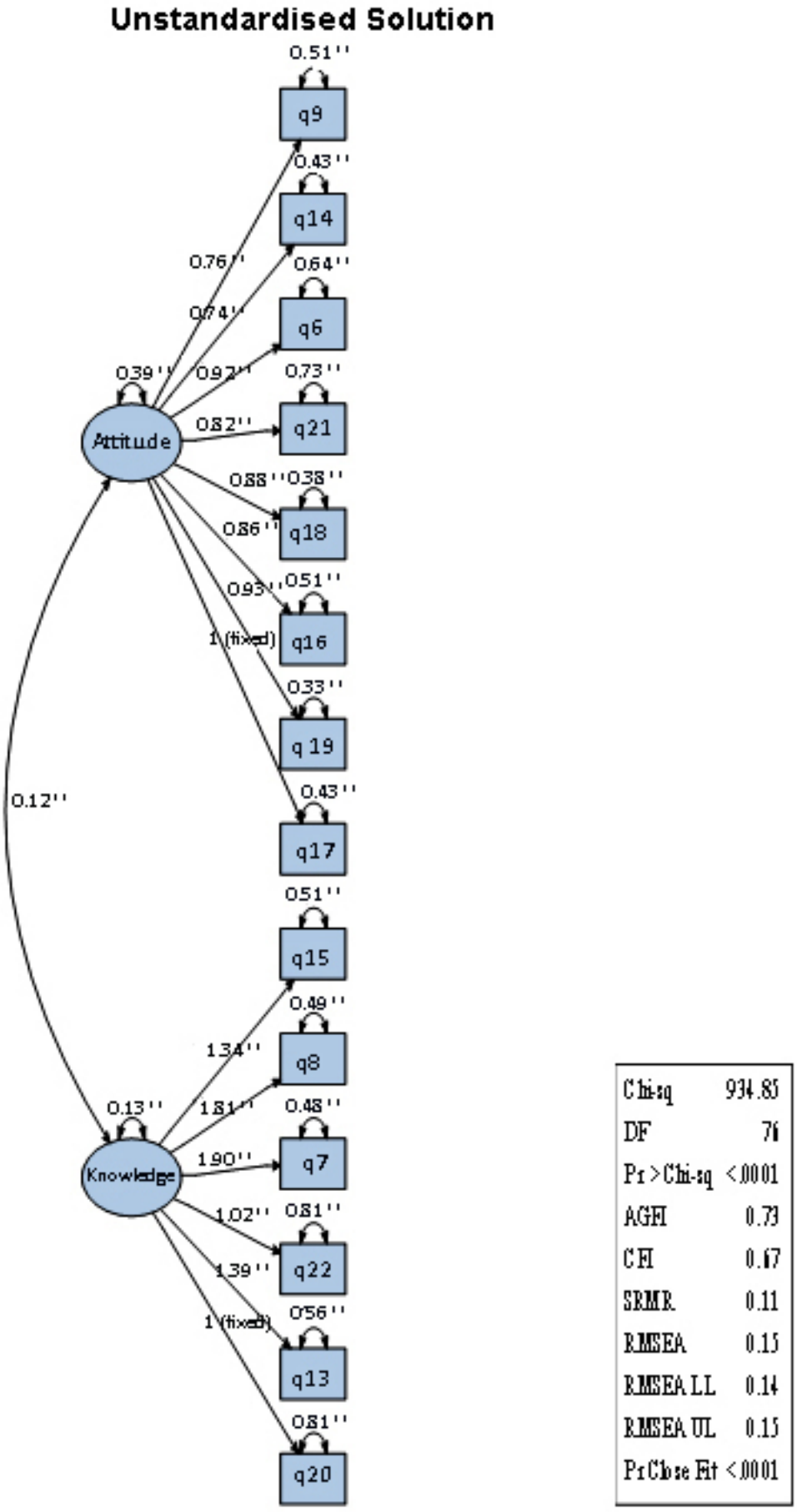


Table 5 and Table 6 indicate the association between Attitude and Knowledge between the demographic variables. From the derived items of factors Attitude and Knowledge above and below means were calculated. Attitude consisted of 10 items with the least score of 8 and a maximum score of 31; 17.80±4.75 and for Knowledge domain had 6 items with the least score at 6 to the highest score at 24; 16.85±3.71. The demographic variables such as gender, age, current year of study, and GPA score were associated, of which age did not have any association between the attitude, or knowledge. There was a significant association between male and female students with respect to the attitude but not with the knowledge. There was a significant association between the current year of study and GPA in both attitude and knowledge.

Table 5: Distribution of Attitude with demographic variables

Attitude	Less than Mean, n (%)	Greater than mean, n (%)	P value
Gender			
Male	175(65.5)	205(75.6)	0.010*
Female	92(34.5)	66(24.4)	
Age in Years			0.322
18-20	31(11.6)	37(13.7)	
21-23	107(40.1)	112(41.3)	
24-26	126(47.2)	114(42.1)	
>26	3(1.1)	8(3.0)	
Current Year of study			<0.001*
First Year	25(9.4)	36(13.3)	
Second year	20(7.5)	17(6.3)	
Third year	21(7.9)	27(10.0)	
Fourth year	17(6.4)	45(16.6)	
Fifth year	132(49.4)	128(47.2)	
Intern	52(19.5)	18(6.6)	
GPA			<0.001*
2-2.74	4(1.4)	14(5.4)	
2.75-3.74	49(17.8)	37(14.0)	
3.75-4.49	138(50.6)	108(40.9)	
4.50-5	70(25.5)	93(35.2)	
Prefer not to answer	13(4.7)	12(4.5)	

*Statistically significant

Table 6: Distribution of Knowledge with demographic variables

Knowledge	Less than Mean, N (%)	Greater than mean, N (%)	P value
Gender			
Male	166(74.1)	214(68.2)	0.135
Female	58(25.9)	100(31.8)	
Age in Years			
18-20	29(12.9)	39(12.4)	0.201
21-23	80(35.7)	139(44.3)	
24-26	111(49.6)	129(41.1)	
>26	4(1.8)	7(2.2)	
Current Year of study			
First Year	32(14.3)	29(9.2)	0.023*
Second year	10(4.5)	27(8.6)	
Third year	13(5.8)	35(11.1)	
Fourth year	23(10.3)	39(12.4)	
Fifth year	111(49.6)	149(47.5)	
Intern	35(15.6)	35(11.1)	
GPA			
2-2.74	7(3.2)	11(3.4)	0.012*
2.75-3.74	34(15.9)	52(16.0)	
3.75-4.49	97(45.3)	149(46.0)	
4.50-5	67(31.4)	96(29.6)	
Prefer not to answer	09(4.2)	16(5.0)	

*Statistically significant

Discussion

The study was conducted to determine medical students' perceptions of ML in otorhinolaryngology, head, and neck surgery and its applications in diagnosis and management, and also to assess medical students' awareness of current challenges facing the application of ML in medical practice in the KSA.

The findings of our study revealed that more than half of the participants (57.3%) have a good knowledge of ML in general. In a similar study, the results showed that 78.9% of their respondents had a good understanding of AI (24), and another study found that approximately 50% believed they had a good understanding of AI; however, when knowledge of AI was tested using five questions, on average, only 22% of the questions were answered correctly (25).

Our study showed that there is a significant difference related to the familiarity of ML application in medical practice as 55.2% of the participants were aware of it; however, only 34.2% of the participants were familiar with ML application in the field of otorhinolaryngology, head, and neck surgery. These findings might be explained by the short duration of the ENT course that is taught in the medical schools in the KSA, during which, there is a limited time to cover the fundamentals of ENT, and ML cannot be covered as well. This notion was supported by the findings of a study conducted by Park SH et al which showed that 32% of the participants agreed that ML was covered very well in the ENT curriculum in their medical school (26) which is similar to the findings of our study where 32.1% had it covered in ENT curriculum. A systematic review showed that although using AI and ML in teaching and practicing medicine is advised, they are still not taught in traditional medical and health informatics curricula (27). To overcome this drawback, ML should be taught as an elective subject for undergraduate medical students. Even some medical colleges in the Republic of Korea such as the University of Ulsan and Yonsei University have recently started providing AI-dedicated elective courses to the students (27).

In our study, we found that the main challenge in applying ML in medical practice will be unfamiliarity with ML (35.1%) and they believe that to overcome this challenge, medical students need more exposure by adding ML to the curriculum in medical schools (32.9%). Although this was not the only challenge, there were other challenges affecting the application of ML in the medical field, such as machine errors that compromise patient care (29.2%) and affordability (28.2%). A survey conducted in the UK showed that 63% of the adults were uncomfortable permitting their personal data to be used to improve healthcare and were opposed to AI systems substituting medical professionals in their usual tasks (28).

The majority of the participants (25.1% and 45.7% were strongly agreeing and agreeing respectively) in our study thought that ML will be important in the field of otorhinolaryngology, head, and neck surgery and have a positive effect in terms of reducing the duration of ENT surgery. Similarly, an online survey conducted on fellows and trainees in Australia and New Zealand of different specialties ophthalmology, radiology/radiation oncology, and dermatology found that the majority (71.0%) considered AI would advance their field of medicine and that medical practitioner's needs would be impacted by the technology over the next decade (29). Sit C et al received 484 responses from 19 UK medical schools and found that 88% of the students believed that AI would play an important role in healthcare and in health complications (30). Similarly, 69.2% of participants in our study considered that ML was important in health practice.

In the present study, a total of 54.8% felt that there was a great future for ML in ENT in the KSA. A study conducted by Park CJ et al among 156 medical students in the US agreed that AI would have a significant role in the future of medicine (75%) (31). Another cross-sectional study conducted by Bin Dahmash A et al in the KSA found that 44.8% of the participants believed that AI would minimize the number of radiologists needed in the future (25).

Deeper knowledge and a good understanding of ML can be a shift toward specialties with high quality and fewer mistakes, not only in ENT or in medicine in general, but also in other careers (32,33). ML has many potential applications in the medical field, not only with diagnosis and treatment but also with the medical education of medical students (34). AI can also help with training and improving the surgical skills of residents (35), and ML can also possibly help with evaluating medical professionals (36).

We faced some limitations in this study. Given the current situation of the COVID-19 pandemic and the restrictions of social distancing and lockdown, we had to work online at the beginning of the study and some work was postponed due to the pandemic. Further, there is limited research on this topic published. Therefore, we could not compare our findings to other studies. We were also limited by the nascency of ML in the medical field; ML is not yet taught or not taught enough in the curriculum in medical schools.

Recommendations

There should be more medical research conducted on ML with clinical trials for an accurate assessment of the efficacy of ML on patients' health care to improve the healthcare system and take the next step toward the future and advancing medical science. Surveys should also be conducted in the KSA to determine whether the adult population is comfortable with allowing their personal data to be used in ML to improve the healthcare system. ML should be more covered in medical schools in the KSA to enhance students' understanding of the possibilities that ML could provide.

Conclusion

To conclude, the medical students in the KSA demonstrated a good knowledge of machine learning in general, although many were not familiar with machine learning applications in the field. Therefore, further research about medical students' attitude toward ML in other medical specialties in the KSA is recommended to evaluate the awareness of current challenges facing the applications of ML in medical practice. Similar studies should also be conducted on medical physicians in the KSA to assess their perception and stance on applying ML to treat and diagnose patients and to know obstructions faced while applying ML.

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