



World Family Medicine Journal

incorporating the Middle East Journal of Family Medicine

ISSN 1839-0188

March 2024 - Volume 22, Issue 3



Australian Humpback Whale

Our planet ~ our health

A time for humanity to unite and end all wars
and together rescue our planetary home

4 Editorial

Dr. Abdulrazak Abyad

Original Contribution**6 Knowledge about the Risk of Cardiovascular Disease among Adults with Type 2 Diabetes in Taif City, Saudi Arabia: A Cross sectional study**

Aisha Al Gethami, Rawan M. Altowairqi, Aryam F. Alqthami, Ruba M. Altowairqi, Khulud A. Alamri, Lamyaa M. Algethami, Fatimah K. Alo
DOI: 10.5742/MEWFM.2024.95257621

14 Treatment of stress incontinence by trans-obturator tension: A retrospective study, Aden, Yemen

Ali Ahmed Salem Hatroom, Ahmed Mohammed Abdullah Alwashali
DOI: 10.5742/MEWFM.2024.95257622

Regional Thesis**21 Knowledge and Practice of taking Influenza Vaccine among Adult Diabetic Patients in Bahrain Defense Force Hospital**

Yasir Abdel Rahaman Abdel Wahid
DOI: 10.5742/MEWFM.2024.95257624

International Health Affairs**43 Review on Implementing Patient-Centered Care in Primary Health Practice in Qatar**

Walaa Abdulmohsin
DOI: 10.5742/MEWFM.2024.95257625

Review**46 Graves Eye Disease Medical and Surgical Management: A Review**

Yazeed Alshahrani, Abdullah Jallwi Korkoman, Fahad Saud M Alremthi, Hdinan Mohammed J Alsadi, Abdulaziz Braik Saleh AlQarni, Ahmed Abdullah Ahmed Alghamdi, Abdullah Hassan F Alsuayri, Abdullah Awon A Alsalooli, Nawaf Saeed O Alshahrani
DOI: 10.5742/MEWFM.2024.95257626

52 Fibromyalgia : A review

Yasir Al-Athari, Mina Mahawish
DOI: 10.5742/MEWFM.2024.95257627

57 Insomnia in adults: a brief review

Jakir Hussain Ullah

DOI: 10.5742/MEWFM.2024.95257628

62 The Prevention of Diabetic Ketoacidosis in Patients with Type 2 Diabetes on Sodium-Glucose Transport Protein 2 Inhibitors

Sara Elsheikh Ahmedana, Musa Basheer Mansour, Amr Musa Basheer

DOI: 10.5742/MEWFM.2024.95257631

Case Report**75 A case of sleep apnoea**

Yasir Al-Athari, Mina Mahawish

DOI: 10.5742/MEWFM.2024.95257629

Editorial

Chief Editor:

A. Abyad
MD, MPH, AGSF, AFCHSE
Email:

aabyad@cyberia.net.lb

Mobile: 961-3-201901

Publisher

Lesley Pocock
medi+WORLD International
AUSTRALIA

Email:

lesleypocock@mediworld.com.au
publishermwi@gmail.com

In this issue we have a good number of papers of interest to primary care in addition to a number of reviews on various issues.

Dr. Abdel Wahid did a descriptive cross-sectional hospital-based study. The objective of this study is to assess the knowledge and practice of taking the annual influenza vaccine among adult diabetic patients in BDF Hospital. Three hundred diabetic patients who are eligible for the study were interviewed, with a structured questionnaire. Results of the survey indicated that males and females included are 48% to 52% respectively, 95.3% of the whole population are doing regular F.U. but only 55.3 were doing regular F.U. The study, it was found that the main reason for not taking the flu vaccine is that they mainly did not know about the vaccine which constituted 49, 33% of the study population. So, knowledge and use are lower than optimal in the literature but here it is the lowest, which may be mostly due to reduced awareness of the benefits of the vaccine and it will most probably increase if there are increased efforts on advising direct contacts with the patients in the diabetic or other PHC clinics or through the media to have the seasonal flu vaccine.

Al Gethami et al., did a cross-sectional study carried out on 300 type 2 diabetic patients through an online survey. The purpose of this study was to ascertain the level of awareness among persons with type 2 diabetes in Taif, Saudi Arabia, regarding their risk of CVDs. The mean knowledge of risk of cardiovascular disease among adults in Taif was 15.4 ± 5.4 . 26% of the participants had an age ranged from 50-59 years and 57.1% were females. Most of the participants had an age of diabetes diagnosis more than 30 years and 41.7% had a duration of disease less than 5 years. This study found that adults

with type 2 diabetes in Taif have a high level of knowledge about the risk of cardiovascular disease. Education and preventive measures for patients about CVD risk factors and diabetes management can improve health and reduce the risk of CVD.

Alshahrani et al., reviewed graves eye disease medical and surgical Management. They stressed that Graves' disease (GD) is the most frequent cause of hyperthyroidism, where iodine levels are abundant. One of the extrathyroidal symptoms is Graves' ophthalmopathy (GO) which presents with ophthalmic symptoms that can range from minor (e.g., dry eye) to sight-threatening (e.g., corneal ulceration and compressive optic neuropathy).

About 79% of Graves' disease cases can be attributed to genetic predispositions, while the remaining 21% are due to environmental factors. A low basal serum Thyroid Stimulating hormone (TSH) level has the highest sensitivity and specificity for diagnosing hyperthyroidism. Moreover, the appearance of Thyroid Stimulating hormone receptors (TSHR) autoantibodies (TRAbs) is presumed to be highly specific for the diagnosis of Graves' disease. Therefore, it is essential to restore the euthyroid state and this can be obtained by either antithyroid medications, radioactive iodine or surgical thyroidectomy.

Dr. Abdulmohsin, reviewed the implementing of Patient-centered care in primary health care. Patient-centered care is a critical component of healthcare delivery, emphasizing the involvement of patients in their care and the consideration of their preferences and needs. In Qatar, a country dedicated to providing high-quality healthcare, the implementation of patient-centered care in primary health practices is of paramount

importance. This literature review examines the existing literature on patient-centered care implementation in primary health practices in Qatar, focusing on strategies, challenges, and outcomes. The review underscores the significance of cultural considerations, patient engagement, provider training, health information technology integration, quality improvement initiatives, multidisciplinary collaboration, and care coordination.

Al-Athari et al., presented a case of sleep apnea. This case report represents a comprehensive overview of the assessment, diagnosis, and subsequent management of a 60 years old patient who sought medical attention due to debilitating fatigue. Despite displaying atypical symptoms and an absence of characteristic signs, polysomnography revealed significant degree of obstructive sleep apnea. This case highlights the importance of considering sleep-related disorders in the differential diagnosis of fatigue and the remarkable efficacy of continuous positive airway pressure (CPAP) therapy in improving the patient's quality of life.

Al-Athari et al., presented a review on Fibromyalgia. Fibromyalgia is a common medical condition which still misdiagnosed with other rheumatological disorders. It can be complex and brings many challenges. Presentation can vary from patient to patient. It is estimated that around up to 5% of population may have fibromyalgia with more cases in women. Although there is no cure for this condition but more understanding of Fibromyalgia can contribute to a well-rounded effective treatment and therapy options via a multidisciplinary approach to help relieving the symptoms.

Ahmedana et al., reviewed the current evidence of incidence, predisposing factors and the prevention of DKA in T2DM patients on SGLT2Is use. Sodium-Glucose Transport Protein 2 Inhibitors (SGLT2Is) effectively controlled diabetes. Diabetic ketoaci-

dosis (DKA) has been reported as a life-threatening adverse effect due to SGLT2Is use. 85 studies were identified in the initial search, 75 records were removed and finally, 10 studies were included. Only studies discussing the prevention of DKA in T2DM patients on SGLT2Is were selected, extracted and categorized into main domains that included SGLT2Is use in T2DM patients and DKA (50%), SGLT2Is use in T2DM patients (20%), the clinical presentation of DKA (20%) and DKA prevention (10%). Six studies showed SGLT2Is increased the risk of DKA and with very low rates in two studies. This review summarized the prevention of DKA in T2DM patients on SGLT2Is use with consideration of incidence, a summary of evidence and predisposing factors. Physicians, health care providers and patients should be aware of SGLT2Is use, regular follow up, precipitating factors, symptoms, signs and prevention of DKA.

Hatroom, et al., evaluate the effectiveness of transobturator approach in the treatment of female stress urinary incontinence and to analyze functional results. They retrospectively reviewed all medical files of patients presenting with urinary incontinence to our Urology Center in Aden, Yemen, over a 2-year period. There were 42 patients treated with TOT and the postoperative follow up of the patients was at least 10 months. The collected data were tabulated and statistical analysis was done by estimating rates, means and standard deviations. The age of the patients ranged between 40 to 80 years and their mean age was 62.1 ± 9.7 years. We grouped the study patients in two age groups, 60 years and > 60 years. The authors concluded that the transobturator approach is an effective treatment of stress urinary incontinence with low morbidity and with acceptable success and outcome.

Dr Ullah, reviewed insomnia in adults. Insomnia is a common and debilitating condition in adults, especially in the elderly. It is associated with poor

mental health and contributes to the development of a wide range of medical conditions, including obesity, cardiovascular disease, diabetes and dementia. The condition is frequently missed or underdiagnosed and poorly managed. This brief review summarizes the etiology, clinical features, diagnosis and latest management strategies.

Knowledge about the Risk of Cardiovascular Disease among Adults with Type 2 Diabetes in Taif City, Saudi Arabia: A Cross sectional study

Aisha Al Gethami ¹, Rawan M. Altowairqi ², Aryam F. Alqthami ³, Ruba M. Altowairqi ³,
Khulud A. Alamri ³, Lamyaa M. Algethami ³, Fatimah K. Alotaibi ³

(1) Consultant Family Medicine and Diabetologist, Diabetes and Endocrine Centre , Prince Mansour Military Hospital, Taif, KSA

(2) Family Medicine Resident, Prince Mansour Military Hospital, Taif KSA

(3) Medical student, Taif University, Taif, KSA

Corresponding author

Dr. Rawan M. Altowairqi

Taif city, Saudi Arabia

Tel.: 0554757641

Email: rawanaltuwirqi@gmail.com

Received: January 2024. Accepted: February 2024; Published: March 1, 2024.

Citation: Aisha Al Gethami et al. Knowledge about the Risk of Cardiovascular Disease among Adults with Type 2 Diabetes in Taif City, Saudi Arabia: A Cross sectional study. World Family Medicine. March 2024; 22(3): 6-13.

DOI: 10.5742/MEWFM.2024.95257621

Abstract

Background: Diabetes patients are significantly more likely to develop cardiovascular diseases (CVDs). Lack of understanding about the disease's risk for CVDs would increase morbidity and mortality.

Objectives: The purpose of this study was to ascertain the level of awareness among persons with type 2 diabetes in Taif, Saudi Arabia, regarding their risk of CVDs. **Methods:** A cross-sectional study was carried out on 300 type 2 diabetic patients through an online survey.

Results: The mean knowledge of risk of cardiovascular disease among adults in Taif was 15.4 ± 5.4 . 26% of the participants had an age range from 50-59 years and 57.1% were females. Most of the participants had an age at diabetes diagnosis more than 30 years and 41.7% had a duration of disease less than 5 years. Regarding knowledge of participants it was reported that, a family history of heart disease 55.8%, old age 66%, smoking 79.5%, high blood pressure 76.9% and bad cholesterol (LDL) 74.4% at higher risk for developing heart disease. 64.4% knew they should keep their blood pressure under control and 80.1% knew regular exercise can reduce their risk of developing heart disease. There was a positive relationship between participants education level and knowledge.

Conclusion: This study found that adults with type 2 diabetes in Taif have a high level of knowledge about the risk of cardiovascular disease. Education and preventive measures for patients about CVD risk factors and diabetes management can improve health and reduce the risk of CVD.

Keywords: knowledge, risk, CVD, DM, adults, Taif

Introduction

Cardiovascular disease (CVD) is one of the leading causes of mortality and disability in diabetics [1, 2]. The risk of CVD increases with rising fasting plasma glucose levels [3]. Adults with diabetes have historically had a higher incidence of CVD than adults without diabetes [4].

Type 2 diabetes mellitus (T2DM) is typically discovered late in the course of cardiovascular disease (CVD). As a result, many patients experience difficulties at the time of diagnosis or shortly thereafter [5]. Ischemic heart disease, heart failure (HF), stroke, coronary artery disease (CAD), and peripheral artery disease are the most common cardiovascular diseases (CVD) associated with T2DM, and they can kill at least half of T2DM patients [6].

Inadequate knowledge of CVD risk in diabetes may result in ineffective early detection and prevention. Thus, it is critical that people with diabetes have adequate 'risk knowledge' of CVD [7]. From 2014 to 2019, several studies have investigated diabetic patients' awareness of CVD risk [8-14]. In an Indian study, only 44% of respondents identified heart disease as a possible outcome of diabetes [8].

More recently, a study in Ethiopia discovered that 63.2% of participants were aware that diabetes can cause heart problems (9). Furthermore, a study in Ghana discovered that 80% of participants were unaware of the risk of heart disease from diabetes [10]. A Pakistani study found that 50-60% of people were unaware of their cardiovascular risk [11]. Furthermore, a study in Nigeria found that while diabetic complications were well-known (90.5%), only 61.9% were familiar with cardiac complications. These results were consistent with the Turkish study, in which 62.81% of participants were aware of the cardiovascular risk [7,12].

A 2018 study in Mecca, Saudi Arabia, discovered that, while general knowledge of diabetes complications was high (80%), only 40.1% had specific knowledge about the risk of heart disease in diabetes [13]. In 2022, a cross-sectional study was conducted at King Saud University Medical City (KSUMC), a tertiary hospital in Riyadh. The study included 377 patients with type 2 diabetes, in Saudis over the age of 18, and discovered a high level of CVD risk knowledge among study participants. The prevalence of multidisciplinary intensive education programs aimed at type 2 diabetes patients, such as those offered at KSUMC, may explain why study participants were more familiar with CVD risk [14].

Although there are numerous studies on the risk of cardiovascular disease among adults with type 2 diabetes in the literature, we are aware of no prior studies conducted in the Taif region of Saudi Arabia. Thus, the purpose of this study was to determine the level of knowledge about the risk of cardiovascular disease among adults with type 2 diabetes in the Taif region of Saudi Arabia.

Subjects and Methods

Study design, location and time frame: a cross sectional study was conducted in Taif City of Saudi Arabia from January to April 2023.

Study participants: the inclusion criteria were type 2 diabetic patients of all ages and both genders, and the exclusion criteria were type I diabetic patients, non-diabetics and those who refused participating in the study.

Data collection: data were collected through an online questionnaire. The questionnaire had two sections. The first section included demographic data (age, gender, level of education, marital status). It also consisted of information about diabetes-related factors (duration of DM, family history of diabetes, and diabetes regimen). The second section of the questionnaire comprised the Arabic-translated version of the Heart Disease Fact Questionnaire (HDFQ). HDFQ is a validated questionnaire of 25 items for measuring heart disease risk knowledge, with possible answers of 'true', 'false', and 'I do not know'. The scores were calculated by giving one point for each correct answer and zero points for incorrect answers or 'I do not know' responses. The total knowledge score was calculated by summing the points for the correct answers and then grading the score out of 25.

Ethical considerations: ethical approval for the study was obtained from the research Ethics Committee of Armed forces Hospital in in Taif city, Saudi Arabia.

Data analysis: data were analyzed statistically using SPSS program version 26. Qualitative data was expressed as numbers and percentages. Quantitative data was expressed as mean and standard deviation (Mean \pm SD), and non-parametric variables were tested using the Mann-Whitney and Kruskal Wallis tests. Correlation analysis was performed using the Spearman's test, and a p-value of less than 0.05 was considered statistically significant.

Results

(Table 1) shows that 26.3% of the participants had an age range from 50-59 years and 57.1% were females. Of them, 50.6% had a university level of education and 72.4% were married.

Most of the participants had an age of DM diagnosis >30 years and 41.7% had a disease duration of less than 5 years. Almost one third (33.3%) of them were on insulin, while 32.7% were on oral hypoglycemic drugs for DM treatment. More than half of the participants (56.4%) had a family history of DM (Table 2).

The participants responses to the 25 items of the HDFQ are illustrated in Table 3. Of them, 22.4% correctly mentioned that the following statements are false:

- 1) a person always knows when they have heart disease (22.4%),
- 2) Eating fatty foods does not affect blood cholesterol levels (55.8%),
- 3) If your 'HDL' cholesterol is high, you are at risk for heart disease (41%),
- 4) Only exercising at a gym or in an exercise class will lower a person's chance of developing heart disease (46.8%) and
- 5) Men with diabetes have higher risk of heart disease than women with diabetes (14.1%).

As for the correct true answers:

- 55.8% reported that if they have a family history of heart disease, they are at risk of developing heart disease, 66% knew that the older a person is, the greater their risk of developing heart disease and 79.5% reported that smoking is a risk factor for heart disease.

- 68.6% reported that a person who stops smoking will lower their risk of developing heart disease, 76.9% knew that high blood pressure is a risk factor for heart disease, 74.4% knew that if their 'bad' cholesterol (LDL) is high, they are at risk of heart disease and 78.2% knew that being overweight increases a person's risk for heart disease.

- 80.1% knew that regular physical activity will lower a person's chance of getting heart disease; 76.9% report that walking and gardening are considered exercise that will help lower a person's chance of developing heart disease, 66.7% correctly knew it is true that diabetes is a risk factor for developing heart disease and 68.6% knew that high blood sugar puts a strain on the heart.

- 60.3% reported that if their blood sugar is high over several months, it can cause their cholesterol level to go up and increase the risk of heart disease, 74.4% knew that a person who has diabetes can reduce their risk of developing heart disease if they keep their blood sugar levels under control and only 28.8% knew that people with diabetes rarely have high cholesterol.

- 69.2% correctly knew that if a person has diabetes keeping their cholesterol under control will help to lower their chance of developing heart disease; 38.5% knew that people with diabetes tend to have low HDL cholesterol and 75% knew that a person who has diabetes can reduce their risk of developing heart disease if they keep their weight under control.

- 41.7% knew that men with diabetes have higher risk of heart disease than women with diabetes and 64.4% knew that a person who has diabetes can reduce their risk of developing heart disease if they keep their blood pressure under control.

The mean knowledge score was 15.4 ± 5.4 . Table 4 demonstrates that participants who were on both oral hypoglycemic drugs and insulin for DM treatment had a significant higher mean HDFQ score compared to other types of DM treatments ($p < 0.05$). On the other hand, a non-significant relationship was found between the mean HDFQ score and all participants' demographics and DM clinical data other than treatment ($p > 0.05$).

Figure 1 illustrates that a significant positive correlation was found between the participants' educational level and the HDFQ score ($r = 0.22$, $p\text{-value} = 0.005$).

Table 1. Distribution of studied participants according their demographic data (No.:156)

Variable	No. (%)
Age (years)	
<30	38 (24.4)
30-39	17 (10.9)
40-49	29 (18.6)
50-59	41 (26.3)
60-70	25 (16)
>70	6 (3.8)
Gender	
Female	89 (57.1)
Male	67 (42.9)
Educational level	
Illiterate	9 (5.8)
Read and write	5 (3.2)
Primary	5 (3.2)
Middle	11 (7.1)
Secondary	37 (23.7)
University	79 (50.6)
Postgraduate	10 (6.4)
Marital status	
Single	43 (27.6)
Married	113 (72.4)

Table 2. Distribution of studied participants according to DM clinical data (No.:156)

Variable	No. (%)
Age at diagnosis	
≤30 years	54 (34.6)
>30 years	102 (65.4)
Disease duration	
<5 years	65 (41.7)
5-10 years	41 (26.3)
>10 years	50 (32.1)
DM treatment	
Oral hypoglycemic drugs	51 (32.7)
Insulin	52 (33.3)
Both	19 (12.2)
Dietary modifications	34 (21.8)
Family history of DM	
No	68 (43.6)
Yes	88 (56.4)

Table 3. Participants responses to the HDFQ (No.:156)

Variable	False No. (%)	True No. (%)	I don't know No. (%)
A person always knows when they have heart disease	35 (22.4) *	57 (36.5)	64 (41)
If you have a family history of heart disease, you are at risk for developing heart disease	32 (20.5)	87 (55.8) *	37 (23.7)
The older a person is, the greater their risk of developing heart disease	22 (14.1)	103 (66) *	31 (19.9)
Smoking is a risk factor for heart disease	11 (7.1)	124 (79.5) *	21 (13.5)
A person who stops smoking will lower their risk of developing heart disease	23 (14.7)	107 (68.6) *	26 (16.7)
High blood pressure is a risk factor for heart disease	10 (6.4)	120 (76.9) *	26 (16.7)
Keeping blood pressure under control will reduce a person's risk for developing heart disease	14 (9)	116 (74.4) *	26 (16.7)
High cholesterol is a risk factor for developing heart disease	12 (7.7)	120 (76.9) *	24 (15.4)
Eating fatty foods does not affect blood cholesterol levels	87 (55.8) *	47 (30.1)	22 (14.1)
If your 'good' cholesterol (HDL) is high, you are at risk for heart disease	64 (41) *	49 (31.4)	43 (27.6)
If your 'bad' cholesterol (LDL) is high, you are at risk for heart disease	14 (9)	116 (74.4) *	26 (16.7)
Being overweight increases a person's risk for heart disease	13 (8.3)	122 (78.2) *	21 (13.5)
Regular physical activity will lower a person's chance of getting heart disease	13 (8.3)	125 (80.1) *	18 (11.5)
Only exercising at a gym or in an exercise class will lower a person's chance of developing heart disease	73 (46.8) *	47 (30.1)	36 (23.1)
Walking and gardening are considered exercise that will help lower a person's chance of developing heart disease	15 (9.6)	120 (76.9) *	21 (13.5)
Diabetes is a risk factor for developing heart disease	19 (12.2)	104 (66.7) *	33 (21.2)
High blood sugar puts a strain on the heart	15 (9.6)	107 (68.6) *	34 (21.8)
If your blood sugar is high over several months, it can cause your cholesterol level to go up and increase the risk of heart disease	20 (12.8)	94 (60.3) *	42 (26.9)
A person who has diabetes can reduce their risk of developing heart disease if they keep their blood sugar levels under control	1 (7.1)	116 (74.4) *	29 (18.6)
People with diabetes rarely have high cholesterol	55 (35.3)	45 (28.8) *	56 (35.9)
If a person has diabetes keeping their cholesterol under control will help to lower their chance of developing heart disease	10 (6.4)	108 (69.2) *	38 (24.4)
People with diabetes tend to have low HDL cholesterol	30 (19.2)	60 (38.5) *	66 (42.3)
A person who has diabetes can reduce their risk of developing heart disease if they keep their blood pressure under control	21 (13.5)	101 (64.4) *	34 (21.8)1
A person who has diabetes can reduce their risk of developing heart disease if they keep their weight under control	5 (9.6)	117 (75) *	24 (15.4)
Men with diabetes have higher risk of heart disease than women with diabetes	22 (14.1) *	65 (41.7)	69 (44.2)

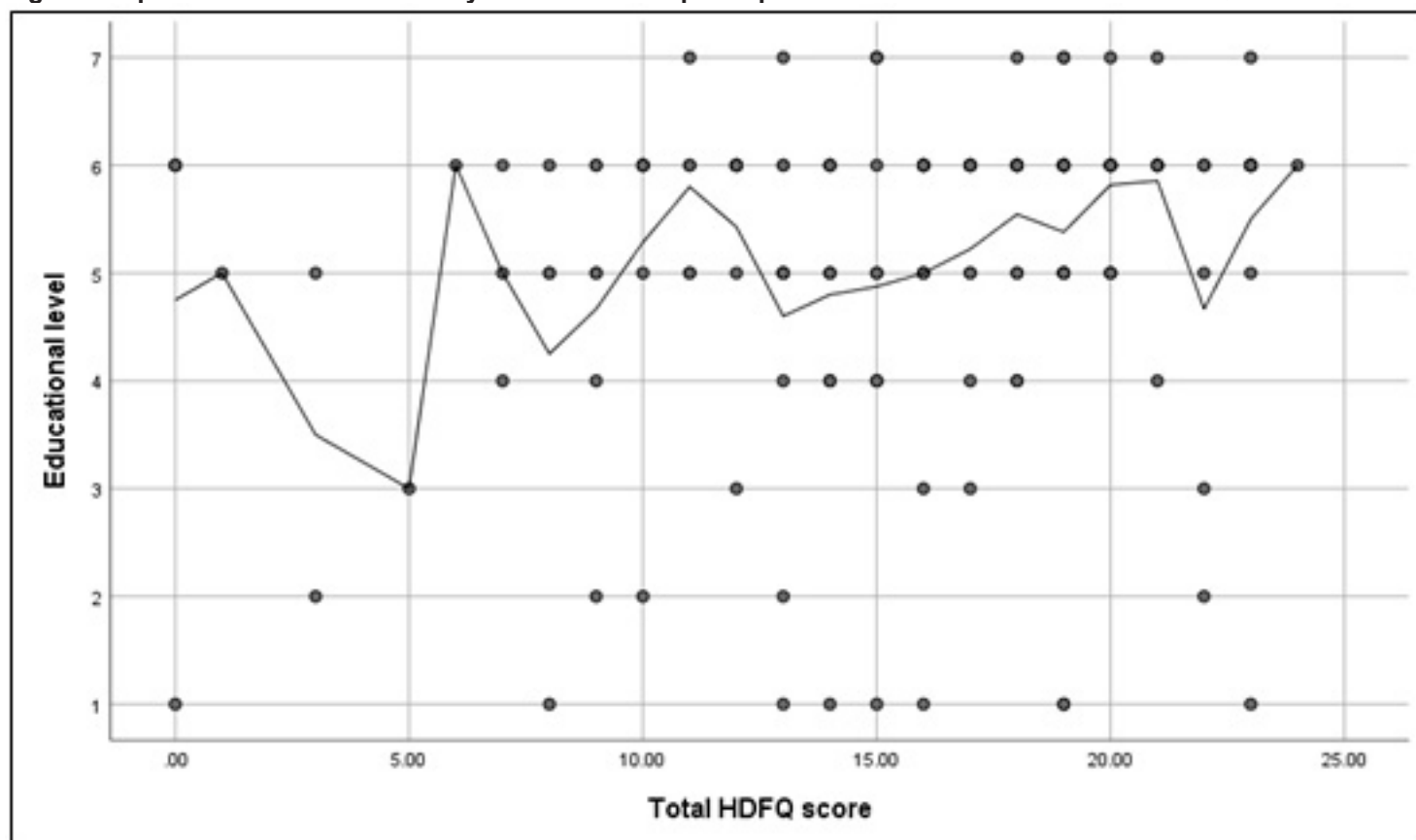
N.B.: * Correct answer

Table 4. Relationship between the mean HDFQ score and participants' demographics and DM clinical data (No.:156)

Variable	Mean HDFQ score (Mean \pm SD)	Test	p-value
Age (years)			
<30	15.18 \pm 5.73	5*	0.558
30-39	16.94 \pm 3.74		
40-49	14.62 \pm 5.21		
50-59	16.04 \pm 5.67		
60-70	15.04 \pm 5.23		
>70	13.33 \pm 7.47		
Gender			
Female	15.26 \pm 5.71	0.05**	0.948
Male	15.58 \pm 5.01		
Educational level			
Illiterate	14.11 \pm 6.79	6*	0.165
Read and write	11.4 \pm 6.94		
Primary	14.4 \pm 6.34		
Middle	14.63 \pm 4.03		
Secondary	14.35 \pm 5.11		
University	16.21 \pm 5.47		
Postgraduate	17.4 \pm 3.77		
Marital status			
Single	15 \pm 5.74	0.31**	0.755
Married	15.55 \pm 5.29		
Age at diagnosis			
\leq 30 years	15.31 \pm 5.41	0.03	0.969
>30 years	15.45 \pm 5.43		
Disease duration			
<5 years	16.23 \pm 4.81	2	0.295
5-10 years	14.46 \pm 6.08		
>10 years	15.1 \pm 5.5		
DM treatment			
Oral hypoglycemic drugs	16.25 \pm 4.97	3	<0.001
Insulin	12.9 \pm 5.29		
Both	17.21 \pm 4.93		
Dietary modifications	16.94 \pm 5.29		
Family history of DM			
No	14.54 \pm 5.56	1.83	0.067
Yes	16.06 \pm 5.22		

N.B.: * = Kruskal Wallis test

** =Mann-Whitney test

Figure 1. Spearman's correlation analysis between the participants' educational level and the HDFQ score

N.B.: ($r = 0.22$, $p\text{-value} = 0.005$)

Discussion

The current study aimed to determine the knowledge about the risk of cardiovascular disease among adults with type 2 Diabetes in Taif region, Saudi Arabia. The study revealed that about two-thirds of the diabetic respondents had the disease recently (less than 5 years), and more than half of them had a family history of DM.

Regarding CVD knowledge, the participants had a mean knowledge score of 15.4 ± 5.4 out of 25 (61.6%) which means that study patients had higher than average knowledge level about the risk of CVDs. The knowledge score was scientifically lower among patients on insulin therapy and borderline lower among others with no family history of DM. Other biodemographics had no significant relationship with diabetic patients' knowledge scores. Zehirlioglu L et al. [7] reported a mean knowledge score of 62.8 ± 17.6 , similar to previous studies. Furthermore, authors discovered that CVD risk was lower in subjects with a high level of knowledge about CVD risk and a shorter duration of diabetes. Similarly, in 2019, a more recent study conducted in Ethiopia found that 63.2% of participants were aware of the potential heart problems associated with diabetes, which is consistent with the current study findings [9]. In Oman, Al Shafae MA et al. [15] discovered that only 20.4% of the population thought heart disease was a possible complication of diabetes. Furthermore, a study conducted in Makkah, Saudi Arabia [13] found that, while 80% of people had a basic understanding of diabetic consequences, only 40.1% had a precise understanding of the risk of heart disease in diabetics.

Other studies revealed a lower level of knowledge about CVD risk, with a study in India showing that only 44% of respondents reported heart disease as a possible complication of diabetes [8]. Furthermore, a study in Ghana [11] found that only 20% of diabetic participants had adequate knowledge of the risk of heart disease in diabetes.

A study in Pakistan [12] also found lower levels of CVD risk knowledge, ranging from 50 to 60% among diabetic patients. According to a study conducted in Nigeria [10], only 61.9% of diabetics had a clear understanding of cardiac problems, despite a high awareness of diabetic complications (90.5%). In contrast, in Saudi Arabia, Alduraywish SA et al. [14] reported a higher knowledge of CVD risk. Age, marital status, and type of residence all had a significant association with higher knowledge levels. Mani K and Shanmugam A in India [16] found that 89% of diabetic patients were aware of macrovascular complications.

Limitations:

The current study's limitation was the use of a self-administered questionnaire, which could lead to recall bias.

Conclusions

The current study found that diabetic patients, particularly those on insulin therapy, had an average level of knowledge about the risk of CVD. The highest knowledge was reported primarily for risk factors of heart disease in diabetes, but the lowest for self-perception of having heart disease. Given the increase in diabetes prevalence in Saudi Arabia over the last decade, health promotion, along with other measures to prevent and control this growing health problem, is critical.

References

- Whiting, D. R., Guariguata, L., Weil, C., & Shaw, J. (2011). IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes research and clinical practice*, 94(3), 311-321.
- Leon, B. M., & Maddox, T. M. (2015). Diabetes and cardiovascular disease: epidemiology, biological mechanisms, treatment recommendations and future research. *World journal of diabetes*, 6(13), 1246.
- Singh, G. M., Danaei, G., Farzadfar, F., Stevens, G. A., Woodward, M., Wormser, D., ... & Prospective Studies Collaboration (PSC). (2013). The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: a pooled analysis. *PloS one*, 8(7), e65174.
- Sarwar, N., Gao, P., Kondapally Seshasai, S. R., Gobin, R., Kaptoge, S., & Di Angelantonio, E. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: A collaborative meta-analysis of 102 prospective studies. *Lancet [Internet]*. 2010; 375 (9733): 2215–22. S0140-6736 (10), 60484-9.
- Huang, D., Refaat, M., Mohammedi, K., Jayyousi, A., Al Suwaidi, J., & Abi Khalil, C. (2017). Macrovascular Complications in Patients with Diabetes and Prediabetes. *BioMed research international*, 2017, 7839101.
- Einarson, T. R., Acs, A., Ludwig, C., & Panton, U. H. (2018). Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007–2017. *Cardiovascular diabetology*, 17(1), 1-19.
- Zehirlioglu, L.; Mert, H.; Sezgin, D.; Özpelit, E. Cardiovascular Risk, Risk Knowledge, and Related Factors in Patients with Type 2 Diabetes. *Clin. Nurs. Res.* 2020, 29, 322–330. [CrossRef]
- Mehta, P. Knowledge of Diabetes and Self Care Practices in Chronic Diabetic Patients Attending a Tertiary Care Teaching Hospital in India. *Natl. J. Integr. Res. Med.* 2014, 5, 91-97.
- Belsti, Y., Akalu, Y., Fekadu, H., & Animut, Y. (2019). Awareness of complications of diabetes mellitus and its associated factors among type 2 diabetic patients at Addis Zemen District Hospital, northwest Ethiopia. *BMC Research Notes*, 12(1), 1-7.
- Obirikorang, Y., Obirikorang, C., Anto, E. O., Acheampong, E., Batu, E. N., Stella, A. D., ... & Brenya, P. K. (2016). Knowledge of complications of diabetes mellitus among patients visiting the diabetes clinic at Sampa Government Hospital, Ghana: a descriptive study. *BMC public health*, 16(1), 1-8.
- Ullah, F., Afridi, A. K., Rahim, F., Ashfaq, M., Khan, S., Shabbier, G., & ur Rahman, S. (2015). Knowledge of diabetic complications in patients with diabetes mellitus. *Journal of Ayub Medical College Abbottabad*, 27(2), 360-363.
- Adeyemi, O., Timothy, T. F., Oluwanmodimu, D. V., & Tosin, T. O. (2018). Knowledge of Diabetic Complications and Practice of Routine Medical Check-up among Type 2 Diabetics in Nigeria. *J. Adv. Med. Med. Res*, 25, 1-8.
- Fatani, E. M., Gari, L. N., Alharbi, A. H., Alzahrani, J. A., Almasoudi, A. S., Babilghaith, E. S., ... & Alsharif, S. K. (2018). Awareness of diabetic complications, perceived knowledge, compliance to medications and control of diabetes among diabetic population of Makkah city, Kingdom Saudi Arabia: cross-sectional study. *Egypt J Hosp Med*, 70(7), 1190-1195.
- Alduraywish SA, Aldakheel FM, Azizalrahman LA, Alzaid LT, Alqahtani SS, Alhussein SH, Almutairi AM. Knowledge about the Risk of Cardiovascular Disease among Adults with Type 2 Diabetes Visiting the Outpatient Clinics at Tertiary Hospital in Riyadh, Saudi Arabia: A Cross-Sectional Study. *International Journal of Environmental Research and Public Health*. 2022 Apr 20;19(9):4996
- Al Shafae MA, Al-Shukaili S, Rizvi SG, Al Farsi Y, Khan MA, Ganguly SS, Afifi M, Al Adawi S. Knowledge and perceptions of diabetes in a semi-urban Omani population. *BMC public health*. 2008 Dec; 8:1-8.
- Mani K, Shanmugam A. Knowledge on Complications of Diabetes Mellitus among Patients with Diabetes Mellitus - A Descriptive Study. *Int. J. Compr. Nurs*. 2014, 1, 18-20.

Treatment of stress incontinence by trans-obturator tension: A retrospective study, Aden, Yemen

Ali Ahmed Salem Hatroom¹, Ahmed Mohammed Abdullah Alwashali ²

(1) Associate Professor of Urology, Department of Special Surgery, Faculty of Medicine, University of Aden, Yemen

(2) Assistant Professor of Urology, Department of General Surgery, Faculty of Medicine, University of Thamar, Yemen

Corresponding author:

Dr. Ali Ahmed Salem Hatroom: Associate Professor of Urology, Department of Special Surgery, Faculty of Medicine, University of Aden, Yemen

Email: hatroom.cl@gmail.com

Received: January 2024. Accepted: February 2024; Published: March 1, 2024.

Citation: Ali Ahmed Salem Hatroom, Ahmed Mohammed Abdullah Alwashali. Treatment of stress incontinence by trans-obturator tension: A retrospective study, Aden, Yemen. World Family Medicine. March 2024; 22(3): 14-20.

DOI: 10.5742/MEWFM.2024.95257622

Abstract

Background: Stress urinary incontinence is the complaint of involuntary leakage on effort or exertion or on sneezing or coughing.

Objectives: To evaluate the effectiveness of transobturator approach in the treatment of female stress urinary incontinence and to analyze functional results.

Materials and methods: We retrospectively reviewed all medical files of patients presenting with urinary incontinence to our Urology Center in Aden, Yemen, over a 2-year period. There were 42 patients treated with TOT and the postoperative follow up of the patients was at least 10 months. The collected data were tabulated and statistical analysis was done by estimating rates, means and standard deviations.

Results: The age of the patients ranged between 40 to 80 years and their mean age was 62.1 ± 9.7 years. We grouped the study patients in two age groups, ≤ 60 years and > 60 years.

We found the patients of the age group > 60 years were (57.1%) while the patients of the age group ≤ 60 years were (42.9%).

The mean weight of the patients is 67.5 ± 7.0 kilograms (kg).

We categorized the number of vaginal deliveries in 2 groups: 5 – 7 vaginal deliveries were (31.0%), and 8 – 10 vaginal deliveries (69.0%). The Mean number of vaginal delivery was 8.0 ± 1.2 .

Concomitant operations were posterior colpotomy (7.0%) and anterior colpotomy (4.8%). The Mean operative time was 48 ± 8.9 minutes.

Four cases developed complications, (4.8%) major bleeding; (2.4%) of them had bladder injury and (2.4%) urine retention. Additionally, (93.0%) of the outcome of operated women were with excellent success while those with failed results were (7.0%).

Conclusion: The transobturator approach is an effective treatment of stress urinary incontinence with low morbidity and with acceptable success and outcome.

Keywords: Stress urinary incontinence, transobturator approach, Aden, Yemen

Introduction

Urinary incontinence is a common, distressing condition which affects women of all ages and can have a profound impact on quality of life. Women often have symptoms for a considerable amount of time before seeking a medical opinion. Stress urinary incontinence (SUI) is the complaint of involuntary leakage on effort or exertion or on sneezing or coughing, usually caused by weak or damaged muscles in the pelvic floor or sphincter [1].

SUI has a significant impact on the quality of life for many women, although estimates of prevalence vary widely due to inconsistencies in the definitions of SUI and differences in populations studied [2].

The most common types of UI in women are stress urinary incontinence and urge urinary incontinence. Women with both problems have mixed urinary incontinence. Stress urinary incontinence was defined by the International Urogynecological Association and International Continence Society as "complaint of involuntary loss of urine on effort or physical exertion (e.g. sporting activities), or on sneezing or coughing" [3,4]. SUI, also known as effort incontinence, is due essentially to insufficient strength of the pelvic floor muscles and caused by loss of support of the urethra. It is characterized by leaking of small amounts of urine during activities which increase abdominal pressure such as coughing, laughing, sneezing, climbing stairs, running and lifting. It can be a common and distressing problem, which may have a profound impact on quality of life, including sexual life. Stress urinary incontinence leads to decreased quality of life in sufferers, especially in women over 60 years old and financial burdens for both the patient and the healthcare industry [5]. An estimated prevalence for urinary incontinence is nearly 30% in women aged 30–60 years, with approximately half of the cases attributed to SUI [6–10].

In 2001, Delorme described a new method of inserting the tape, which passes through the obturator foramen [11].

The transobturator approach (TOT) for sub-urethral tension-free vaginal tapes has since gained wide popularity in the surgical treatment of SUI.

TOT was introduced by Delorme et al. in 2001 and modified by de Leval in 2003 to allow insertion of the tape via the inside-out technique [12,13].

This approach has a theoretical advantage of less obstruction and postoperative voiding dysfunction, as well as avoiding some of the complications, such as bladder perforation and bowel perforation. Subsequently, deTayrac reported a 1-year cure rate of 84% with the TOT procedure [11].

Objectives:

To evaluate the effectiveness of transobturator tape (TOT) in the treatment of female stress urinary incontinence (SUI) and to analyze functional results.

Materials and Methods

We retrospectively reviewed all medical files of patients presenting with urinary incontinence to our Urology Center in Aden, Yemen, over a 2-year period from January 2018 to December 2019.

During the period, there were 42 patients with urinary incontinence treated with TOT and the postoperative follow up of the patients was at least 10 months in our Urology Center.

The collected data were age, residency, body weight, number of vaginal deliveries, complication, concomitant operation, operation time and result.

The collected data were tabulated and statistical analysis was done by estimating rates, means and standard deviations. We used IBM SPSS version 22 for statistical analysis.

Results

Forty-two women were operated for SUI under this study. The age of the study women ranged between 40 to 80 years and their mean age was 62.1 ± 9.7 years (Table 1). We grouped the study women in two age groups, ≤ 60 years and > 60 years. We found the patients of the age group > 60 years were 24 (57.1%) while the patients of the age group ≤ 60 years were 18 (42.9%) as shown in Table 1.

Most of the patients were from the three southern governorates, Abian 13 (31%) followed by Aden 12 (28.6%) and Lahj 11 (26.2%). The mean body weight of the patients is 67.5 ± 7.0 kilograms (kg) and ranged between 55 and 80 kg, as shown in Table 1.

As shown in Table 2 the number of vaginal deliveries ranged between 5 and 10. We categorized the number of vaginal deliveries in 2 groups: 5 – 7 vaginal deliveries were 13 (31.0%), and 8 – 10 vaginal deliveries vaginal deliveries 29 (69.0%).

The Mean number of vaginal deliveries was 8.0 ± 1.2 . Concomitant operations were posterior colpotomy 3 (7.0%) and anterior colpotomy 2 (4.8%). The Mean operative time was 48 ± 8.9 minutes.

Four cases developed complications, 2 (4.8%) major bleeding, 1 (2.4%) of them was with bladder injury and 1 (2.4%) urine retention, (Table 3 & Figure 2). Additionally, 39 (93.0%) of the outcome of operated women were with excellent success while with failed results were 3 (7.0%), as shown in Table 3 & Figure 2 .

Table 1: Demographic variables of the study women (n=42)

Variables	No	%
Range of age (years):	40 - 80	
Mean age (years):	62.1 ± 9.7	
Age groups (years):		
≤ 60	18	42.9
> 60	24	57.1
Governorate:		
Abian	13	31.0
Aden	12	28.6
Lahj	11	26.2
Taiz	3	7.0
Shabwah	2	4.8
Aldhale	1	2.4
Mean body weight (Kilogram)	67.5 ± 7.0	
Range (Kilogram)	55 to 80	

Figure 1: Age proportions of the study women

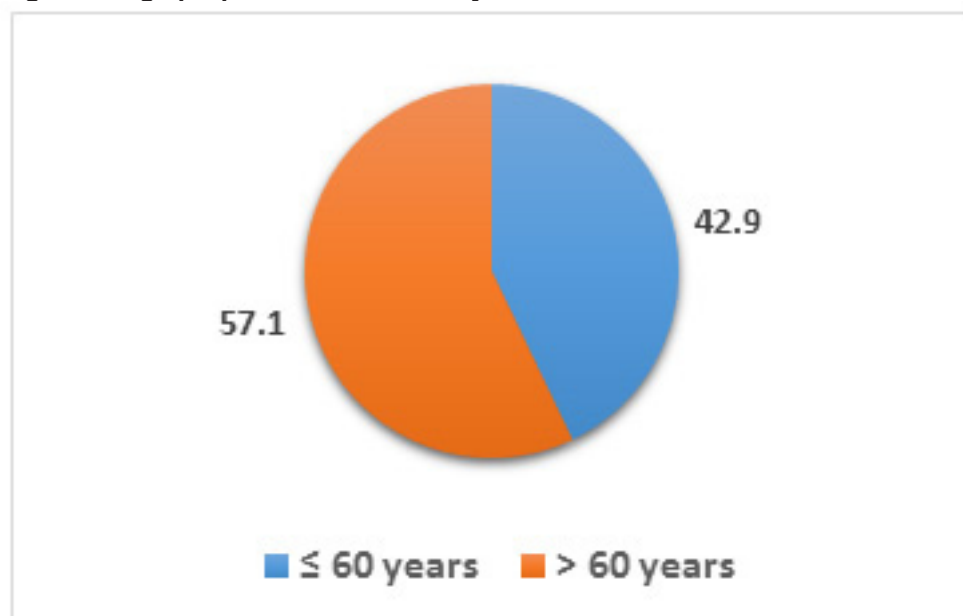


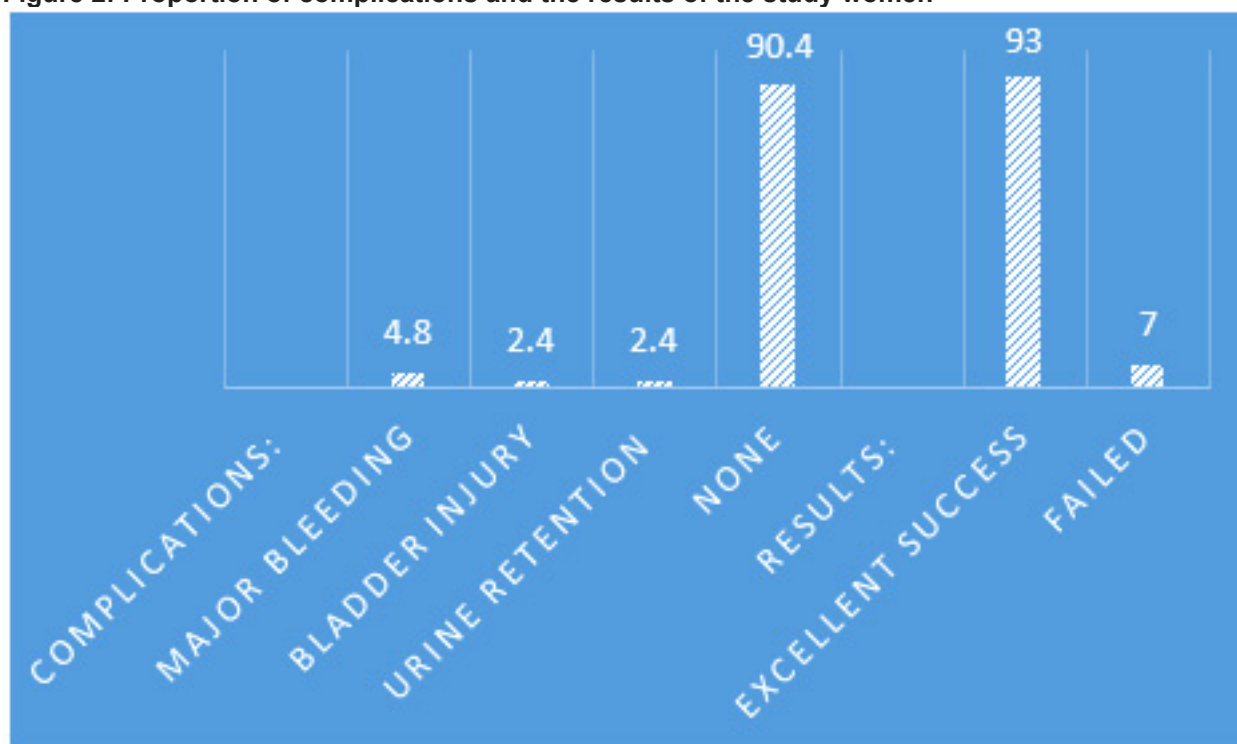
Table 2: Frequency of different variables of the study women (no = 42)

Variables	No	%
Number of vaginal deliveries:		
5 – 7	13	31
8 – 10	29	69
Mean number of vaginal deliveries:	7.0 ± 1.2	
Treatment:		
Trans-obturator tape	42	100
Concomitant operations:		
Posterior colpotomy	3	7.0
Anterior colpotomy	2	4.8
None	37	88.2
Mean operative time (minutes):	48 ± 8.9 0	

Table 3: Frequency of complications and results among the study women (42)

Variables	No	%
Complications:		
Major bleeding	2	4.8
Bladder injury	1	2.4
Urine retention	1	2.4
None	38	90.4
Results:		
Excellent success	39	93.0
Failed	3	7.0

Figure 2: Proportion of complications and the results of the study women



Discussion

Cooper et al [14] mentioned that UI is not a normal part of ageing; up to 40% of older women (≥ 55 years of age) report experiencing UI in everyday life. UI may lead to a significant reduction in women's quality of life, psychological health, confidence, sexuality, and societal inclusion [15]. This occurs to different degrees of severity; some women experience infrequent leakage, and others experience more frequent problems or total inability to control their bladder function [16].

Causes of UI for older women vary from functional causes, such as damage to the urethra, or pelvic floor muscles [17], to other issues, including an overactive bladder or lower urinary tract and bladder infections. The likelihood is increased for those who have experienced vaginal birth, are obese, or have familial risk [18].

SUI refers to the involuntary leakage of urine from the external urethral orifice when abdominal pressure increases due to actions such as sneezing, coughing and laughing [19].

Stress urinary incontinence affects 15.7% of adult women; 77.5% of women report the symptoms to be bothersome and 28.8% report the symptoms to be moderate to severe [20]. Prevalence of stress urinary incontinence will increase with age particularly with menopause. One study found that 41% of women older than 40 years old will have urinary incontinence [21]. Up to 77% of elderly females in nursing homes will have urinary incontinence [22].

In our present study, there were 42 women operated for SUI. We found in the present study that most of the patients were from the rural governorates with 30 (71.4%).

The age of the study women ranged between 40 to 80 years and their mean age was 62.1 ± 9.7 years.

The mean age of the patients operated for SUI reported by Magon et al [23] was 46.2 years (SD 11.2 years; range 24–70 years). The mean age of patients reported by Taweel in his series was 52 ± 9 years (range 34–70 years) [24].

Kaelin-Gambirasio et al [25] in their analysis of 233 cases had patients with an average age of 57.9 years (SD 13.2 years).

In our study, we grouped the study women in two age groups, ≤ 60 years and > 60 years. We found the patients of the age group > 60 years were (57.1%) while the patients of the age group ≤ 60 years were (42.9%).

We found in our current study that the mean body weight of the patients is 67.5 ± 7.0 kilograms (kg) and ranged between 55 and 80 kg.

Obesity is one of the important risk factors for the development of urinary incontinence with old age [26,27]. Some authors have described an increase of intra-abdominal pressure in obese patients [28], and this phenomenon may stress the pelvic floor, possibly causing nerve and muscular injury that might lead to a higher prevalence of SUI [29].

In our present study, the number of vaginal deliveries

ranged between 5 and 10. We categorized the number of vaginal deliveries in 2 groups: 5 – 7 vaginal deliveries were 13 (31.0%), and 8 – 10 vaginal deliveries 29 (69.0%). In the present study, we found the mean number of vaginal delivery was 8.0 ± 1.2 .

Gari et al [30] found in their published study, that the presence of SUI increased with the number of pregnancies, and among women who had at least one vaginal delivery and no delivery via cesarean section. They added that the likely explanation for this is that mechanical strain during repetitive delivery may cause muscle, fascia, and ligamentous disruption, as well as damage to connective and neurological structures of the pelvic organs and pelvic floor. Similar findings have been reported in two congruent studies. The first study, was conducted by Gyhagen et al which reported up to a 20–30% increase in the prevalence of SUI due to pregnancy, and this increased to 43% if the delivery was vaginal [31].

The second study carried out by Altman et al [32] reported an increase in the prevalence of SUI by 12% due to pregnancy and vaginal delivery.

In the current study, we observed 4 (9.6%) cases developed complications. They were (4.8%) major bleeding, (2.4%) of them was bladder injury and (2.4%) were urine retention. Magon et al [23] reported that in their study, there was one bladder and one urethral injury intra-operatively. They added that in their opinion, it is mandatory to inspect the lateral vaginal wall after passing the needle through transobturator foramen. In the immediate postoperative period, only one patient (1.7%) had transient urinary retention after removal of urinary catheter, which was relieved by recatheterization and subsequently had successful voiding on the next day.

Additionally, we found in our present study, (93.0%) of the outcome of operated women had excellent success while with failed results were 3 (7.0%), at six months postoperatively.

Buhur et al [33] reported in their study that TOT operation is effective in treating stress urinary incontinence, 89.6% at six months postoperatively.

Chrysostomou [34] reported in his published study that the TOT is a simple, effective and safe procedure for treating SUI. He added the cure rate of SUI, defined as the disappearance of subjective and objective SUI, was 94.5% during the follow up period. Success rate of our current study is also similar to other reported series [35–37].

Conclusion

We concluded that urinary incontinence is a common health problem, which affects women of all ages in Aden and the surrounding governorates. Stress urinary incontinence has a negative impact on quality of life in both the physical and mental health domains. The transobturator approach is an effective treatment of stress urinary incontinence with low morbidity and with acceptable success and outcome. Further studies are needed to determine the magnitude of this health problem in our country.

References

1. National Collaborating Centre for Women's and Children's Health (UK). Urinary Incontinence in Women: The Management of Urinary Incontinence in Women. London: Royal College of Obstetricians and Gynaecologists (UK); 2013.
2. Luber KM. The definition, prevalence, and risk factors for stress urinary incontinence. *Rev Urol.* 2004; 6:S3.
3. Nygaard IE, Heit M. Stress urinary incontinence. *Obstet Gynecol.* 2004; 104: 607-620.
4. Haylen BT, de Ridder D, Freeman RM, et al. International Urogynecological Association; International Continence Society. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Neurourol Urodyn.* 2010;29:4-20.
5. Keyock KL, Newman DK. Understanding stress urinary incontinence. *Nurse Practitioner.* 2011;36:24-36.
6. Hampel C, Weinhold D, Benken N, Eggersmann C, Thuroff JW. Definition of overactive bladder and epidemiology of urinary incontinence. *Urology.* 1997; 50:4.
7. Hampel C, Artibani W, Espuña Pons M, Haab F, Jackson S, Romero J, et al. Understanding the burden of stress urinary incontinence in Europe: A qualitative review of the literature. *Eur Urol.* 2004; 46:15.
8. Minaglia S, Ozel B, Hurtado E, Klutke CG, Klutke JJ. Effect of Transobturator tape procedure on proximal urethral mobility. *Urology.* 2005; 65:55-59.
9. Juma S, Brito CG. Transobturator tape: Two years follow-up. *Neurourol Urodyn.* 2007; 26:37.
10. Abdel-Fattah M, Ramsay I, Pringle S, Bjornsson S, Hardwick C, Tierney J, et al. Transobturator suburethral tapes in the management of urinary incontinence: Success, safety and impact on sexual life. *Gynecol Surg.* 2007; 4:267-73.
11. Delorme E. Transobturator urethral suspension: mini-invasive procedure in the treatment of stress urinary incontinence in women. *Prog Urol.* 2001; 11: 1306-13.
12. Delorme E, Droupy S, de Tayrac R, Delmas V. Transobturator tape (Uratape): a new minimally invasive procedure to treat female urinary incontinence. *Eur Urol.* 2004; 45(2):203-207.
13. De Leval J. Novel surgical technique for the treatment of female stress urinary incontinence: transobturator vaginal tape inside-out. *Eur Urol.* 2003; 44(6):724-730.
14. Cooper J, Annappa M, Quigley A, et al. Prevalence of female urinary incontinence and its impact on quality of life in a cluster population in the United Kingdom (UK): a community survey. *Prim Health Care Res Dev* 2015; 16(4): 377-382.
15. Abrams P, Smith AP, Cotterill N. The impact of urinary incontinence on health-related quality of life (HRQoL) in a real-world population of women aged 45-60 years: results from a survey in France, Germany, the UK and the USA. *BJU Int* 2015; 115(1): 143-152.
16. Healthcare Quality Improvement Partnership (HQIP) and Royal College of Physicians. National audit of continence care: combined organizational and clinical report. 2010. <https://www.hqip.org.uk/wp-content/uploads/2010/01/2010-NACC-Annual-Report.pdf>.
17. Tennstedt SL, Link CL, Steers WD, et al. Prevalence of and risk factors for urine leakage in a racially and ethnically diverse population of adults: the Boston Area Community Health (BACH) survey. *Am J Epidemiol.* 2008; 167: 390-399.
18. Handa VL, Blomquist JL, Knoop LR, et al. Pelvic floor disorders 5-10 years after vaginal or cesarean childbirth. *Obstet Gynecol* 2011; 118: 777-784.
19. Zhu L, Lang J, Liu C, Han S, Huang J, Li X. The epidemiological study of women with urinary incontinence and risk factors for stress urinary incontinence in China. *Menopause.* 2009; 16: 831-836.
20. Nygaard I, Barber MD, Burgio KL, Kenton K, Meikle S, Schaffer J, Spino C, Whitehead WE, Wu J, Brody DJ., Pelvic Floor Disorders Network. Prevalence of symptomatic pelvic floor disorders in US women. *JAMA.* 2008 Sep 17; 300(11):1311-6.
21. Minassian VA, Yan X, Lichtenfeld MJ, Sun H, Stewart WF. The iceberg of health care utilization in women with urinary incontinence. *Int Urogynecol J.* 2012; 23(8):1087-93.
22. Offermans MP, Du Moulin MF, Hamers JP, Dassen T, Halfens RJ. Prevalence of urinary incontinence and associated risk factors in nursing home residents: a systematic review. *Neurourol Urodyn.* 2009; 28(4):288-94.
23. Magon N, Chopra SVSM. Trans-obturator Tape in Treatment of Stress Urinary Incontinence: It is Time for a New Gold Standard. *N Am J Med Sci.* 2012; 4(5): 226-230.
24. Taweel WA, Rabah DM. Transobturator tape for female stress incontinence: Follow-up after 24 months. *Can Urol Assoc J.* 2010;4:33-6.
25. Kaelin-Gambirasio I, Jacob S, Boulvain M, Dubuisson JB, Dällenbach P. Complications associated with transobturator sling procedures: Analysis of 233 consecutive cases with a 27 months follow-up. *BMC Womens Health.* 2009; 9:28.
26. Parazzini F, Colli E, Origgi G, Surace M, Bianchi M, Benzi G, et al. Risk factors for urinary incontinence in women. *Eur Urol.* 2000;37:637-643.
27. Park YK. Female stress urinary incontinence. *J Korean Continence Soc.* 2008;12:1-9.
28. Noblett KL, Jensen JK, Ostergard DR. The relationship of body mass index to intra-abdominal pressure as measured by multichannel cystometry. *Int Urogynecol J Pelvic Floor Dysfunct.* 1997;8:323-326.
29. Rafii A, Darai E, Haab F, Samain E, Levardon M, Deval B. Body mass index and outcome of tension-free vaginal tape. *Eur Urol.* 2003;43:288-292.
30. Gari AM, Alamer EHA, Almalayo RO, Alshaddadi WA, Alamri SA, Aloufi RS, et al. Prevalence of stress urinary incontinence and risk factors among Saudi females. *Medicina (Kaunas).* 2023; 59(5): 940.
31. Gyhagen M, Åkervall S, Molin M, Milsom I. The effect of childbirth on urinary incontinence: A matched cohort study in women aged 40-64 years. *Am. J. Obstet. Gynecol.* 2019; 221: 322.e1-322.e17.

32. Altman D, Ekström A, Gustafsson C, López A, Falconer C, Zetterström J. Risk of urinary incontinence after childbirth: A 10-year prospective cohort study. *Obstet. Gynecol.* 2006; 108: 873–878.
33. Buhur A, Öncü N. Evaluation of the Effectiveness of Trans Obturator Tape Operation in the Treatment of Stress Incontinence. *J Contemp Med* 2023;13(1):24-29.
34. Chrysostomou A. The management of stress urinary incontinence using transobturator tapes in a tertiary hospital in South Africa. *Pelviperrineology.* 2012; 32: 82-86.
35. Nilsson C, Palva K, Rezapour M, Falconer C. Eleven years prospective follow-up of the tension-free vaginal tape procedure for treatment of stress urinary incontinence. *International Urogynecology Journal* 2008; 19:1043-1047.
36. deTayrac R, Deffieux X, Droupy S, Chauveaud-Lambling A, Calvanèse-Benamour L, Fernandez H. A prospective randomized trial comparing tension-free vaginal tape and transobturator suburethral tape for surgical treatment of stress urinary in86 continence. *American journal of obstetrics and gynecology* 2004; 190:602-608.
37. Domingo S, Alama P, Ruiz N, Lazaro G, Morell M, Pellicer A. Transobturator tape procedure outcome: a clinical and quality of life analysis of a 1-year follow-up. *International Urogynecology Journal* 2007; 18:895-900.

Knowledge and Practice of taking Influenza Vaccine among Adult Diabetic Patients in Bahrain Defense Force Hospital

Yasir Abdel Rahaman Abdel Wahid

MD in Family Medicine (SMSB)

Correspondence:

Dr. Yasir Abdel Rahaman Abdel Wahid

Email: yasirfamily19@gmail.com

Received: January 2024. Accepted: February 2024; Published: March 1, 2024.

Citation: Yasir Abdel Rahaman Abdel Wahid. Knowledge and Practice of taking Influenza

Vaccine among Adult Diabetic Patients in Bahrain Defense Force Hospital. World Family Medicine. March 2024; 22(3): 21-42.

DOI: 10.5742/MEWFM.2024.95257624

Abstract

The objective of this study is to assess the knowledge and practice of taking the annual influenza vaccine among adult diabetic patients in BDF Hospital. The study is a descriptive cross-sectional hospital-based study.

Three hundred diabetic patients who were eligible for the study were interviewed, using a structured questionnaire.

Results of the survey indicated that males and females included are 48% to 52% respectively, 95.3% of the cohort were doing follow up, but only 55.3% were doing it regularly.

Although 65.3% are aware and have heard about the flu vaccine only 10% have taken the flu vaccine in the last 2 years. Only 27.3% were advised to take the flu vaccine, 30% of the study population know that the vaccine helps reduce the flu illness and 47.33% know that it helps prevent seasonal influenza.

From our study, it was found that the main reason for not taking the flu vaccine is that they mainly did not know about the vaccine which constituted 49.33% of the study population.

So, knowledge and use are lower than optimal compared to the literature but here it is the lowest, which may mostly be due to reduced awareness of the benefits of the vaccine and vaccination. This will most probably increase if there are increased efforts on advising direct contacts with the patients in the diabetic or other PHC clinics or through the media, to have the seasonal flu vaccine.

Keywords: Influenza vaccine, diabetes patients

Abbreviations

BDF	Bahrain defense force
CMC	Christian Medical College
DFID	Distance Fellowship in Diabetes Management
DM	Diabetes mellitus
MOH	Ministry Of Health
FU	Follow up
HCW	Health Care Workers
CDC	Centers for Disease Control and Prevention
NIAID	National Institute of Allergy and Infectious Diseases
HCP	Health Care Provider

UK	United Kingdom
NHS	National Health Surveys
COPD	Chronic Obstructive Pulmonary Disease
RIV3	Trivalent Recombinant Hemagglutinin

Introduction

No one questions the important role of vaccination in protecting and preventing or reducing the incidence rate of fatal diseases.

From this point vaccinations worldwide are programmed according to vaccine recommendations, from birth till later for the elderly with different forms and compositions.

Vaccination is well known to enhance immunity and usually starts when the body is building its defenses against diseases early in childhood. It is a well-known program from birth, with some modulation in different (MOH) systems depending on many factors which are geographical and endemic in the region.

Also, there is a role for adult vaccinations especially for those who are vulnerable to be attacked due to some illness, or due to less immunity, such as those with chronic illness and at the top of the list comes diabetic patients.

Hence this study was conducted to evaluate the knowledge and practice of taking influenza vaccine among adult diabetic patients in BDF hospital outpatient clinics, as diabetes is now one of the most common non communicable diseases globally and presents as a huge burden for the whole health system, and is one of the recommended areas for vaccination during adult life.

The study evaluates the factors that are taken as variables affecting the knowledge and practice of taking the flu vaccine, where these variables are to be used in an open and closed questionnaire. The interview was guided by doctors and Nurses in the GP clinics. The variables taken were age, sex, level of education, duration of being diabetic, whether the patient is on regular follow up for DM, source of knowledge about flu vaccine, basic knowledge about the vaccine, when, how, and why it should be taken, and any concerns or doubts about taking the flu vaccine, and if the patient had ever had the flu vaccine.

Literature Review

Although the flu vaccine is well known and has been shown in many studies to reduce the incidence, morbidity and mortality of influenza and hence the cost of management of this contagious disease, many people are not aware of the recommendations to take the vaccine. Of those who know, very few respond to the message of Flu vaccine usage.

The influenza vaccination is an annual vaccination using a vaccine specific for a given year to protect against the highly variable influenza virus [1]. Each seasonal influenza vaccine contains antigens representing three or four influenza virus strains: one influenza type A subtype H1N1 virus strain, one influenza type A subtype H3N2 virus strain, and either one or two influenza type B virus strains [2]. Influenza vaccines may be administered as an injection, also known as a flu shot, or as a nasal spray.

The U.S. Centers for Disease Control and Prevention (CDC) recommends that everyone over the age of 6 months should receive the seasonal influenza vaccine. [3], Vaccination campaigns usually focus on people who are at high risk of serious complications if they catch the flu, such as the elderly and people living with chronic illness or those with weakened immune systems, as well as health care providers (HCP) [3][4].

Despite somewhat limited research, the safety of flu vaccines is reassuring; there is no evidence that they can cause serious harm and no reason for serious side effects to be a concern. [5].

Purpose and benefits of annual flu vaccination:

Influenza vaccines cut the risk that elderly people will die of the virus by 50% and reduces the incidence of hospitalization by more than 25%, according to a study released by the New England Journal of Medicine [6] [7]. Having the flu vaccine is the best way to protect against the flu and helps prevent its spread throughout a community. The influenza vaccine can also reduce the severity of the flu should a person contract a strain of the flu that the vaccine did not contain [8].

An influenza epidemic emerges during flu season each winter. There are two flu seasons annually, corresponding to the occurrence of winter in the Northern and Southern Hemispheres.

Although difficult to assess, these annual epidemics are thought to result in between three and five million cases of severe illness and between 250,000 and 500,000 deaths around the world every year [9].

A review at the National Institute of Allergy and Infectious Diseases (NIAID) division of the National Institutes of Health (NIH) in 2008 concluded that "Seasonal influenza causes more than 200,000 hospitalizations and 41,000 deaths in the U.S. each year, and is the seventh leading cause of death in the U.S." [10]. The average total economic costs caused by the annual influenza outbreak in the U.S. has been estimated at over \$80 billion [12] [13]. The number of annual influenza-related hospitalizations is many times the number of deaths [14].

Benefits of vaccination:

According to research published in July 2010, vaccination against influenza is also thought to be important for members of high-risk groups who would be likely to suffer complications [15][16].

Vaccination of school-age children has a strong protective effect on the adults and elderly with whom the children are in contact [17].

For healthy, working adults, influenza vaccines can provide moderate protection against confirmed influenza, but such protection is greatly reduced in some seasons. Evidence for protection in adults aged 65 years or older is lacking [18].

Influenza vaccination has been shown to be highly effective in Healthcare Workers (HCW), with minimal adverse effects. In a study of forty matched nursing homes, staff influenza vaccination rates were 69.9% in the vaccination arm versus 31.8% in the controls. The vaccinated staff experienced a 42% reduction in sick leave from work ($P=.03$) [19].

An analysis of data and patient population health in New Mexico's 75 long-term care facilities and nursing homes found that as vaccination rates of HCPs with direct patient contact rose from 51 to 75 %, the chances of a flu outbreak among patients in that facility went down by 87%. The New Mexico study showed that vaccinating HCPs provided more protection to residents than vaccinating the residents themselves [20].

In a 2010 survey in United States HCW, 63.5% reported that they received the flu vaccine during the 2010–11 seasons, an increase from 61.9% reported the previous season. Health professionals with direct patient contact had higher vaccination uptake, such as physicians and dentists (84.2%) and nurse practitioners (82.6%) [21][22][23].

It is important to note that the flu vaccine takes about two weeks to build up enough antibodies to protect against the flu, [2] and that the vaccine does not protect against every strain of the flu [2].

Safety:

Flu vaccination may lead to side effects such as runny nose and sore throat, which can last for up to several days. Egg allergy may also be a concern since flu vaccines are typically made using eggs [24][25], however, research into egg allergy and influenza vaccination [26] has led some advisory groups to recommend vaccine delivery protocols for egg allergic persons [27].

Some injection-based flu vaccines intended for adults in the United States contain thiomersal (also known as thimerosal), a mercury-based preservative. Despite some controversy in the media, [28] it was concluded that there is no evidence of toxicity from thiomersal in vaccines as it is in tiny concentration and with no health safety risk. [29]

Although Guillain-Barre syndrome had been feared as a complication of vaccination, the CDC states that some of the studies on modern influenza vaccines have seen no link with Guillain-Barre [30] [31].

Efficacy and effectiveness:

A vaccine is assessed by its efficacy; the extent to which it reduces risk of disease under controlled conditions, and its effectiveness, and the observed reduction in risk after the vaccine is put into use [32].

In the case of influenza, effectiveness is expected to be lower than efficacy because it is measured using the rates of influenza-like illness, which is not always caused by influenza [33]. Influenza vaccines generally show high efficacy, as measured by the antibody production induced

in animal models or vaccinated people, [34] or most rigorously, by immunizing healthy adult volunteers and then challenging them with virulent influenza virus [35]. Studies on the effectiveness of flu vaccines in the real world are uniquely difficult; vaccines may be imperfectly matched, virus prevalence varies widely between years, and influenza is often confused with other influenza-like illnesses [36]. But even a mismatched vaccine can often provide cross-protection [37].

Nevertheless, multiple clinical trials of both live and inactivated influenza vaccines against seasonal influenza have been performed and their results pooled and analyzed in several 2012 meta-analyses. Studies on live vaccines have very limited data, but these preparations may be more effective than inactivated vaccines [35]. The meta-analyses examined the efficacy and effectiveness of inactivated vaccines against seasonal influenza in adults [33], children [38], and the elderly [39][40]. In adults, vaccines show a three quarters reduction in risk of contracting influenza (4% influenza rate among the unvaccinated versus 1% among vaccinated persons) when the vaccine is perfectly matched to the virus and a one-half reduction (2% getting flu without vaccine versus 1% with vaccine) when it is not, but with no significant effect on the rate of hospitalization [33].

In children, vaccines again showed high efficacy, but low effectiveness in preventing "flu-like illness". In children under the age of two the data are extremely limited, but vaccination appeared to confer no measurable benefit [38].

In the elderly, while many studies show effectiveness [41] [42] [43], the overall evidence is still insufficient [39] [40] [44].

Available evidence indicates that the high-dose vaccine produces a stronger immune response [46].

During an influenza pandemic, where a single strain of virus is responsible for illnesses, an effective vaccine could produce a large decrease in the number of cases and be highly effective in controlling an epidemic [47]. However, such a vaccine would have to be produced and distributed rapidly to have maximum effect [48]. A 2011 meta-study published in *The Lancet*, "Efficacy and Effectiveness of Influenza Vaccines," analyzed 31 prior studies on the effectiveness of influenza vaccination trials conducted between 1967 and 2011. The analysis found that flu shots were efficacious 67 % of the time; the populations that benefited the most were HIV-positive adults aged 18 to 55 (76 %), healthy adults aged 18 to 46 (approximately 70%), and healthy children aged 6 to 24 months (66%) [45].

The group most vulnerable to non-pandemic flu, the elderly, is also the least to benefit from the vaccine. There are multiple reasons behind this steep decline in vaccine efficacy, the most common of which are declining immunological function and frailty associated with advanced age [49].

As mortality is also high among infants who contract influenza, household contacts and caregivers of infants should be vaccinated to reduce the risk of passing an influenza infection to the infant [4].

Data from the years when Japan required annual flu vaccinations for school-aged children indicate that vaccinating children, the group most likely to catch and spread the disease, has a strikingly positive effect on reducing mortality among older people, due to herd immunity: one life saved for every 420 children who received the flu vaccine [50].

In working adults, a 2010 Cochrane review found that vaccination reduced both influenza symptoms and working days lost, without affecting transmission or influenza-related complications [33].

Duration of protection:

According to work published in 1973, 1983, and 2004, after vaccination against seasonal flu, antibody titers peak after typically two to four weeks. They decrease by about 50% over the next six months (the decrease is less for older adults), then remain stable for two to three years; protection without revaccination persists for at least three years for children and young adults [51]. It was previously thought that vaccination provided lifelong protection against specific strains [52]. This is not untrue; a 2010 study found a significantly enhanced immune response against the 2009 pandemic H1N1 in study participants who had received vaccination against the swine flu in 1976 [53].

Injection versus Nasal Spray

Flu vaccines are available either as, TIV, QIV (flu shot (injection), or trivalent (three strains; usually A/H1N1, A/H3N2, and B), quadrivalent (four strains; usually A/H1N1, A/H3N2, and representatives of B/Yamagata and B/Victoria lineages) inactivated (killed) vaccine), or LAIV; Q/LAIV (nasal spray (mist) of live attenuated influenza vaccine).

TIV induces protection after injection (typically intramuscular, though subcutaneous and intradermal routes are also immunogenic) [54], based on an immune response to the antigens present in the inactivated virus. While cold-adapted LAIV works by establishing infection in the nasal passages [55], LAIV is not recommended for individuals under age 2 or over age 50 [56], but might be comparatively more effective among children over age 2 [57].

A study of military personnel in the USA showed that flu shots yielded less illness than nasal sprays. This study was based on one of the largest head-to-head studies comparing LAIV and TIV. It was conducted by the U.S. Armed Forces Surveillance Center, on military personnel stationed in the U.S. during three flu seasons from 2004 through 2007.

Cross protection

Annual seasonal flu vaccination provides some protection against flu viruses that the vaccine was not designed for, including novel viruses [57]. The CDC made the following statement regarding the 2007-2008 vaccine; antibodies made in response to vaccination with one strain of influenza viruses can protect against different, but related strains [57].

In addition, it is important to remember that the influenza vaccine contains three virus strains so the vaccine can also protect against another two viruses.

For these reasons, even during seasons when there is a less-than-ideal match, CDC continues to recommend influenza vaccination. This is particularly important for people at high risk for serious flu complications and their close contacts [57].

Vaccination recommendations

Various public health organizations, including the WHO, have recommended that yearly influenza vaccination be routinely offered to patients at risk of complications of influenza and those individuals who live with or care for high-risk individuals, including: the elderly (UK recommendation is those aged 65 or above), Patients with chronic lung diseases (asthma, COPD, etc.), patients with chronic heart diseases (congenital heart disease, chronic heart failure, ischemic heart disease), patients with chronic liver diseases (including cirrhosis), patients with chronic renal diseases (such as the nephrotic syndrome), patients who are immunosuppressed (those with HIV or who are receiving drugs to suppress the immune system such as chemotherapy and long-term steroids) and their household contacts, people who live together in large numbers in an environment where influenza can spread rapidly, such as prisons, nursing homes, schools, and dormitories, people who plan to attend or participate in a high profile important event with large numbers of people from various places (such as Olympic Games etc.), people who are in the armed forces and HCW [58]. For pregnant women, however, a 2009 review concluded that there was insufficient evidence to recommend routine use of trivalent influenza vaccine during the first trimester of pregnancy [59]. Influenza vaccination during flu season is part of the recommendations for influenza vaccination of pregnant women in the United States [60].

Both types of flu vaccines are contraindicated for those with severe allergies to egg proteins and people with a history of Guillain-Barre syndrome [61].

According to the recommendations of the Advisory Committee on Immunization Practices, (ACIP) United States, 2013-14, recommend the Flu vaccination to all children aged 6 through to 59 months; all persons aged ≥50 years; adults and children who have chronic pulmonary (including asthma) or cardiovascular (except isolated

hypertension), renal, hepatic, neurological, hematologic, or metabolic disorders (including diabetes mellitus); persons who have immune-suppression (including immune-suppression caused by medications or by HIV infection); women who are or will be pregnant during the influenza season; children and adolescents (aged 6 months-18 years) who are receiving long-term aspirin therapy and who might be at risk for experiencing Reye's syndrome after influenza virus infection; residents of nursing homes and other long-term care facilities; American Indians/Alaska Natives; persons who are morbidly obese (BMI ≥ 40) [10].

When vaccine supply is limited, vaccination efforts should focus on delivering vaccination to persons at higher risk for influenza-related complications listed above, as well as these persons: HCW; Household contacts (including children), and caregivers of children aged ≤ 59 months (i.e., aged < 5 years) and adults aged ≥ 50 years, with particular emphasis on vaccinating contacts of children aged < 6 months; and Household contacts (including children) and caregivers of persons with medical conditions that put them at higher risk for severe complications from influenza. HCPs and persons who are contacts of persons in these groups and who are not contacts of severely immune-compromised persons (those living in a protective environment) may receive any influenza vaccine that is otherwise indicated.

Individuals who care for the severely immune-compromised should receive either IIV or RIV3. Women who are or will be pregnant during influenza season should receive IIV. Live attenuated influenza vaccine (LAIV) is not recommended for use during pregnancy. Postpartum women can receive either LAIV or IIV. Pregnant and postpartum women do not need to avoid contact with persons recently vaccinated with LAIV.

Persons who report having had reactions to egg involving such symptoms as angioedema, respiratory distress, lightheadedness, or recurrent emesis; or who required epinephrine or another emergency medical intervention may receive RIV3 if aged 18 through to 49 years and there are no other contraindications. If RIV3 is not available or the recipient is not within the indicated age range, such persons should be referred to a physician with expertise in the management of allergic conditions for further risk assessment before receipt of the vaccine.

Administration of IIV to persons receiving influenza antiviral drugs for treatment or chemoprophylaxis is acceptable. LAIV should not be administered until 48 hours after cessation of influenza antiviral therapy. If flu antiviral medications are administered within 2 weeks after receipt of LAIV, the vaccine dose should be repeated 48 or more hours after the last dose of antiviral medication.

Persons receiving antiviral drugs within the period 2 days before to 14 days after vaccination with LAIV should be revaccinated at a later date with any approved vaccine formulation.

After administration of a live vaccine, at least 4 weeks should pass before another live vaccine is administered [10].

Also, the former abbreviation TIV (Trivalent Inactivated Influenza Vaccine, previously used for inactivated influenza vaccines) has been replaced with the new abbreviation IIV (Inactivated Influenza Vaccine) [10].

Cost effectiveness

The cost-effectiveness of seasonal influenza vaccination has been widely evaluated for different groups and in different settings. In the elderly (aged over 65 years) the majority of published studies have found that vaccination is cost saving, with the cost savings associated with influenza vaccination (e.g. prevented health care visits) outweighing the cost of vaccination [62]. In older adults (aged 50–64 years), several published studies have found that influenza vaccination is likely to be cost-effective, however, the results of these studies were often found to be dependent on key assumptions used in the economic evaluations [63]. The uncertainty in influenza cost-effectiveness models can partially be explained by the complexities involved in estimating the disease burden [63], as well as the seasonal variability in the circulating strains and the match of the vaccine [65]. In children, the majority of studies have found that influenza vaccination was cost-effective [66]. Several studies have attempted to predict the cost-effectiveness of interventions (including pre-pandemic vaccination) to help protect against a future pandemic, however estimating the cost-effectiveness has been complicated by uncertainty as to the severity of a potential future pandemic and the efficacy of measures against it [67].

Vaccine production

Flu vaccine is usually grown by vaccine manufacturers in fertilized chicken eggs [68] [69]. In the Northern Hemisphere, the manufacturing process begins following the announcement (typically in February) of the WHO recommended strains for the winter flu season [68] [70]. Three strains (representing an H1N1, an H3N2, and a B strain) of flu are selected and chicken eggs are inoculated separately; these monovalent harvests are then combined to make the trivalent vaccine [71]. Both the conventional injection and the nasal spray are manufactured using chicken eggs. The European Union has also approved Opta flu, a vaccine produced by using vats of animal cells [69]. This technique is expected to be more scalable and avoid problems with eggs, such as allergic reactions and incompatibility with strains that affect avians, like chickens [69].

Research continues into the idea of a “universal” influenza vaccine that would not require tailoring to particular strains, but would be effective against a broad variety of influenza viruses under trial [69].

Regional research

Study about Influenza Vaccination among HCWs and their Attitude in Three Middle Eastern Countries, aimed to determine the current influenza vaccination rates among HCWs in three Middle Eastern countries namely the United Arab Emirates (UAE), Kuwait, and Oman, and also to identify the different variables associated with the noncompliance of HCWs to the recommendations of the Advisory Committee on Immunization Practices (ACIP) set in those countries, using 1500 questionnaires which were distributed to HCW.

The study results showed that a total of 42.5% of all the respondents self reported influenza vaccination in the three countries. There was a statistically significant difference in the rate of vaccination among participants in the three countries (p -value <0.0001) with the highest vaccination rate in Kuwait (67.2%) compared to 46.4% in Oman and only 24.7% in UAE.

A small proportion of the respondents reported that they got influenza like symptoms regularly (11.6%) and the majority of the participants reported that they got it rarely (53.0%). When the respondents were asked about their awareness of the CDC recommendations for influenza vaccination, around fifty-one percent of the respondents reported that they were aware of the CDC recommendations regarding immunization against seasonal influenza.

The association between the respondents' characteristics and their vaccination status was tested to identify the different variables associated with the likelihood of influenza-like symptoms. Results from UAE and Kuwait showed that there is no association between respondents' previous history of influenza illness and their vaccination status (p -value > 0.05 , χ^2 test) in fact in Oman, the highest vaccination rate (66.4%) was obtained for individuals who never got influenza-like symptoms. Multivariate analysis of the results showed that having a history of influenza illness was less likely to occur in the vaccinated group in Oman (OR=0.662).

Participants' awareness of the CDC recommendations for vaccination against seasonal influenza was assessed which revealed that almost half of the participants (48.5%) were aware of these recommendations. Despite this fact, the vaccination rate was low in all three countries; in the UAE, only

26.7% of the vaccinated workers were aware of the CDC recommendations. In Oman, the majority of the vaccinated individuals (56.5%) were aware of the CDC recommendations and those HCWs were 2.2 times considered more likely to be vaccinated than other groups in the other two countries.

On the other hand, self reported reasons among HCWs for refusal to take the influenza vaccine were assessed and showed that the most common reason that discouraged HCWs from taking the vaccine was "lack of time" as reported by 31.8% of the respondents. Other reasons for not taking the vaccine were unawareness of vaccine availability (29.4%), unavailability of vaccine (25.4%),

doubts about vaccine efficacy (24.9%), lack of information about importance (20.1%) and concerns about its side effects (17.3%).

The most common reason for not taking the vaccine in UAE and Oman was the unawareness of vaccine availability (21.5% and 31.6%, respectively) while in Kuwait "lack of time" was the main reason for not being vaccinated (90.9%) among HCWs.

The most common reasons among HCWs for not taking the vaccine were similar in the three countries but there were statistically significant differences for some factors among the three countries. The results of the present study revealed that the vaccination rate in the UAE (27%) was low compared to 46.4% in Oman and 67.2% in Kuwait [79].

Global research

A similar study done in Singapore in January 2007 using a pilot-tested questionnaire was conducted for a total of 307 diabetics who participated in the study.

Of these, 139 (45.3%) claimed to know the difference between influenza and the common cold, while 98 (31.9%) and 18 (5.9%) participants thought that influenza vaccines protected against all influenza strains and provided lifelong immunity. 247 (80.4%) participants were aware that they were at a moderate or higher risk for influenza-related complications, while 181 (58.9%) considered vaccination to be effective in preventing influenza and its complications. Only 94 (30.6%) participants were previously vaccinated. Among those unvaccinated, 117 (54.9%) did not think vaccination was necessary, while 104 (48.8%) had never considered it. As observed from the multivariate analysis, income was a key predictor of influenza vaccination. While 241 (78.5%) participants cited healthcare professional advice as the main guiding factor for getting vaccinated, 199 (64.8%) had never been advised on flu vaccination. Of the 108 (35.1%) participants who had received previous advice on influenza vaccination, the majority had received it from their healthcare professionals [76].

So uptake of influenza vaccination among diabetics in Singapore is low, and the key predictor is income. Perception and knowledge are the main barriers among diabetics [76].

Another descriptive cross-sectional study was conducted on adult subjects (age >16 years) in Spain using individualized secondary data furnished by the 1993 and 2001 NHS. The total number of subjects finally analyzed in the 1993 and 2001 NHSs amounted to 20,880 and 21,034, respectively.

Of these, 911 in 1993 (4.4%, 95% CI 4.1– 4.6) and 1,232 in 2001 (5.9%, 5.5– 6.2) were classified as people with diabetes. The proportion of diabetic subjects who reported having been vaccinated was 43.2% (95% CI 40–46.4) in 1993 and 48.8% (46–51.6) in 2001. Furthermore, influenza

coverage was significantly higher among diabetic versus non-diabetic subjects in both 1993 (43.2 vs. 16.7%) and 2001 (48.8 vs. 17.5%). In both years, after adjusting for potential confounders (age, sex, and comorbidity), the likelihood of being vaccinated was significantly higher among diabetic than among non-diabetic subjects (OR = 1.68 and 1.65, respectively).

The most relevant results of this study are that influenza vaccination coverage among Spanish diabetic adults is below desirable levels and that, after controlling for the influence of confounding variables, there has been no significant improvement in coverage between 1993 and 2001.

Arguably, the main limitation of this study is that the use of invalidated self-report data on vaccination might entail possible bias.

In this respect, however, several studies observe that self-response on influenza vaccination is highly sensitive and evinces a high degree of agreement [72,73]. The coverage described for Spain is appreciably lower than that reported for the U.S. and other European countries [74, 75].

Other studies in Slovakia have been analyzed in selected target groups. A questionnaire study was focused on the level of knowledge about flu vaccination and the attitudes towards it among three target groups: medical students, nurses, and printing company workers. The questionnaire survey revealed several surprising facts. Although almost all the respondents knew about the existence of the influenza vaccine, only less than one quarter had ever received an influenza shot. Despite our expectations that the main source of information about influenza prevention in medical students and nurses would be from their medical and nursing studies, it was shown to be from mass media instead. Even more staggering was the distrust towards the vaccination as a reason for not being vaccinated in a high proportion of both the medical students and the nurses. The majority of medical students would not even want to get a vaccination, even if it were to be provided for free [77].

A study in Germany as a population-based cross-sectional analysis of the seasons 2002/2003 and 2003/2004, conducted by random sampling, was a telephone-based household survey among non-institutionalized individuals representative of the population aged ≥ 14 . The surveys for 2002/2003 and 2003/2004 used the same questionnaire and were subsequently pooled. Four target groups were determined for analysis: (1) persons aged ≥ 60 ; (2) people working in the medical field; (3) persons suffering from chronic illness; and (4) a group composed of persons aged ≥ 60 or working in the medical field or suffering from a chronic illness.

The overall sample consisted of 4,011 people. The influenza vaccination coverage rate in Germany increased from 22.3% in 2002/2003 to 25.1% in 2003/2004. This increase is not significant. The most frequent reasons for being

vaccinated given by vaccinated clients were: influenza considered to be a serious illness, that people wanted to avoid influenza (90.1%), having received advice from the family doctor or nurse to be vaccinated (71.3%), and not wanting to infect family and friends (70.4%). Reasons for not being vaccinated mentioned by people who have never been vaccinated were: thinking about it, however, not being vaccinated in the end (47.7%), not expecting to catch influenza (43.6%), and not having received a recommendation from their family doctor to be vaccinated (36.6%). Options encouraging influenza vaccination are recommendations by the family doctor or nurses (66.6%), more available information on the vaccine regarding efficacy and tolerance (54.2%), and more information available about the disease (52.4%). [78]

Justification

The risk of influenza is very serious as a cause of morbidity and mortality, especially if it comes in an epidemic as it happened at the beginning of the last century where this could be repeated unless faced by wise protection through the use of the recommended vaccine which is efficacious in those vulnerable to be affected, and where diabetic patients came on the top of the list.

Diabetes emerges as an enormous healthcare dilemma all over the world and is growing day by day, especially in the Gulf area and far Southeast. In Asia, vaccination for this sector of patients is an inevitable demand. Hence the budget for the management of seasonal flu is much needed considering morbidity, mortality, and sick leave days in comparison with vaccination which was proved in many studies to give a hope of better immunity and control of the disease at a lower cost.

Where the precious role of the HCP is to forward the idea of vaccination for a better life without flu and its complications by spreading knowledge and health education to all clients, especially diabetic patients.

Study Objectives

General Objectives

Assess the patients' knowledge and practice of taking the annual influenza vaccine among adult diabetic patients in BDF hospital.

Specific Objectives

To measure the knowledge gained throughout diabetic education.

To evaluate the factors that affect taking the annual influenza vaccine.

Methodology

Study Design

Descriptive cross sectional hospital-based study.

Study Area

BDF Hospital, a PHC-out patient clinic in The Kingdom of Bahrain, the hospital is serving a definitive population with specific criteria with insurance and gives holistic primary, secondary, and tertiary care levels all working in coordination to deliver maximum care for the sponsors.

Study Population

All diabetic patients who attended the outpatient clinic in BDF Hospital.

Study Sample

All diabetic patients who came to the GP clinics during the period of the research.

Sampling

Total coverage samples of patients who agree to be included in the study.

Sample Size

It was calculated according to the standard formula

$$N = \frac{Z^2 (PQ)}{D^2}$$

N= sample size

Z= critical value

P= proportion of the problem

D= degree of perception.

The sample size is 300 participants.

Data Collection

Patients were interviewed by a standardized questionnaire.

Inclusion criteria

- Diabetic patients who are willing to be enrolled in the research
- Adult patients of 20-60 years age range.
- Patients who are mentally normal, not seriously ill patients.

Exclusion criteria

- Diabetic patients who are severely ill
- Those less than 20 or more than 60 years old
- Mentally retarded or with psychiatric illness
- Diabetic patients who refused the interview

Data Analysis

The data analysis was done by using the SPSS program.

Results

After analyzing the data collected, where three hundred diabetic patients were interviewed about the knowledge and practice of taking the influenza vaccine and the findings were as follows:

Figure 1: Sex distribution: Females constitute 52% and males were 48%

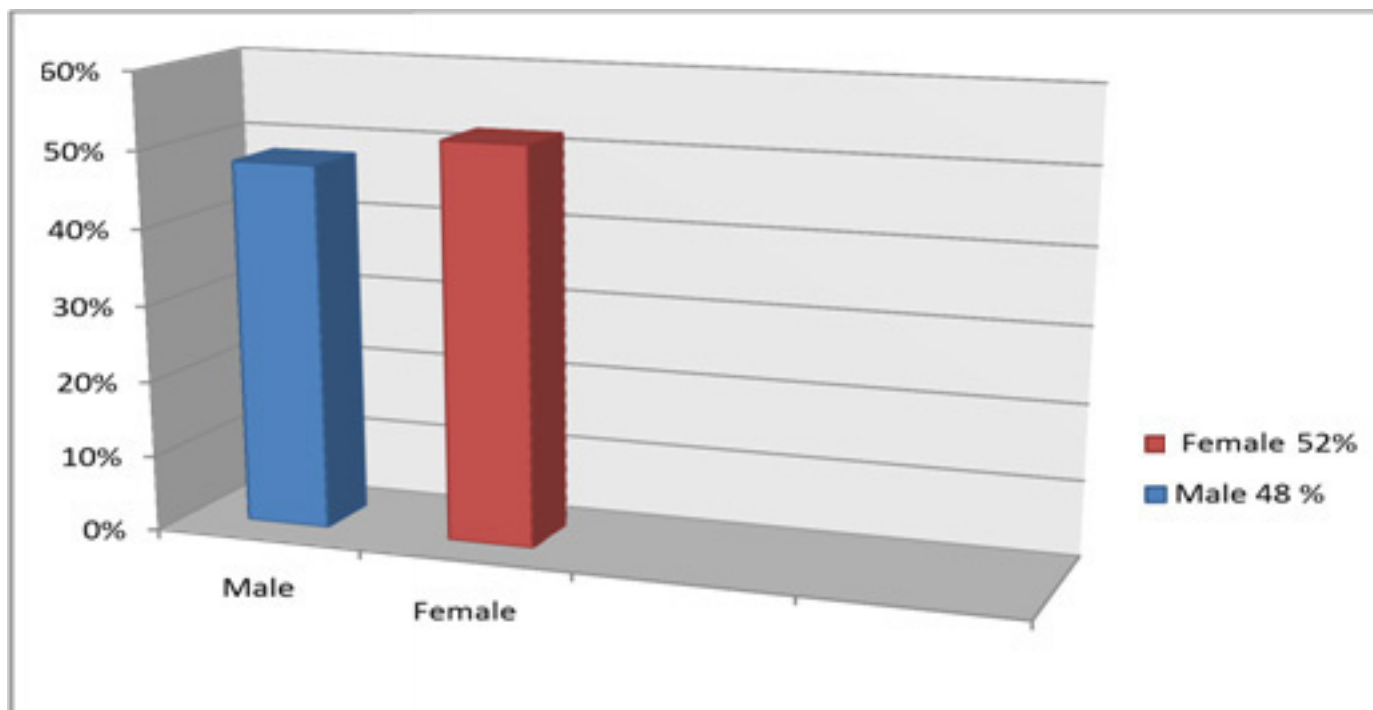


Figure 2: the distribution of the study population according to the duration of being diabetic

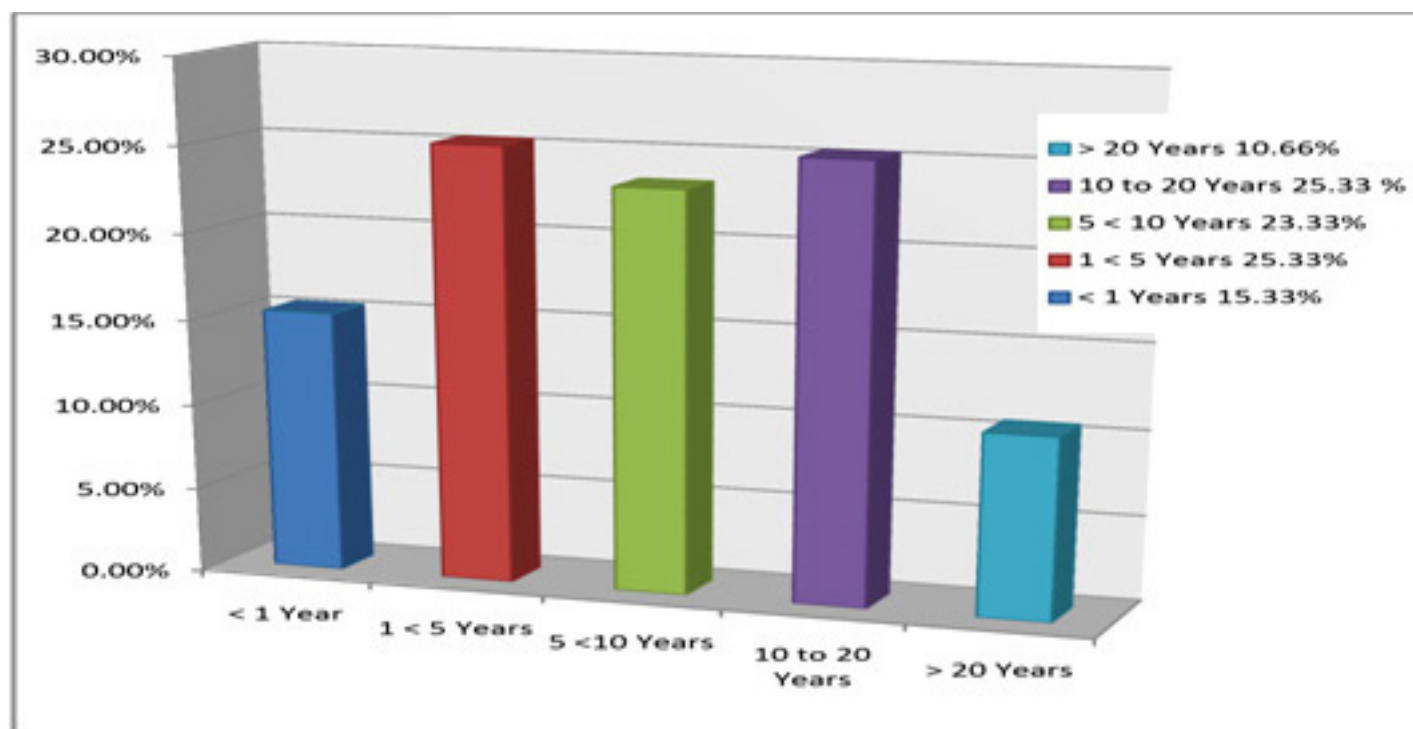


Figure 3: the distribution of the population of the study according to regular follow up

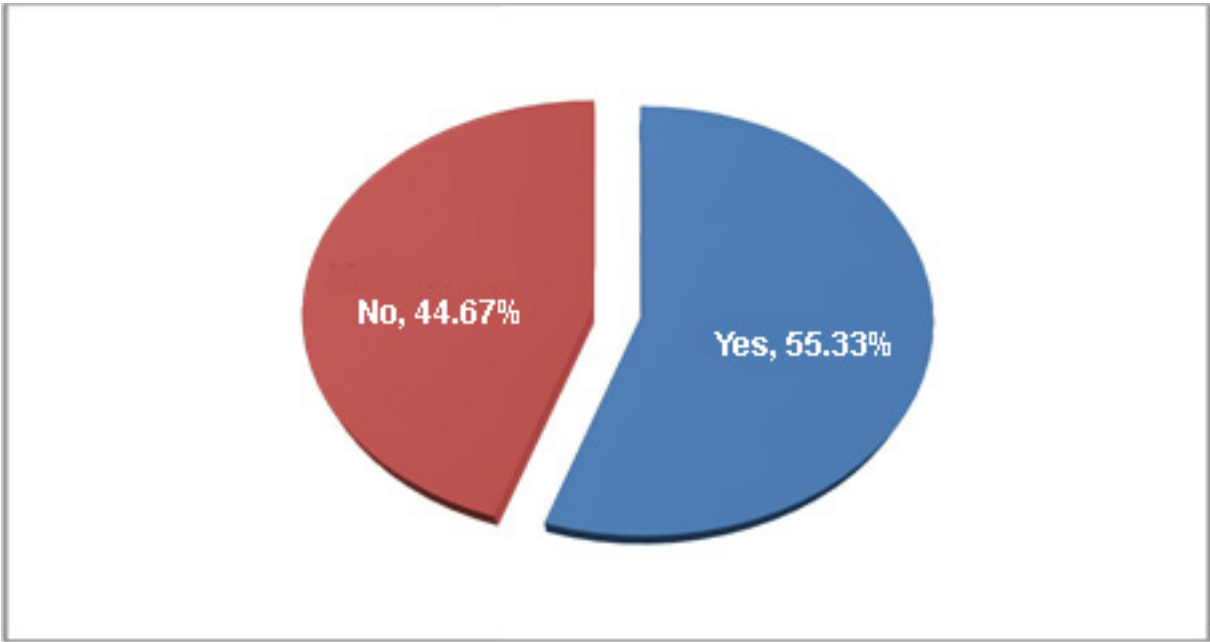


Figure 4: the distribution of the population of the study according to Place where follow up occurs

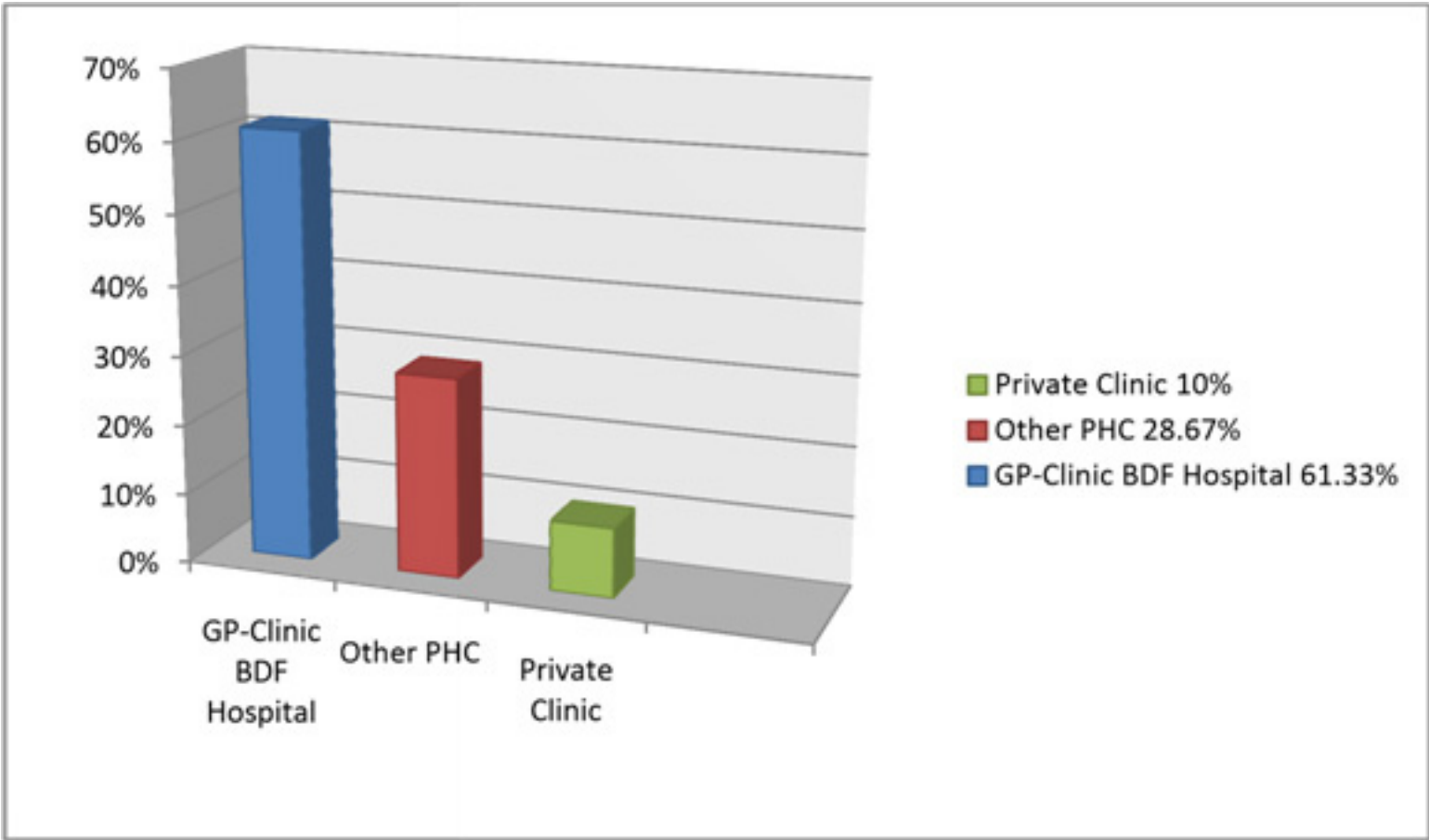


Figure 5: Shows the distribution of the population of the study according to Influenza Vaccine Awareness or if they have heard about the vaccine

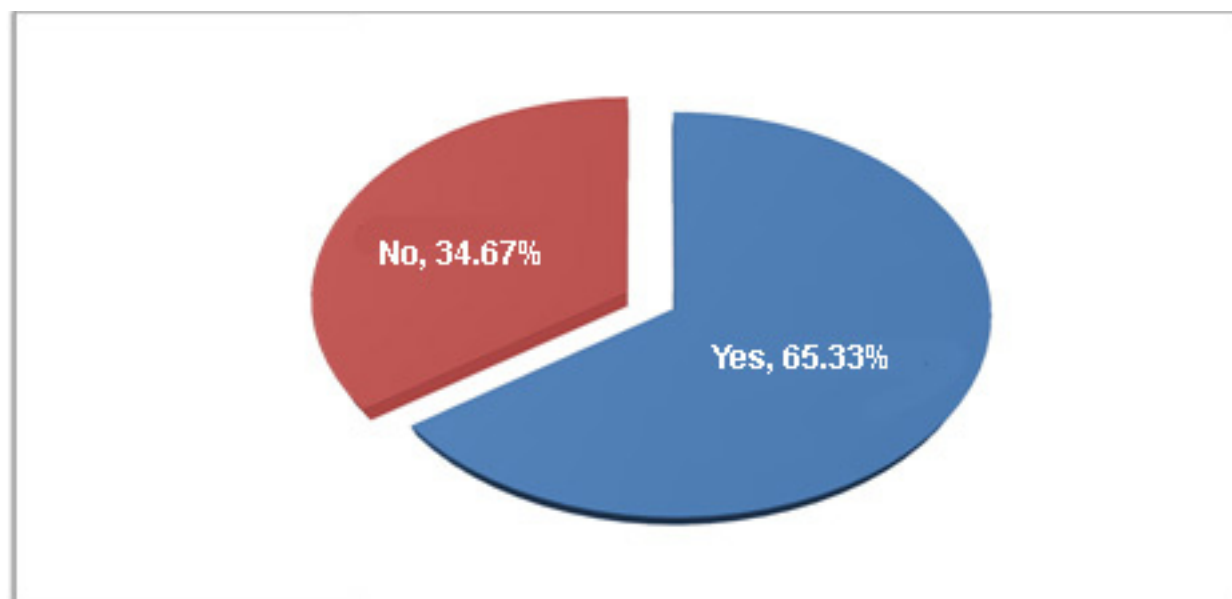


Figure 6: the distribution of the population of the study according to the source of Influenza Vaccine Awareness

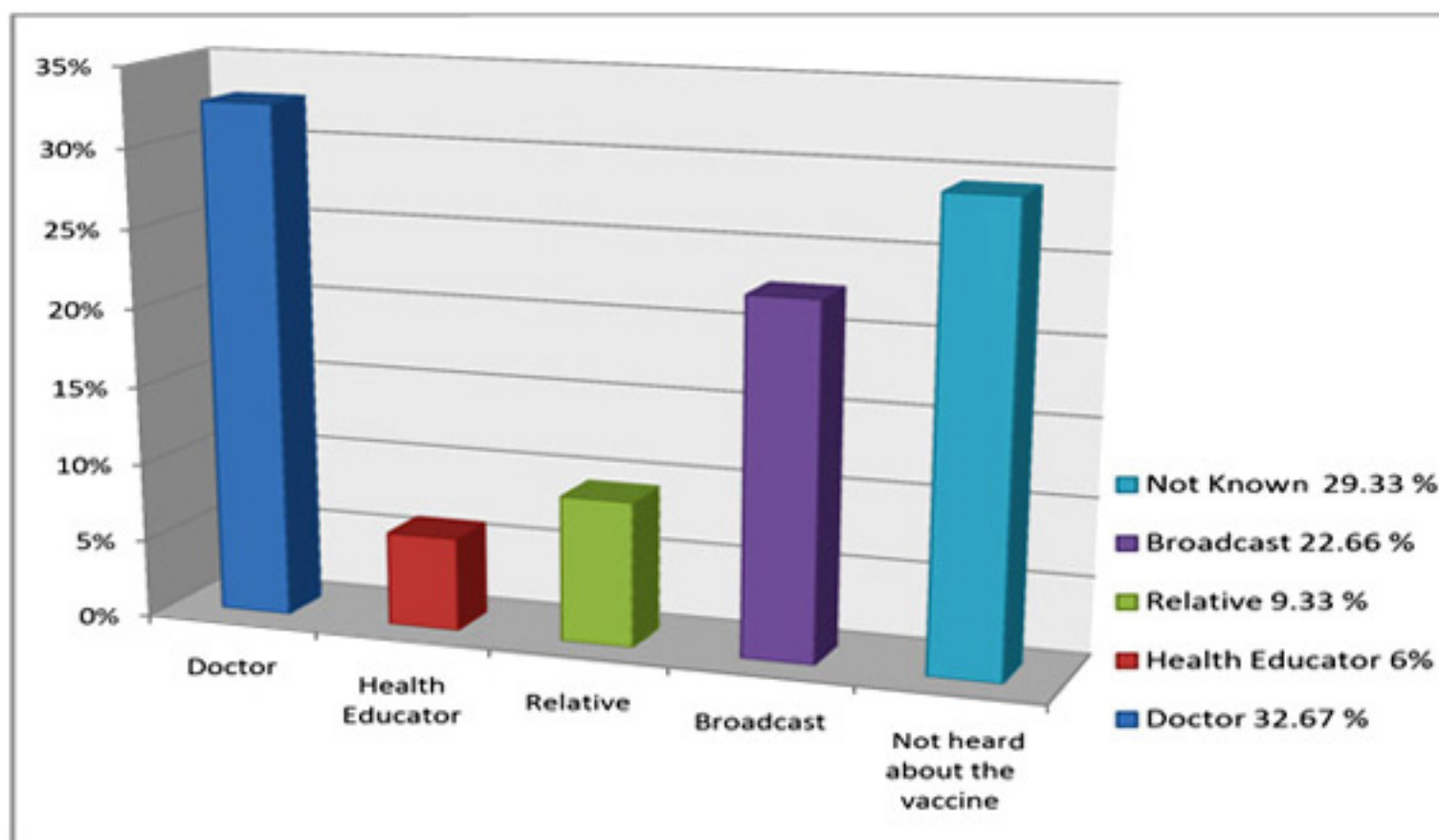


Figure 7: the distribution of the population of the study according to being advised to take the Influenza

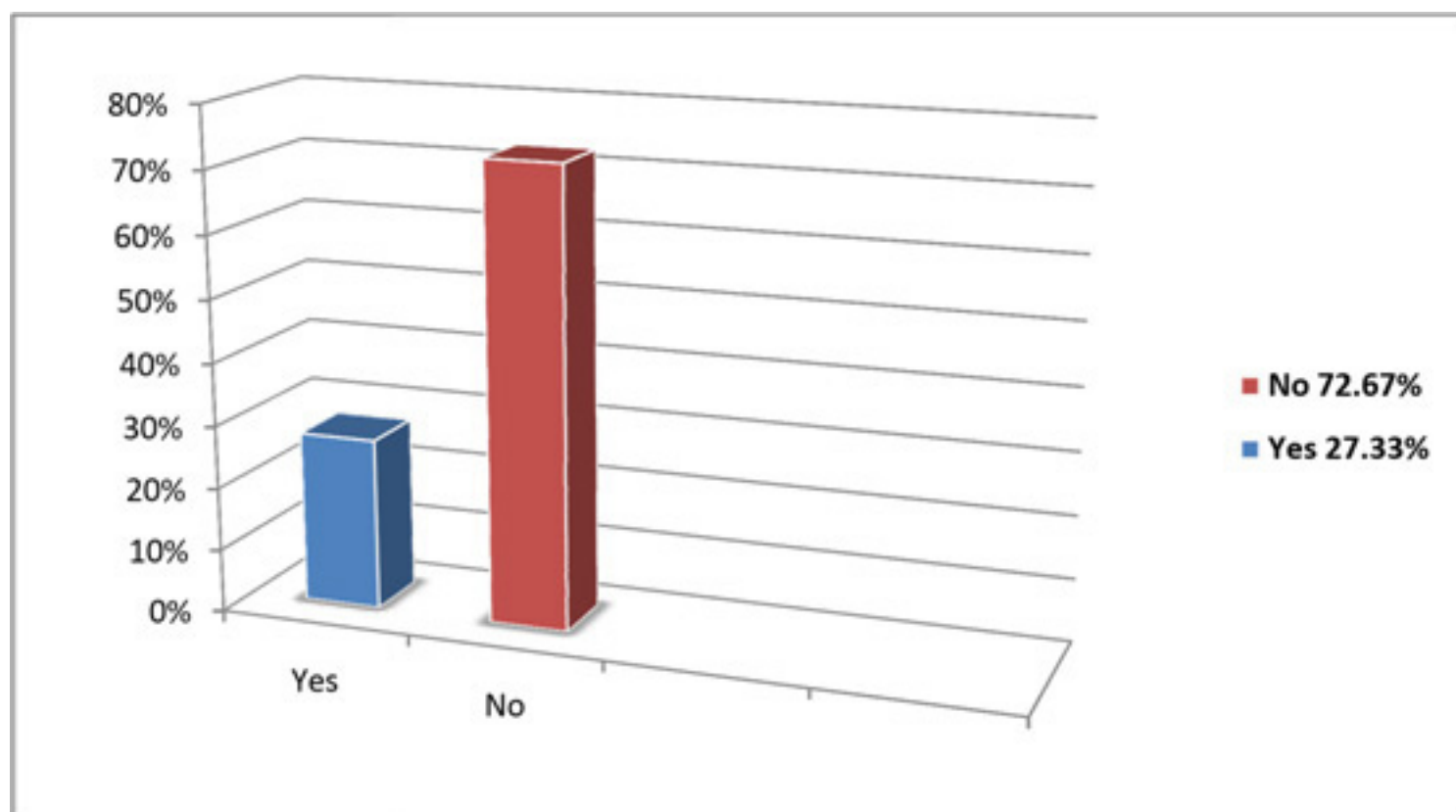


Figure 8: the distribution of the population of the study according to the last time of taking Influenza Vaccine

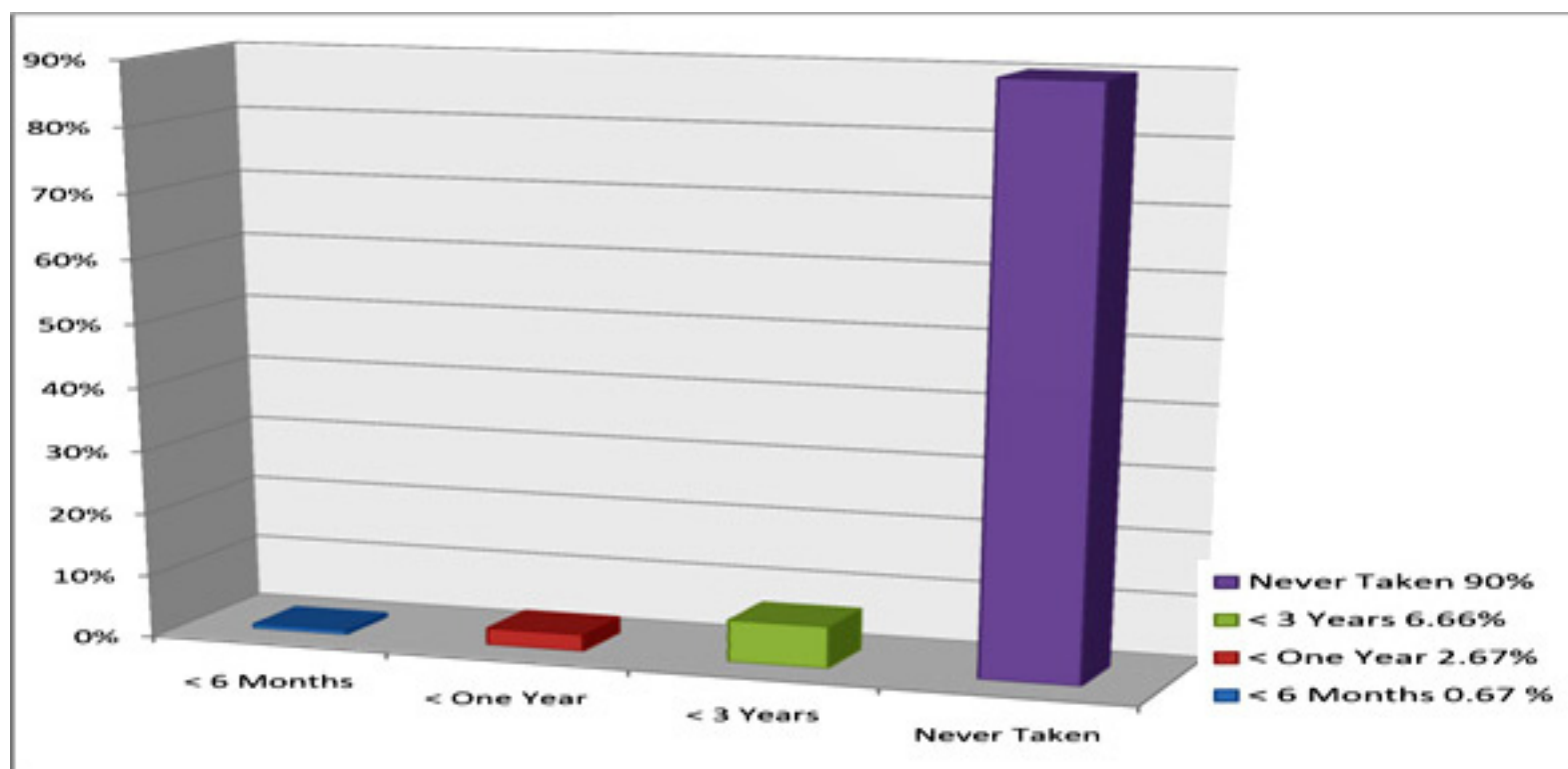


Figure 9: the distribution of the population of the study according to the benefit of taking the Influenza Vaccine

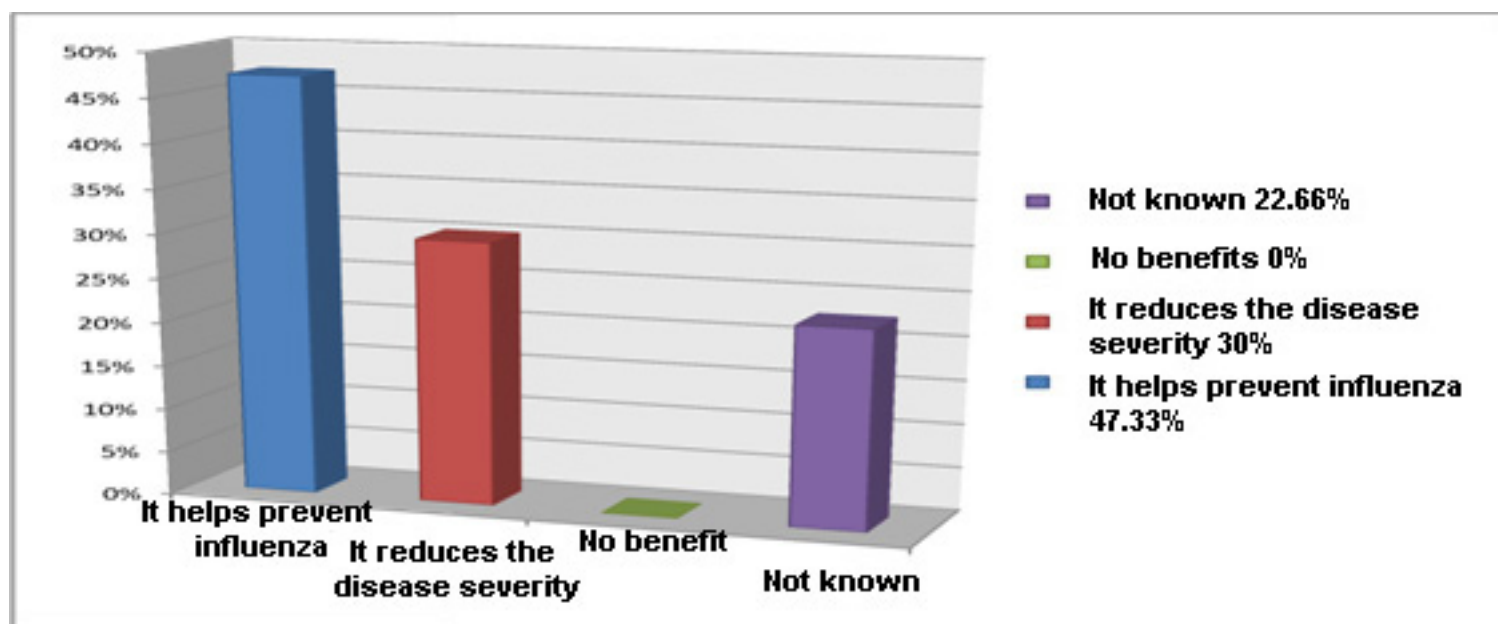


Figure 10: the distribution of the population of the study according to how frequently they take Influenza Vaccine.

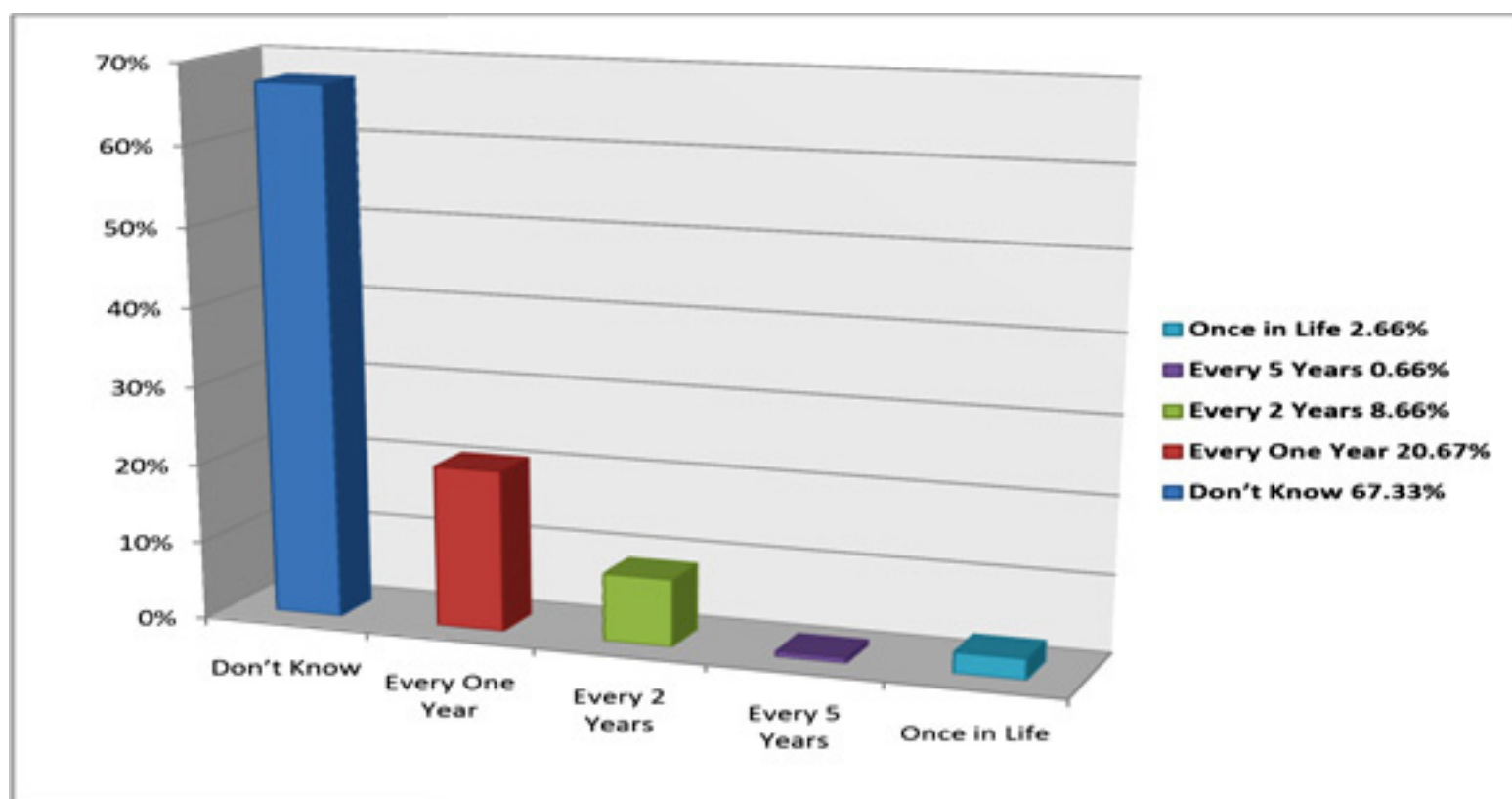


Figure 11: distribution of the population of the study according to Influenza Vaccine optimum time.

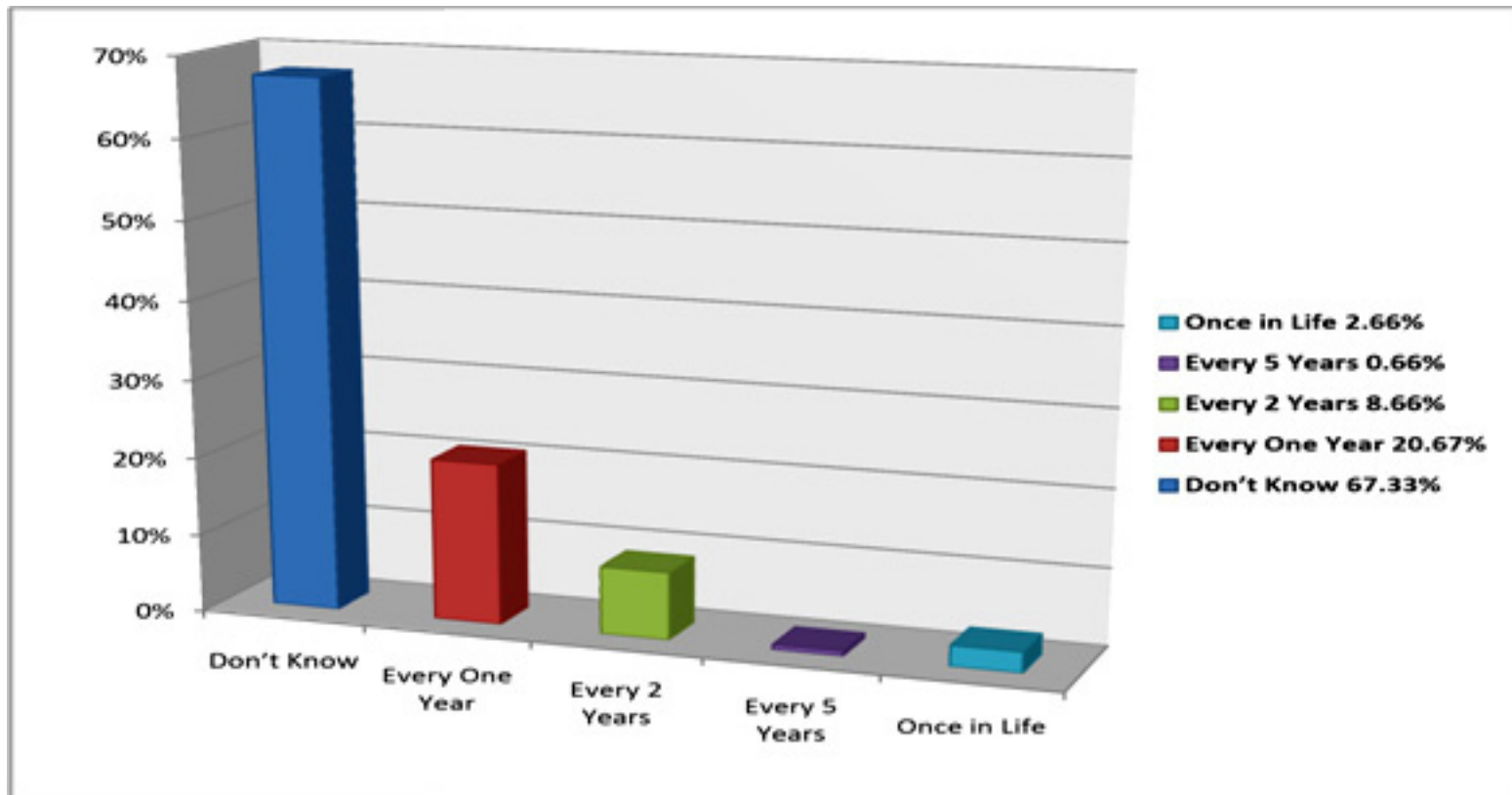


Figure 12: distribution of the population of the study according to the route of taking the Influenza Vaccine

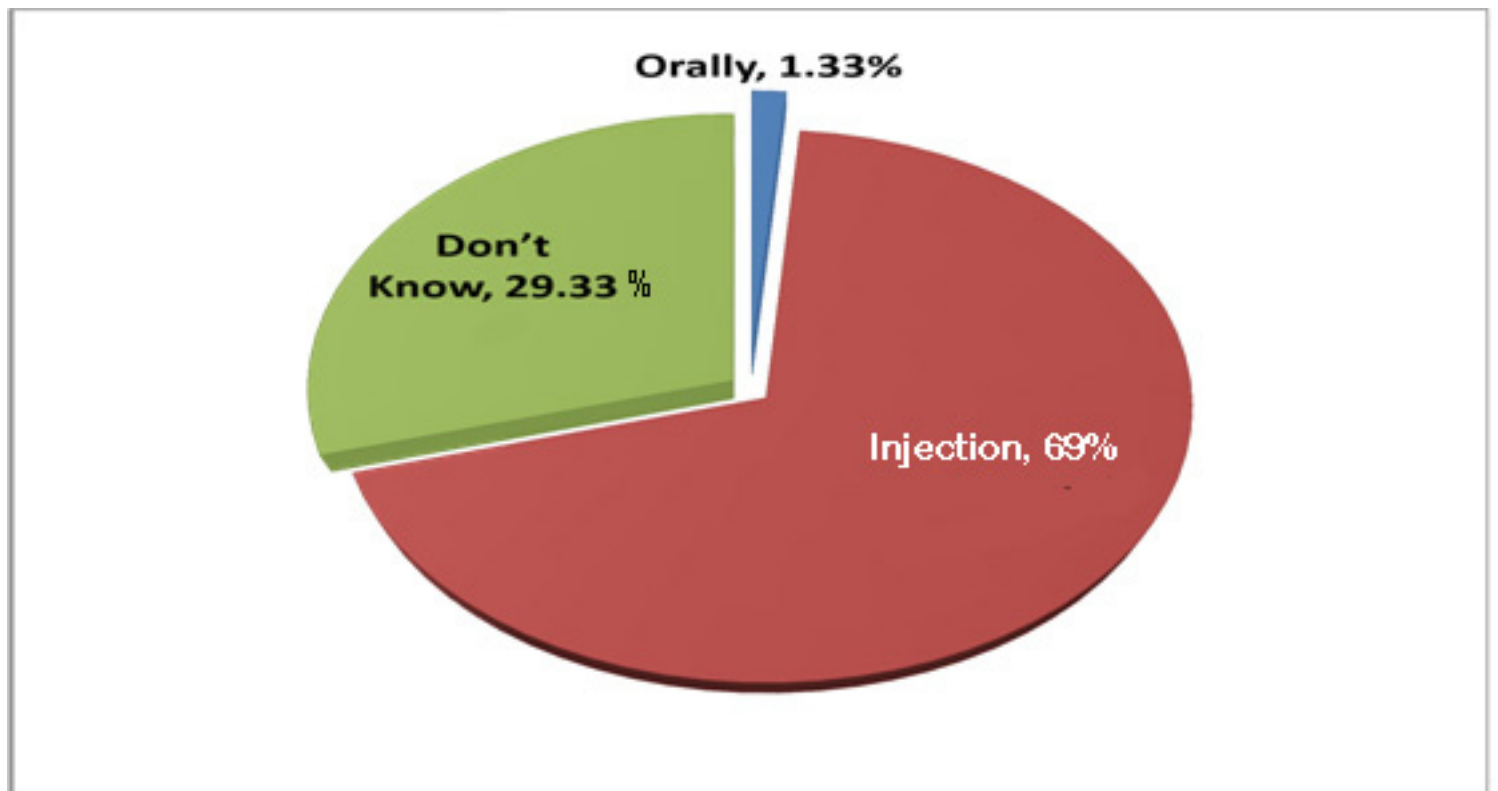


Figure 13: distribution of the population of the study according to reasons why not taking the Influenza Vaccine

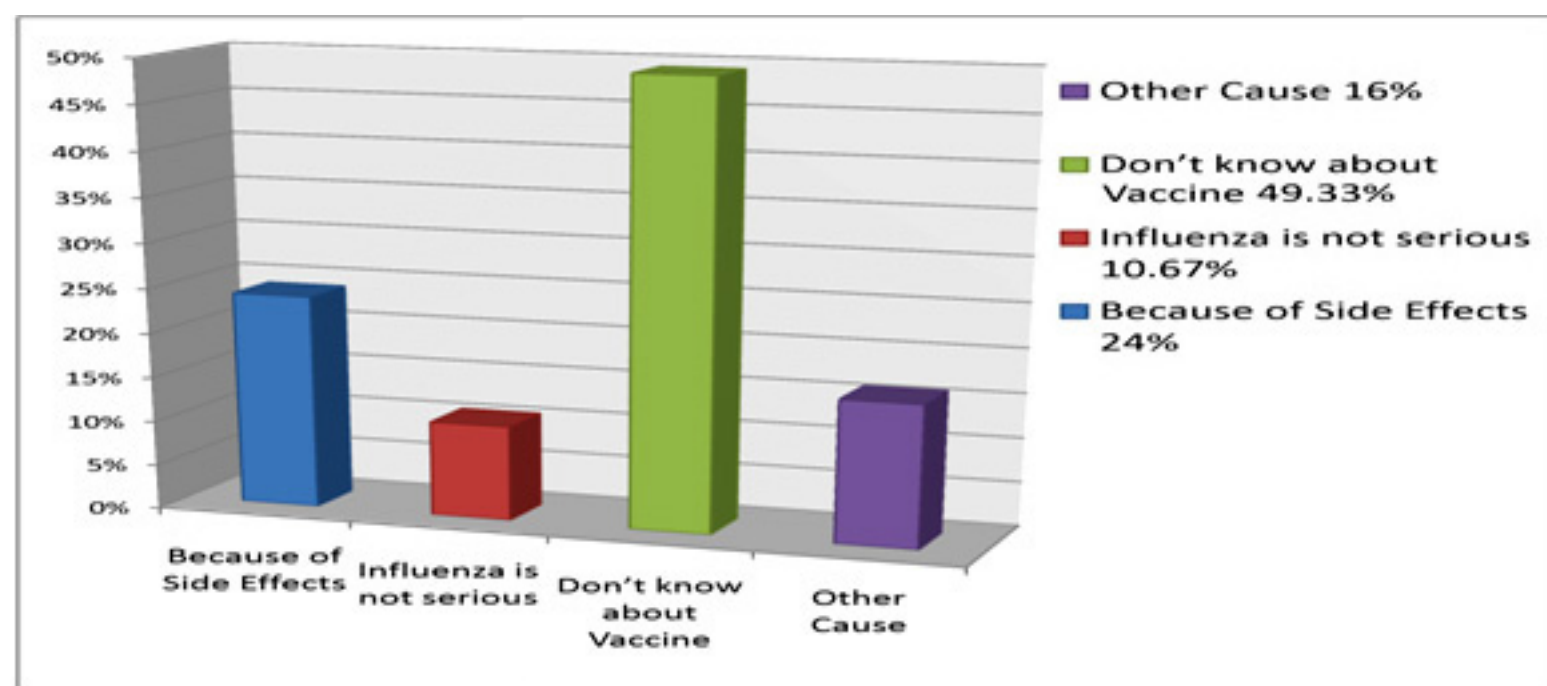


Table 1: distribution of the population of the study according to age.

Patient Age	Frequency	Percent	Valid Percent	Cumulative Percent
20-35	22	7.3	7.3	7.3
36-50	96	32	32	39.3
51-60	182	60.7	60.7	53.4
Total	300	100	100	100

Table 2 distribution of the population of the study according to the Level of Education.

Education	Frequency	Percent	Valid Percent	Cumulative Percent
HIGHER SEC	134	44.7	44.7	44.7
ILLITERATE	8	2.7	2.7	47.3
INTERMED	32	10.7	10.7	58
PRIMARY	46	15.3	15.3	73.3
UNIVERSITY	80	26.6	26.6	76.6
Total	300	100	100	300

Table 3: distribution of the population of the study according to doing follow up for Diabetes.

Follow Up	Frequency	Percent	Valid Percent	Cumulative Percent
NO	14	4.7	4.7	4.7
YES	286	95.3	95.3	95.3
Total	300	100	100	100

Table 5: distribution of the population of the study according to the relation between the duration of DM against advice to take the flu vaccine

Duration of DM	Advice		Total
	NO	YES	
1-5 Years	30	36	66
10-20 Years	57	0	57
20-30 Years	18	0	18
5-10 Years	80	0	80
< 1 Year	0	46	46
>20	22	0	22
>20	11	0	11
Total	218	82	300

a. 2 cells (14.3%) have an expected count of less than 5. The minimum expected count is 3.01.
Chi-Square Tests

	Value	df	Asymp. Sig. (2 sided)
Pearson Chi-square	217.614 ^a	6	.000
Chi-square Likelihood Ratio	260.978	6	.000
No. of Valid Cases	300		

Table 6: distribution of the population of the study according to the relation between sexes against advice to take the flu vaccine

Count	Advice		Total
	NO	YES	
Female	156	0	156
Male	62	82	144
Total	218	82	300

Table 7: distribution of the population of the study according to the frequency of flu illness against the last vaccination

Count of frequency of flu illness	Last vaccination				Total
	1	2	3	4	
1	2	8	20	58	88
2	0	0	0	102	102
3	0	0	0	84	84
4	0	0	0	26	26
10	2	8	20	270	300

a. 9 cells (56.3%) have an expected count of less than 5. The minimum expected count is .17
Chi-Square Tests

	Value	df	Asymp. Sig. (2 sided)
Pearson Chi-square	80.303 ^a	9	.000
Chi-square Likelihood Ratio	82.122	9	.000
N of Valid Cases	300		

Table 8: distribution of the population of the study according to the relation between the level of education against awareness or if they have heard about the flu vaccine

	N	Percent	N	Percent	N	Percent
Education Awareness	300	100	0	0	300	100

a. 1 cells (10.0%) have an expected count of less than 5. The minimum expected count is 2.77.

Chi-Square Tests

	Value	df	Asymp. Sig. (2 sided)
Pearson Chi-square	213.013 ^a	4	.000
Likelihood Ratio	261.246	4	.000
No. of Valid Cases	300		

Table 9: the distribution of the population of the study according to the relation between awareness sources about flu vaccine against the optimum time for vaccination

Awareness source *	300	100.0 %	0	.0%	300	100.0%
Time of vaccination						

a. 12 cells (60.0%) have an expected count of less than 5. The minimum expected count is .12.

Chi-Square Tests

	Value	df	Asymp. Sig. (2 sided)
Pearson Chi-square	100.664 ^a	12	.000
Likelihood Ratio	109.128	12	.000
No. of Valid Cases	300		

Discussion

Professional healthcare organizations must activate internal policies and provide educational and informational resources to support seasonal influenza immunization programs in general and for diabetic patients as an urgent need due to the rising number of diabetic patients.

Concerning the results propounded from our study, though 65.3% were aware and had heard about the flu vaccine only 10% were vaccinated which is among the lowest in the literature as shown in a study done in Singapore where those vaccinated were 30.6%, and another study done in three Middle East countries namely United Arab Emirates (UAE), Kuwait and Oman also show vaccination rate in Kuwait (67.2%), 46.4% in Oman and 24.7% in UAE. Also, there was a similar result to our study done in Slovakia concerning both populations having a good knowledge and awareness about the flu vaccine, but only 10% and 25% of the populations respectively take the seasonal flu shots. Also, another result propounded from our study is that most of the knowledge or awareness about the vaccine is from doctors 32, 6% and secondly from mass media 22.6%, where there should be a role for the health educators, which is deficient.

Hence the doctors leading a busy clinic find it difficult to cover education and advice for patients to be vaccinated against the flu in most occasions, where there is a major role for the health educators to give the message and follow the response aiming at the target in the global recommendations.

Even though the response rate was good the study has some limitations with respect to that the questionnaire assessed self-reported vaccination rate and are not based on chart review which may resulted in a biased, over-reported vaccination rate.

Conclusion

The purpose of this study was to describe the knowledge and practice of taking seasonal flu vaccine among diabetic patients where the study population was taken as a sample. Our study results show clearly that neither the knowledge nor the practice of taking the seasonal flu vaccine is enough to reduce the risk of morbidity and mortality encountered by influenza.

In our study the practice of taking the vaccine constitutes the lowest rate compared with other studies in the literature.

Recommendations

- It is recommended to enhance the knowledge about influenza vaccine esp., among diabetic patients who constitute of more than 20% of the population in Bahrain and almost the same percentage in the Gulf according to their huge number vaccination will lower the risk of a pandemic flu illness or at least the rate of the incidence of the disease will be reduced significantly.
- Targeting the CDC recommendations regulatory bodies must increase the awareness about flu vaccination by the use of the mass media, preparing training courses, educational programs, and vaccination campaigns about Flu vaccination, and activating the protocol for its usage in all the PHC centers.
- To introduce the knowledge about Flu in the schedule of the elementary and secondary level of education which should be supervised by the school health system with an important role for health educators.
- To increase diabetic patients' compliance with influenza vaccination, diabetic clinics and healthcare facilities should implement appropriate follow-up and reminder systems which would be successful and supposedly have a positive effect on increasing the rate of flu vaccinations.
- Also, it is mandatory, for family physicians, health educators, and PHW to provide education about this vaccine an important part of their daily practice.
- The idea of fixed or one vaccination for both hemispheres will be promising as it will aid international efforts and give more knowledge, confidence, and compliance to clients towards the flu vaccine

Dedication

I would like generously to give my dedication to those who have suffered with me all over the past years, Before Birth and since childhood, my beloved parents, and siblings.

And for my wife, 'who stands beside me, and supports me with all her love to complete this project in an honorable view.

My thanks extend to all those who devote themselves seek a new life full of pleasure and health.

Acknowledgments

I would like to express my sincere appreciation to the following people, who gave me support, encouragement and help during my study and research, to Dr. Nihal Thomas, Dr. Jachin Velavan, Dr. Jachin Danielraj and to all whom I did not mention in the DFID department; in Christian Medical College (CMC), Vellore, for their keen supervision, knowledge, advice, and guidance.

To my entire, participants' who were cooperative throughout the period of the study, and also to mention my appreciation to my colleagues; in (BDF) hospital for their collaboration and Help.

To Mr. Muhammad Usman Saleh and Mr. Ayoub for their precious technical experience in analysis and statistics

References

1. Couch, RB (2008). "Seasonal Inactivated Influenza Virus Vaccines. Vaccine. 26 Suppl 4 (Suppl 4): D5–9. doi:10.1016/j.vaccine.2008.05.076. PMC 2643340. PMID 18602728.
2. "Key Facts About Seasonal Flu Vaccine"
3. [No authors listed] (2011-09-09). "Who Should Get Vaccinated Against Influenza". U.S. Centers for Disease Control and Prevention. Retrieved 2013-04-07.
4. World Health Organization. Seasonal Influenza
5. Manzoli L, Ioannidis JP, Flacco ME, De Vito C, Villari P (July 2012). "Effectiveness and harms of seasonal and pandemic influenza vaccines in children, adults and elderly: a critical review and reanalysis of 15 meta-analyses". *Hum Vaccin Immunother* 8 (7): 851– 62. doi:10.4161/hv.19917. PMC 3495721. PMID 22777099.
6. ^pid=20601081&sid=aoDQn_PvtPGw&refer=Australia[verification needed]
7. McNeil, Donald G. Jr. (March 28, 2008). "A Multitude of Vaccine Benefits, Yet Controversy Persists,". *The New York Times*. "Public health experts generally agree that after clean water and flush toilets, the most important health advances in history have been vaccinations"
8. Center for Disease Control and Prevention. "Key Facts About Seasonal Flu Vaccine". Retrieved 7 February 2013.
9. WHO Influenza Overview
10. Kroger AT, Sumaya CV, Pickering LK, Atkinson WL. General recommendations on immunization -- recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. [Practice Guideline]. 2011 Jan 28;60(2):1-64.
11. Beigel, J. H. (2008). "Influenza". *Critical Care Medicine* 36 (9): 2660–2666. doi:10.1097/CCM.0b013e318180b039. PMC 3431208. PMID 18679129. edit
12. WHO Influenza Overview <http://www.who.int/mediacentre/factsheets/2003/fs211/en/>
13. "In the United States of America, for example, recent estimates put the cost of influenza epidemics to the economy at US\$ 71-167 billion per year."
14. Molinari NA, Ortega-Sanchez IR, Messonnier ML, et al. (June 2007). "The annual impact of seasonal influenza in the US: measuring disease burden and costs". *Vaccine* 25 (27): 5086–96. doi:10.1016/j.vaccine.2007.03.046. PMID 17544181. (Estimates that in the United States, annual influenza epidemics result in approximately 600,000 life-years lost, 3 million hospitalized days, and 30 million outpatient visits, resulting in direct medical costs of \$10 billion annually. Lost earnings due to illness and loss of life added over \$15 billion in direct costs annually and the average of all direct and indirect economic burdens of annual influenza epidemics (funeral expenses, lost productivity, etc.) amounts to over \$80 billion.
15. Fiore, AE; Uyeki, TM; Broder, K; Finelli, L; Euler, GL; Singleton, JA; Iskander, JK; Wortley, PM et al. (August 2010). "Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010". *MMWR Recomm Rep* 59 (RR–8): 1–62. PMID 20689501.

16. Fiore, AE; Shay, DK; Broder, K; Iskander, JK; Uyeki, TM; Mootrey, G; Bresee, JS; Cox, NJ et al. (2009). "Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009". *MMWR Recomm Rep* 58 (RR-8): 1–52.
17. Benowitz, I.; Esposito, D. B.; Gracey, K. D.; Shapiro, E. D.; Vázquez, M. (December 2010). "Influenza Vaccine Given to Pregnant Women Reduces Hospitalization Due to Influenza in Their Infants". *Clin Infect Dis* 51 (12): 1355–61. doi:10.1086/657309. PMC 3106242. PMID 21058908.
18. Lemaitre, M.; Meret, T.; Rothan-Tondeur, M.; Belmin, J.; Lejonc, J. L.; Luquel, L.; Piette, F.; Salom, M. et al. (September 2009). "Effect of influenza vaccination of nursing home staff on mortality of residents: a cluster-randomized trial". *Journal of the American Geriatrics Society* 57 (9): 1580–1586.
19. Burls, A.; Jordan, R.; Barton, P.; Olowokure, B.; Wake, B.; Albon, E.; Hawker, J. (2006). "Vaccinating healthcare workers against influenza to protect the vulnerable—Is it a good use of healthcare resources? A systematic review of the evidence and an economic evaluation". *Vaccine* 24 (19): 4212–4221. doi:10.1016/j.vaccine.2005.12.043. PMID 16546308. edit
20. Coverage in healthcare workers
20. "Influenza Vaccination Coverage Among Health-Care Personnel --- United States, 2010--11 Influenza Season". *Morbidity and Mortality Weekly Report (MMWR)*
21. "Influenza vaccination coverage among health-care personnel: 201112 influenza season, United States". *MMWR Morb. Mortal. Wkly. Rep.* 61 (38): 753–7. September 2012. ISSN 0149-2195. PMID 23013720.
22. CDC - Inactivated Influenza Vaccine 2007-2008 - What You Need To Know
23. Flu - LAIV
24. Gagnon, R; Primeau MN, Des Roches A, Lemire C, Kagan R, Carr S, Ouakki M, Benoît M, De Serres G (August 2010). "Safe vaccination of patients with egg allergy with an adjuvanted pandemic H1N1 vaccine.". *The Journal of Allergy and Clinical Immunology* 126 (2): 317–323. doi:10.1016/j.jaci.2010.05.037. PMID 20579720.
25. National Advisory Committee on Immunization (August 2012). "Statement on Seasonal Influenza Vaccine for 2012-2013". *Canadian Communicable Disease Report*
38. Retrieved 18 July 2013.
26. Offit PA (September 2007). "Thimerosal and vaccines—a cautionary tale" (PDF). *N Engl J Med* 357 (13): 1278–9. doi:10.1056/NEJMp078187. PMID 17898096.
27. Global Advisory Committee on Vaccine Safety (2006-07-14). "Thiomersal and vaccines". World Health Organization. Retrieved 2007-11-20.
28. Haber P, Sejvar J, Mikaeloff Y, DeStefano F (2009). "Vaccines and Guillain-Barré syndrome". *Drug Safety* 32 (4): 309–23. doi:10.2165/00002018-200932040-00005. PMID 19388722.
29. Kaplan JE, Katona P, Hurwitz ES, Schonberger LB (August 1982). "Guillain-Barré syndrome in the United States, 1979-1980 and 1980-1981. Lack of an association with influenza vaccination". *JAMA* 248 (6): 698–700. doi:10.1001/jama.248.6.698. PMID 7097920.
30. Denise Grady (December 4, 2009). "Review Shows Safety of H1N1 Vaccine, Officials Say". *The New York Times*. "No substantial differences between H1N1 and seasonal influenza vaccines were noted in the proportion or types of serious adverse events reported"
32. Stephenson, I.; Zambon, M. C.; Rudin, A.; Colegate, A.; Podda, A.; Bugarini, R.; Del Giudice, G.; Minutello, A. et al. (May 2006). "Phase I Evaluation of Intranasal Trivalent Inactivated Influenza Vaccine with Nontoxicogenic Escherichia coli Enterotoxin and Novel Biovector as Mucosal Adjuvants, Using Adult Volunteers". *J Virol* 80 (10): 4962–70. doi:10.1128/JVI.80.10.4962-4970.2006. PMC 1472052. PMID 16641287.
33. Treanor, J.; Kotloff, K.; Betts, R.; Belshe, R.; Newman, F.; Iacuzio, D.; Wittes, J.; Bryant, M. (December 1999). "Evaluation of trivalent, live, cold-adapted (CAIV-T) and inactivated (TIV) influenza vaccines in the prevention of virus infection and illness following challenge of adults with wild-type influenza A (H1N1), A (H3N2), and B viruses". *Vaccine* 18 (9–10): 899–906. doi:10.1016/S0264410X(99)00334-5. PMID 10580204.
34. Jefferson, T. (October 2006). "Influenza vaccination: policy versus evidence". *BMJ* 333 (7574): 912–5. doi:10.1136/bmj.38995.531701.80. PMC 1626345. PMID 17068038.
35. CDC - Influenza (Flu) | Q & A: 2007-08 Flu Season
36. Jefferson T, Rivetti A, Di Pietrantonj C, Demicheli V, Ferroni E (2012). "Vaccines for preventing influenza in healthy children". *Cochrane Database Syst Rev* 8: CD004879. doi:10.1002/14651858.CD004879.pub4. PMID 22895945.
37. Jefferson T, Di Pietrantonj C, Al-Ansary LA, Ferroni E, Thorning S, Thomas RE (2010). "Vaccines for preventing influenza in the elderly". *Cochrane Database Syst Rev* (2): CD004876. doi:10.1002/14651858.CD004876.pub3. PMID 20166072.
38. Jefferson T, Rivetti D, Rivetti A, Rudin M, Di Pietrantonj C, Demicheli V (2005). "Efficacy and effectiveness of influenza vaccines in elderly people: a systematic review". *Lancet* 366 (9492): 1165–74. doi:10.1016/S0140-6736(05)67339-4. PMID 16198765.
39. Nichol, K.L.; Nordin, J.D.; Nelson, D.B.; Mullooly, J.D.; Hak, E. (2007). "Effectiveness of Influenza Vaccine in the community-dwelling elderly". *The New England Journal of Medicine* 357 (14): 1373–1381. doi:10.1056/NEJMoa070844. PMID 17914038.
40. Vu, T.; Farish, S.; Jenkins, M.; Kelly, H. (2002). "A meta-analysis of the effectiveness of influenza vaccine in persons aged 65 years and over living in the community". *Vaccine* 20 (13–14): 1831–1836. doi:10.1016/S0264-410X(02)00041-5. PMID 11906772.

41. Nordin, J.; Mullooly, J.; Poblete, S.; Strikas, R.; Petrucci, R.; Wei, F.; Rush, B; Safirstein, B et al. (2001). "Influenza vaccine effectiveness in preventing hospitalizations and deaths in persons 65 years or older in Minnesota, New York, and Oregon: Data from 3 health plans". *The Journal of Infectious Diseases* 184 (6): 665–670. doi:10.1086/323085. PMID 11517426.
42. Simonsen L, Viboud C, Taylor RJ, Miller MA, Jackson L (October 2009). "Influenza vaccination and mortality benefits: new insights, new opportunities". *Vaccine* 27 (45): 6300–4. doi:10.1016/j.vaccine.2009.07.008. PMID 19840664.
43. Osterholm, MT; Kelley, NS; Sommer, A; Belongia, EA (2012). "Efficacy and effectiveness of influenza vaccines: A systematic review and meta-analysis". *The Lancet Infectious Diseases* 12 (1): 36–44. doi:10.1016/S1473-3099(11)70295-X. PMID 22032844. Also discussed in "Efficacy and Effectiveness of Influenza Vaccines: A Systematic Review and Meta-analysis". *JournalistsResource.org*, Retrieved February 2, 2012
44. <http://www.sciencebasedmedicine.org/index.php/high-dose-fluvaccine-for-the-elderly/>
45. Nuño, M.; Chowell, G.; Gumel, A. B. (June 2007). "Assessing the role of basic control measures, antivirals and vaccine in curtailing pandemic influenza: scenarios for the US, UK, and the Netherlands". *Journal of the Royal Society Interface* 4 (14): 505–521. doi:10.1098/rsif.2006.0186. PMC 2373400. PMID 17251132.
46. Ferguson, N. M.; Cummings, D. A.; Fraser, C.; Cajka, J. C.; Cooley, P. C.; Burke, D. S. (July 2006). "Strategies for mitigating an influenza pandemic". *Nature* 442 (7101): 448–452. Bibcode:2006Natur.442..448F. doi:10.1038/nature04795. PMID 16642006.
47. Simpson, CR; Ritchie, LD; Robertson, C; Sheikh, A; McMenamin, J (2012). "Effectiveness of H1N1 vaccine for the prevention of pandemic influenza in Scotland, UK: A retrospective observational cohort study". *The Lancet Infectious Diseases* 12 (9): 696–702. doi:10.1016/S1473-3099(12)70133-0. PMID 22738894.
48. Thompson WW, Shay DK, Weintraub E, Brammer L, Cox N, Anderson LJ, Fukuda K (2003). "Mortality associated with influenza and respiratory syncytial virus in the United States". *The Journal of the American Medical Association* 289 (2): 179–186. doi:10.1001/jama.289.2.179. PMID 12517228.
49. Thomas RE, Jefferson T, Lasserson TJ (2010). "Influenza vaccination for healthcare workers who work with the elderly". *Cochrane Database Syst Rev* (2): CD005187. doi:10.1002/14651858.CD005187.pub3. PMID 20166073.
50. New York Times: IDEAS & TRENDS; Flu, 1 December 1991. "Once infected with a strain of flu, people develop lifelong immunity to it." Example of earlier belief in lifelong immunity.]
51. McCullers JA, Van De Velde LA, Allison KJ, Branum KC, Webby RJ, Flynn PM (June 2010). "Vaccines against the 1976 "swine flu" have enhanced neutralization responses to the 2009 novel H1N1 influenza virus". *Clin. Infect. Dis.* 50 (11): 1487–92. doi:10.1086/652441. PMC 2946351. PMID 20415539.
52. Science News, Survivors of the 1918 flu pandemic are protected with a lifetime immunity to virus
53. Product Monograph: Flumist, Astrazeneca Canada Inc., 2011
54. immunize.org article Summary of Recommendations for Adult Immunization, which is linked from CDC website CDC
55. "The Nasal-Spray Flu Vaccine (Live Attenuated Influenza Vaccine [LAIV])" Centers for Disease Control and Prevention (CDC)
56. Thomas RE, Jefferson TO, Demicheli V, Rivetti D (2006). "Influenza vaccination for health-care workers who work with elderly people in institutions: a systematic review". *Lancet Infect Dis* 6 (5): 273–279. doi:10.1016/S1473-3099(06)70462-5. PMID 16631547.
57. Skowronski DM, De Serres G (2009). "Is routine influenza immunization warranted in early pregnancy?". *Vaccine* 27 (35): 4754–70. doi:10.1016/j.vaccine.2009.03.079. PMID 19515466.
58. Health Care Guideline: Routine Prenatal Care. Fourteenth Edition. By the Institute for Clinical Systems Improvement. July 2010.
59. CDC
60. Postma, M.J; Baltussen, R.P.M., Palache, A.M, Wilschut, J.C. (2006). "Further evidence for favorable cost-effectiveness of elderly influenza vaccination". *Expert Review of Pharmacoeconomics and Outcomes Research* 6 (2). doi:10.1586/14737167.6.2.215. PMID 20528557.
61. Newall, AT; Kelly, H; Harsley, S; Scuffham, PA (2009). "Cost Effectiveness of Influenza Vaccination in Older Adults". *PharmacoEconomics* 27 (6): 439–50. doi:10.2165/00019053200927060-00001. PMID 19640008.
62. Newall, AT; Viboud, C; Wood, JG (2009). "Influenza-attributable mortality in Australians aged more than 50 years: A comparison of different modeling approaches". *Epidemiology and Infection* 138 (6): 836–42. doi:10.1017/S095026880999118X. PMID 19941685.
63. Newall, A.T.; Scuffham, P.A (2011). "Uncertainty and variability in influenza cost-effectiveness models". *Australian and New Zealand Journal of Public Health* 35 (6). doi:10.1111/j.17536405.2011.00788.x. PMID 22151168.
64. Gatwood, J; Meltzer, MI; Messonnier, M; Ortega-Sanchez, IR; Balkrishnan, R; Prosser, LA (2012). "Seasonal Influenza Vaccination of Healthy Working-Age Adults". *Drugs* 72 (1): 35–48. doi:10.2165/11597310-000000000-00000. PMID 22191794.
65. Newall, A.T.; Wood, J.G., Oudin, N., MacIntyre, C.R. (2010). "Cost-effectiveness of pharmaceutical-based pandemic influenza mitigation strategies". *Emerging Infectious Diseases* 16 (2). doi:10.3201/eid1602.090571.
66. How it's made
67. New and Old Ways to Make Flu Vaccines, November 8, 2007, National Public Radio.
68. WHO: Influenza vaccine viruses and reagents

69. "Recommendations for the production and control of influenza vaccine (inactivated)". World Health Organization. Retrieved 27 May 2013.
70. MacDonald R, Baken L, Nelson A, Nichol KL: Validation of self-report of influenza and pneumococcal vaccination status in elderly outpatients. *Am J Prev Med* 16: 173–177, 1999
71. Singleton JA, Greby SM, Wooten KG, Walker FJ, Strikas R: Influenza, pneumococcal, and tetanus toxoid vaccination of adults: United States, 1993–7. *Mor Mortal Wkly Rep CDC SurveillSumm* 49:39–62, 2000
72. Kroneman MW, van Essen GA, Tacken MA, Paget WJ, Verheij R: Does a population survey provide reliable influenza vaccine uptake rates among high-risk groups? A case study of The Netherlands. *Vaccine* 22:2163–2170, 2004
73. PMID: 20848058 [PubMed - indexed for MEDLINE]
74. PMID: 15168869 [PubMed - indexed for MEDLINE]
75. PMID: 15654537 [PubMed - indexed for MEDLINE]
76. International Journal of Medical Sciences Ivy Spring International Publisher
77. [PubMed - indexed for MEDLINE])
78. FluMistQuadrivalent [Package Insert]. Gaithersburg, MD: MedImmune; 2013.

Appendix

Questionnaire for Diabetic Patients about Knowledge and Practice of Taking the Influenza Vaccine

1. AGE: > 20 YEARS () > 35 YEARS () > 50 YEARS ()
2. SEX: MALE () FEMALE ()
3. LEVEL OF EDUCATION:
ILLITERATE () PRIMARY SCHOOL () INTERMEDIATE () HIGHER SECONDARY SCHOOL ()
UNIVERSITY AND POSTGRADUATE ()
4. DURATION OF BEING A DIABETIC:
< 1 YEAR () < 5 YEARS () < 10 YEAR ()
10 TO 20 YEARS () > 20 YEARS ()
5. ARE YOU DOING F.U. FOR DIABETES? YES () NO ()
6. IS IT A REGULAR F.U? YES () NO ()
7. WHERE ARE YOU DOING F.U. FOR DIABETES?
GP-CLINIC BDFHOSPITAL () OTHER PHC () PRIVATE CLINIC ()
8. DID YOU HEAR ABOUT THE INFLUENZA VACCINE?
YES () NO ()
9. FROM WHERE DID YOU HEAR ABOUT THE INFLUENZA VACCINE?
DOCTOR () HEALTH EDUCATOR ()
RELATIVE () BROADCAST () NOT HEAR ABOUT THE VACCINE ()
10. DID ANYONE ADVISE YOU TO TAKE AN INFLUENZA VACCINE SINCE YOU BECAME DIABETIC? YES ()
NO ()
11. WHAT IS THE LAST TIME YOU TAKE INFLUENZA VACCINE?
< 6 MONTHS () < ONE YEAR () < 3 YEAR () NEVER TAKE IT ()
12. WHAT DO YOU THINK IS THE BENEFIT OF TAKING THE INFLUENZA VACCINE?
IT HELP PREVENT INFLUENZA () IT REDUCE THE DISEASE SEVERITY () NO BENEFIT
() not known to me ()
13. DO YOU KNOW HOW FREQUENTLY YOU HAVE TO TAKE THE SEASONAL INFLUENZA VACCINE?
Do not know () EVERY ONE YEAR () EVERY 2 YEARS () EVERY 5 YEARS () ONCE IN LIFE ()
14. YOU HAVE TO TAKE THE INFLUENZA VACCINE ON: OCTOBER () APRIL () JUNE ()
DO NOT KNOW ()
15. INFLUENZA VACCINE IS TO BE TAKEN:
ORALLY () INJECTION () DO NOT KNOW ()
16. HOW MANY TIMES HAVE YOU GOTTEN INFLUENZA-LIKE DISEASE DURING THE LAST
YEAR?
ONCE () 2- 3 TIMES () > 3TIMES () DID NOT GET FLU ON THE LAST EAR ()
17. IF YOU DID NOT TAKE THE INFLUENZA VACCINE, WHAT IS THE REASON FOR NOT TAKING IT?
BECAUSE OF SIDE EFFECTS () INFLUENZA IS NOT
SERIOUS () YOU DID NOT KNOW ABOUT THIS VACCINE () OTHER CAUSE ()

Review on Implementing Patient-Centered Care in Primary Health Practice in Qatar

Walaa Abdulmohsin

PHCC Qatar

Correspondence:

Dr. Walaa Abdulmohsin

PHCC Qatar

Email: Waabdulmohsin@phcc.gov.qa

Received: January 2024. Accepted: February 2024; Published: March 1, 2024.

Citation: Walaa Abdulmohsin. Review on Implementing Patient-Centered Care in Primary Health Practice in Qatar. World Family Medicine. March 2024; 22(3): 43-45. DOI: 10.5742/MEWFM.2024.95257625

Abstract

Patient-centered care is a critical component of health-care delivery, emphasizing the involvement of patients in their care and the consideration of their preferences and needs. In Qatar, a country dedicated to providing high-quality healthcare, the implementation of patient-centered care in primary health practices is of paramount importance. This literature review examines the existing literature on patient-centered care implementation in primary health practices in Qatar, focusing on strategies, challenges, and outcomes. The review underscores the significance of cultural considerations, patient engagement, provider training, health information technology integration, quality improvement initiatives, multidisciplinary collaboration, and care coordination. Findings highlight the need for cultural competency training, effective communication, shared decision-making, provider education, health information technology integration, patient feedback mechanisms, multidisciplinary teamwork, and patient involvement in quality improvement efforts. While limited research specifically focuses on Qatar, international evidence supports the positive outcomes of patient-centered care, including improved patient satisfaction, treatment adherence, health outcomes, and potentially reduced healthcare costs. Further research is needed to evaluate the outcomes and impacts of implementing patient-centered care in primary health practices in Qatar and develop tailored guidelines and strategies for successful implementation.

Keywords: Patient centered care, Primary health practice, Qatar

Introduction

Early in its formation, the FMAHealth Board recognized the importance of including a patient advocate voice on the board to inform policy decisions (Stollenwerk et al., 2019). Patient-centered care is a fundamental aspect of healthcare delivery that places the patient at the center of their care and is a core principle in healthcare that focuses on involving patients as active participants in their care, considering their values, preferences, and needs. In Qatar, a country that is committed to providing high-quality healthcare services, implementing patient-centered care in primary health care settings is crucial. This literature review examines the existing literature on the implementation of patient-centered care in primary healthcare settings in Qatar, exploring key strategies, challenges, and outcomes.

Methods

A comprehensive search was conducted using electronic databases, including PubMed, Medline, and Google Scholar, to identify relevant articles published in English between 2013 and 2023. The Studies and review articles focusing specifically on patient-centered care in primary health practices in Qatar were included in this review.

Key words: “patient-centered care,” “primary health care,” “Qatar,” “implementation,” and related keywords.

Results

Strategies for Implementing Patient-Centered Care:

In addition to adding a patient representative to the board and in pursuit of obtaining a greater understanding of how best to approach transformation of primary care delivery to promote patient-centeredness, the board also created and charged an Engagement Tactic Team with two primary objectives:

1. To engage patients as partners in transforming primary care practices and the health care system at large in order to enhance the patient experience, improve community health, and reduce costs; and
2. To strengthen working alliances with other primary care professions and other stakeholders in order help all speak with a unified voice for primary care (Stollenwerk et al., 2019).

Several strategies have been proposed to promote patient-centered care in Qatar. These include improving healthcare provider communication skills, fostering a collaborative and empathetic patient-provider relationship, involving patients in decision-making through shared decision-making approaches, and integrating patient perspectives into quality improvement initiatives. Features implemented to demonstrate PFCC in Qatar's health centers include access to a physician whenever required, and automated confirmation of an appointment to hospital outpatients by Short Message Service (SMS) (Verjee & Robertson-Malt, 2013).

1. Cultural Considerations:

Patient-centered care cultural transformation is a complex and long-term endeavor (Bokhour et al., 2018). Qatar has a diverse population with varying cultural backgrounds. Implementing patient-centered care requires understanding and respecting cultural values, beliefs, and preferences. Studies emphasize the importance of cultural competency training for healthcare providers to effectively communicate and provide care that aligns with patients' cultural expectations.

2. Patient Engagement and Shared Decision-Making:

Such signs orienting both staff and patients to the innovations driving PCC cultural change were present throughout the facility (Bokhour et al., 2018). Patient engagement and shared decision-making are fundamental to patient-centered care. Studies in Qatar highlight the importance of empowering patients to actively participate in their healthcare decisions. Strategies such as friends of the health center, effective communication, patient education, and decision aids are identified as effective tools for facilitating shared decision-making in primary health practices.

3. Provider Training and Education:

It was critical that staff see PCC as essential to care, not as another fleeting VA initiative (Bokhour et al., 2018). Healthcare provider training and education play a crucial role in implementing patient-centered care. Studies underscore the need for training programs that enhance communication skills, empathy, cultural competency, and shared decision-making among healthcare providers in Qatar. Continuing education programs and workshops are recommended to support providers in delivering patient-centered care.

4. Health Information Technology (HIT) Integration:

The abrupt onset of the coronavirus disease 2019 (COVID-19) pandemic required a rapid implementation of telemedicine—the synchronous delivery of health care in an audio-plus-video or audio-only modality—in primary care (Rabinowitz et al., 2023). The integration of health information technology (HIT) can support patient-centered care in primary health practices. Studies highlight the importance of implementing electronic health records (EHRs), patient portals, and telemedicine platforms in Qatar. Unique benefits of telemedicine over in-person visits, ranging from reduced concerns regarding transmission of infections to improved access for patients with limited mobility (Rabinowitz et al., 2023). HIT integration can improve communication, enhance care coordination, and facilitate patient access to medical information by My health mobile application or Sehaty.

5. Quality Improvement Initiatives:

Quality improvement initiatives are essential for implementing patient-centered care. Capturing the patients' voices, obtaining patient perspectives, and finding out what matters most to patients and families were essential to selecting, planning, and implementing PCC initiatives (Bokhour et al., 2018). Studies emphasize the need for collecting patient feedback, conducting

patient satisfaction surveys, and involving patients in quality improvement efforts in primary health practices in Qatar. Feedback mechanisms and patient engagement in quality improvement initiatives contribute to the delivery of patient-centered care.

6. Multidisciplinary Collaboration and Care Coordination:

Collaboration with other people-centered organizations such as government ministries, academic institutions, and civil society associations locally, regionally and internationally, will raise awareness of PFCC (Verjee & Robertson-Malt, 2013). Patient-centered care necessitates collaboration among healthcare professionals in primary health practices. Studies in Qatar highlight the importance of multidisciplinary teamwork and care coordination to provide comprehensive and coordinated care. Effective communication channels, regular team meetings, and care planning are identified as facilitators of patient-centered care.

7. Recognizing the Outcomes and Impacts:

Limited studies directly investigating the outcomes and impacts of implementing patient-centered care in primary health practices in Qatar were found. However, international evidence suggests that patient-centered care leads to improved patient satisfaction, better adherence to treatment plans, enhanced health outcomes, and potentially reduced healthcare costs and improved healthcare provider-patient relationships.

Conclusion

The literature on implementing patient-centered care in primary health practices in Qatar highlights the significance of cultural considerations, patient engagement, provider training, health information technology integration, quality improvement initiatives, multidisciplinary collaboration, and care coordination. It also highlights the conceptual framework, benefits, and strategies for implementing patient-centered care in clinical practice. By embracing patient-centered care principles, Qatar can enhance the patient experience, improve health outcomes, and strengthen its primary health care system to meet the evolving needs of its diverse population.

While there is limited research specifically focusing on Qatar, the existing evidence underscores the importance of these factors in delivering patient-centered care. Further research is needed to evaluate the outcomes and impacts of implementing patient-centered care in primary health practices in Qatar and to develop tailored guidelines and strategies for successful implementation.

References

- Bokhour, B. G., Fix, G. M., Mueller, N. M., Barker, A. M., LaVela, S. L., Hill, J. N., Solomon, J. L., & Lukas, C. V. (2018). How can healthcare organizations implement patient-centered care? Examining a large-scale cultural transformation. *BMC Health Services Research*, 18(1). <https://doi.org/10.1186/s12913-018-2949-5>
- Rabinowitz, G., Cho, L. D., Benda, N. C., Goytia, C., Andreadis, K., Lin, J. J., Horowitz, C., Kaushal, R., Ancker, J. S., & Poeran, J. (2023). The telemedicine experience in primary care practices in the United States: Insights from practice leaders. *Annals of Family Medicine*, 21(3), 207–212. <https://doi.org/10.1370/afm.2967>
- Stollenwerk, D., Kennedy, L. B., Hughes, L. S., & O'Connor, M. (2019). A systematic approach to understanding and implementing patient-centered care. *Family Medicine*, 51(2), 173–178. <https://doi.org/10.22454/FamMed.2019.320829>
- Verjee, M. A., & Robertson-Malt, S. (2013). Patient- and family-centered care in Qatar: A primary care perspective. *Avicenna*, 2013(1). <https://doi.org/10.5339/avi.2013.1>

Graves Eye Disease Medical and Surgical Management: A Review

Yazeed Alshahrani ¹, Abdullah Jallwi Korkoman ¹, Fahad Saud M Alremthi ¹,
Hdinan Mohammed J Alsadi ², Abdulaziz Braik Saleh AlQarni ³, Ahmed Abdullah Ahmed Alghamdi ¹,
Abdullah Hassan F Alsuayri ⁴, Abdullah Awon A Alsalooli ¹, Nawaf Saeed O Alshahrani ⁵

(1) Resident, King Abdullah Hospital, Bisha, Saudi Arabia

(2) Internal medicine resident, King Fahad armed force hospital, Khamis Mushait, Saudi Arabia

(3) Medical intern, University of Bisha, College of Medicine, Bisha, Saudi Arabia

(4) Internal medicine resident, Prince Sultan medical city, Riyadh, Saudi Arabia

(5) Internal medicine resident, King Fahad Medical City, Riyadh

Corresponding author:

Dr. Yazeed Alshahrani

Resident, King Abdullah Hospital, Bisha,
Saudi Arabia

Email: dr.yazeed.fahad@gmail.com

Received: January 2024. Accepted: February 2024; Published: March 1, 2024.

Citation: Yazeed Alshahrani et al. Graves Eye Disease Medical and Surgical Management: A Review. World Family Medicine. March 2024; 22(3): 46-51. DOI: 10.5742/MEWFM.2024.95257626

Abstract

Graves' disease (GD) is the most frequent cause of hyperthyroidism, where iodine levels are abundant.

One of the extrathyroidal symptoms is Graves' ophthalmopathy (GO) which presents with ophthalmic symptoms that can range from minor (e.g., dry eye) to sight-threatening (e.g., corneal ulceration and compressive optic neuropathy) features.

About 79% of Graves' disease cases can be attributed to genetic predispositions, while the remaining 21% are due to environmental factors. Acute stress, active or passive smoking, and past radioactive iodine therapy have all been linked to the development or aggravation of thyroid eye disease (TED).

The devastating effects of GO or TED might include diplopia, ocular hypertension, optic nerve degeneration, and glaucoma.

A low basal serum Thyroid Stimulating hormone (TSH) level has the highest sensitivity and specificity for diagnosing hyperthyroidism. Moreover, the appearance

of Thyroid Stimulating hormone receptors (TSHR) autoantibodies (TRAbs) is presumed to be highly specific for the diagnosis of Graves' disease.

Imaging studies of the orbit that use ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI), for example, can confirm the diagnosis of TED.

In order to treat Graves's eye disease optimally, a multidisciplinary approach must be applied involving primary care physicians, ophthalmologists, internists and endocrinologists. Therefore, it is essential to restore the euthyroid state and this can be obtained by either antithyroid medications, radioactive iodine or surgical thyroidectomy.

Treatment of GO ranges from supportive treatment (lubricants and moisturizer drops), to medical intervention, preferably corticosteroid, and variable surgical interventions.

Key words: Graves' disease,
Medical and surgical management

List of abbreviations:

GD: Graves disease

TED: thyroid eye disease

GO: Graves ophthalmopathy

TSH: thyroid stimulating hormone

TSHR: thyroid stimulating hormone receptors

TRAbs: Thyroid receptors autoantibodies

CT: computed tomography

MRI: magnetic resonance imaging

RAI: radioactive iodine

ATD: Antithyroid drugs

HLA: human leukocyte antigen

Introduction

Graves' disease (GD) is the most frequent cause of hyperthyroidism, where iodine levels are abundant. The existence of antibodies against the TSH receptor is termed TSH receptor antibodies (TRAb) [1]. The incidence of GD is approximately 40/100,000 per year [2]. Women are more likely than men to have GD, and individuals aged between 30 and 50 years are most commonly affected. Extrathyroidal symptoms such as Graves' ophthalmopathy (GO), thyroid dermopathy, and acropachy may also be present in addition to hyperthyroidism [3].

The development of this autoimmune illness is influenced by both genetic and environmental factors. Antithyroid drugs (ATDs) are the mainstay of medical treatment for GD [4,5]. However, thyroid ablation, either thyroidectomy or radioiodine (RAI) treatment, is necessary in around half of cases due to the high recurrence rate of hyperthyroidism. The devastating effects of GO or thyroid eye disease (TED) might include diplopia, ocular hypertension, optic nerve degeneration, and glaucoma. A patient's quality of life may be negatively impacted by even mild TED [7]. Although TED is more common in younger women, studies suggest that men and older people are at a higher risk of developing this serious illness [8]. Those with unstable thyroid function or specific anatomical features of the orbit, such as a larger lateral orbital wall angle, are also more likely to develop TED [9]. Acute stress, active or passive smoking, and past radioactive iodine therapy have all been linked to the development or aggravation of TED [10,11].

The current review article aims to summarize recent advances in our understanding of the pathophysiology of GD and clinical considerations for diagnosing, prognosticating, and treating GD patients [6].

Methodology

A review of the literature was performed to find scholarly publications about TED through a systematic web search. Multiple keywords, including epidemiology, etiology, pathophysiology, clinical features, diagnosis, medical and surgical interventions of TED, were used to search in research databases Google Scholar and PubMed. Among 84 articles retrieved (published between 1988 and 2021), 48 articles were included in the study. Articles were excluded if they are not directly linked to the research topic. Duplicates were also removed after the final retrieving process.

The Review of Literature

Graves' Disease Epidemiology

Graves' disease is the leading cause of hyperthyroidism. Many studies have examined the incidence of hyperthyroidism, but only a few assessed Graves' disease as a cause of hyperthyroidism. Graves' disease is caused by an immune system malfunction, which fights diseases

in the body. About 79% of Graves' disease cases can be attributed to genetic predispositions, while the remaining 21% are due to environmental factors [12]. Common environmental risk factors include vitamin D and selenium deficiency, smoking, and changes in iodine levels. The depletion of iodine in the body can significantly increase its incidence, but the long-term changes in iodine level are not considered a risk factor. It is also believed that stress and pregnancy may increase the risk of developing Graves' disease [12].

Statistics indicate that Graves' disease affects about 40 in every 100,000 people yearly, with an estimated prevalence of 0.4%. However, these statistics are from the retrogressive analysis of available medical records. Hence, these figures may be underestimated and not representative, as patients with mild symptoms are often undiagnosed. The prevalence of Graves' disease is higher in women than men. Its prevalence in the United States was about 0.4% in the 1970s. A United States survey found Graves' disease to be more common among Caucasians than other races [13]. Research conducted in the United Kingdom showed a prevalence rate of about 1.1% to 1.6%. As far as demographics are concerned, people can be affected at any age, but its prevalence is higher between the ages of 30 and 50 years.

The prevalence of Graves' disease is fairly evenly distributed across the globe; however, its incidence is higher in areas with rich iodine consumption, such as India. A recent population study in India indicated that 16.7% of the population suffered from Graves' disease, with those with metabolic syndrome accounting for more than 40%. The same study also indicated that the prevalence was higher in women than in men [14].

Epidemiology of Thyroid Eye Disease (TED)

Graves' ophthalmopathy is a complex inflammation disease of the orbit. Most patients with TED have a biochemical indication of hyperthyroidism, with Graves' disease being the most common. Thyroid eye disease affects about 16 in 100,000 people among women and 3 in 100,000 men, with an average prevalence of about 0.25% [15]. There is no defined ethnic predisposition of TED. The high incidence of TED among women can be attributed to the higher incidence of hyperthyroidism disease among women; however, the disease severity is more pronounced among men [15].

Common risk factors of TED include the female gender, smoking, young age, and hyperthyroidism. The treatment of hyperthyroidism using radioiodine is also a risk factor. The presence of other autoimmune thyroid illnesses can account for up to 15% of the total TED diseases; however, genetic factors are the main risk factors, especially for people with susceptibility alleles [15]. TED usually manifests itself at the beginning of hyperthyroidism and could take five years of treatment. A significantly small proportion of patients have no history of hyperthyroidism. Research shows a decrease in the prevalence in the last two decades, but little justification exists [16]. It is challenging

to determine the definitive prevalence of the TED disease due to insufficient data. However, a study conducted in Olmstead County in the United States showed a bimodal peak for men and women aged between 40 and 44 years and 60 and 64 years. The same study also indicated that about 50% of the patients with Graves' disease have clinically apparent TED [17].

More than 66% of the patients will experience TED either six months before the onset of thyroid disease, or thyroid dysfunction. The natural history of TED consists of two phases; the active inflammatory stage and the static stage. The active inflammatory stage is the first phase; the static stage follows. Only about 5% of TED patients have a late reactivation. Despite TED having no ethical depositions, people of Asian origin tend to have mild manifestations compared to Caucasians [18].

Pathophysiology of GD and GO:

It is widely acknowledged that GD has a substantial hereditary component, with genetic factors playing a key role. Several investigations have established that the main genes causing GD include human leukocyte antigen (HLA), CD40, CTLA-4, PTPN22, Tg, and TSHR. On chromosome 6, the HLA complex contains sequences that code for genes important in controlling the immune response [6]. The involvement of the central tolerance, which is impacted by the production of self-antigens (such as TSHR) within the thymus for negative selection of autoreactive T cell clones, is another factor in the genesis and pathophysiology of GD. Polymorphisms of certain tissue-restricted genes that encode autoantigenes might affect their degree of expression in the thymus, becoming a risk factor for autoimmunity [19,20].

As a component of GD, Graves' ophthalmopathy (GO, often referred to as Graves' orbitopathy) is an autoimmune inflammatory disorder [21]. There are several risk factors for GD-related GO. GO is more prevalent in women than men, and the risk of developing severe GO seems to be higher in males with GD [22]. Moreover, there are ethnic disparities in the frequency of GO, with Asians being less likely than Caucasians to contract the disease [23]. Moreover, the aforementioned hereditary variables are relevant, and smoking is a significant additional risk factor [24]. The activation of autoantibodies to thyroid stimulating hormone (TSH, thyrotropin) receptors (TSHR) appears to be the triggering event in thyroid eye disease, despite the complex underlying molecular mechanisms [25,26]. TSHR is overexpressed in the retrobulbar tissue of Graves' and hyperthyroidism patients compared to controls, especially in orbital fibroblasts, which are crucial to the pathophysiology of thyroid eye disease [21,25,27,28].

Orbital fibroblasts multiply and produce pro-inflammatory cytokines and hydrophilic hyaluronan in the interstitial space when activated [21,25,27]. These mechanisms cause a high osmotic pressure gradient in the orbit, causing greater fluid collection between the muscle fibers. Moreover, some orbital fibroblasts develop into mature adipocytes, resulting in orbital adipose tissue growth [26–28]. This cycle continues, and orbital congestion may result

[21,27]. Long-lasting edema causes fibrosis, sclerosis, and the extraocular muscles to atrophy, resulting in restricted strabismus [29].

Clinical Features

Clinical symptoms are linked to both the autoimmune and hyperthyroidism processes. The signs and symptoms of GD can vary greatly and significantly impact general health since excess thyroid hormones affect many different body systems. Tremors, heat sensitivity and warmth, weight loss despite regular eating habits, anxiety and irritability, goiter, and changes in menstrual cycles are common symptoms [30]. Ophthalmic symptoms can range from minor (e.g., dry eye) to sight-threatening (e.g., corneal ulceration and compressive optic neuropathy) problems, and treatment can range from supportive (e.g., lubrication of the ocular surface) to surgical (e.g., orbital decompression) approaches. Due to various clinical presentations, various disorders, such as allergic conjunctivitis and orbital tumors, are included in the differential diagnosis [31].

The devastating effects of GO and TED might include diplopia, ocular hypertension, optic nerve degeneration, and glaucoma [7]. Lid retraction, proptosis, soft tissue edema, strabismus, and compressive optic neuropathy are some of the clinical signs and symptoms of GO. The globe is pushed forward by the enlarged soft tissues inside the bony orbit, which also prevents venous outflow from the orbit. The adipogenesis and glycosaminoglycan buildup that follows the local fibroblasts' activation due to inflammation, causes enlarged soft tissues. Furthermore, lymphocyte infiltration and tissue remodeling are seen in the GD orbital symptoms, which might lead to fibrosis [32].

Diagnosing Graves' Disease

A low basal serum TSH level has the highest sensitivity and specificity for diagnosing hyperthyroidism and should, therefore, be used as an initial screening parameter. However, if Graves' disease is strongly suspected, diagnostic accuracy improves when serum TSH, free T4, and free T3 are also assessed [33]. Moreover, the appearance of TSHR autoantibodies (TRAbs) is presumed to be highly specific for the diagnosis of Graves' disease. Therefore, the diagnosis is usually confirmed by demonstrating elevated TRAbs [34].

Imaging studies of the orbit that use ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI), for example, can confirm the diagnosis of TED while excluding other diagnoses such as orbital tumor and idiopathic orbital inflammation (previously known as orbital pseudotumor). Computerized tomography without contrast remains the standard radiographic technique because of its ability to display the bony anatomy of the orbit and its low cost relative to MRI [35].

In ultrasound research, Graves' disease is usually characterized by hypoechoic and heterogeneous parenchyma, diffusely enlarged, and hypervascularity. In

contrast, Technetium-99 (99Tc) scanning of the thyroid is limited in diagnosing GD due to the high sensitivity and specificity of TRAb measurement [36,37].

Diagnosing Graves' Ophthalmopathy

The diagnosis of TED is straightforward based on the clinical history and physical examination of patients. Ophthalmic manifestations are present in up to 50% of Graves' hyperthyroidism patients [25]. TED follows a biphasic course: a progressive or active phase lasting up to three years, followed by a stable or inactive phase [26]. Ophthalmic manifestations can vary from mild (for example, dry eye) to sight-threatening (for example, corneal ulceration and compressive optic neuropathy) problems.

There is no single clinical finding or laboratory test that can diagnose TED. Frequently, the presenting symptoms are non-specific dry eye complaints, such as foreign body sensation, redness, blurring of vision, photophobia, glare, or excessive tearing [3,21]. However, there are many additional symptoms, including concern about cosmesis, retrobulbar discomfort, swelling of the eyelids worse in the morning, diplopia, and uncommon loss of vision [38, 39]. Common clinical signs are upper eyelid retraction, conjunctival and caruncle injection and/or edema, eyelid edema and/or erythema with diurnal variation, ocular motility disruption, or strabismus and proptosis [38,40]. Paradoxically, upper eyelid ptosis can also be a presenting sign of TED [41]. The clinical evaluation for TED focuses on determining clinical activity and severity by assessing visual acuity, pupils, color vision, extraocular movements, visual field, exophthalmometry, external eyelid evaluation, slit-lamp examination, and dilated fundus examination.

Medical and surgical treatment of Graves eye disease

Managing thyroid disease:

In order to treat Graves's eye disease optimally, a multidisciplinary approach must be applied involving primary care physicians, ophthalmologists, internists and endocrinologists [42, 43]. Therefore, it is essential to restore the euthyroid state and this can be obtained by either antithyroid medications, radioactive iodine or surgical thyroidectomy[40]. Some reports have shown that Radioactive iodine may result in the development or aggravation of thyroid eye disease by 15-20% in those who are smokers [44]. These adverse effects could be minimized by using oral corticosteroids post-radioactive iodine [43,45]. Smoking is a known risk factor for the progression of thyroid eye diseases [46,11]. Smoking cessation is considered one of the most important modifiable risk factors in the prevention of thyroid eye disease [47]. Therefore, it is advised for the patient with thyroid disease to stop smoking [42,48].

Graves eye disease treatment

Supportive treatment:

Some mild cases of graves eye diseases can be managed conservatively, for patients with dry eye manifestation, lubricants and moisturizer drops could be used [26]. Sunglasses are recommended to minimize photosensitivity and glare. For eyelids retraction, botulinum toxin injections could be used on the levator palpebrae superioris and Muller's muscles [31].

Medical treatment:

For patients with moderate to severe Graves' eye disease, corticosteroid is the mainstay treatment option. Almost 80% of patients on high intravenous corticosteroid show improvement in their condition in comparison to oral steroid which is less effective and with more side effects [31]. An immunosuppressive agent such as rituximab has shown some potential in the treatment of thyroid eye disease. However, some studies reported conflicting results [31]. Selenium supplementation has been shown to have the potential to improve the quality of life and reduces the severity and progression of thyroid eye disease [31].

Surgical treatment

When there is a significant impact on visual function or quality of life, individuals with moderate-to-severe inactive thyroid eye disease may consider surgical rehabilitation [42, 31]. In general, orbital decompression is done first, then extraocular muscle surgery, and finally eyelid procedures are done while treating inactive thyroid eye illness [26].

Several methods of orbital bone decompression and the amount of removed orbital walls have been researched. One approach hasn't proven itself to be better than the others up to this point [26].

For the purpose of reducing proptosis and improving diplopia, orbital fat decompression can be done either in conjunction with bone decompression or on its own [31]. Temporary tarsorrhaphy can be used to treat exposure keratopathy while waiting for orbital decompression [26]. In order to maintain enough corneal covering, eyelid surgery is only done for symptomatic eyelid retraction or asymmetric lid position [26].

Complications of thyroid eye diseases

Thyroid eye disease may lead to diplopia, ocular hypertension, glaucoma and optic nerve damage. Even mild thyroid eye disease could have a significant effect on the patient's quality of life [7].

Conclusion

Graves' disease is a common condition that can be associated with ocular manifestations that range from mild symptoms like dry eye to severe ones like corneal ulceration and compression to optic disc. Presentation in the eye could be devastating to the patient hence affecting the quality of life. Management of TED can range from medical options to a variety of surgical interventions. Therefore, healthcare providers must be aware of its clinical presentations and treatment modalities.

References

- 1- Bartalena L, Chiovato L, Vitti P. Management of hyperthyroidism due to Graves' disease: frequently asked questions and answers (if any). *Journal of endocrinological investigation*. 2016 Oct;39:1105-14
- 2- Weetman AP. Graves' Disease 1835–2002. *Hormone Research in Paediatrics*. 2003;59(Suppl. 1):114-8.
- 3-Bartalena L, Fatourechi V. Extrathyroidal manifestations of Graves' disease: a 2014 update. *Journal of endocrinological investigation*. 2014 Aug;37:691-700.
- 4-Burch HB, Cooper DS. Management of Graves disease: a review. *Jama*. 2015 Dec 15;314(23):2544-54.
- 5-Marinò M, Latrofa F, Menconi F, Chiovato L, Vitti P. An update on the medical treatment of Graves' hyperthyroidism. *Journal of Endocrinological Investigation*. 2014 Nov;37:1041-8.
- 6-Ehlers M, Schott M, Allelein S. Graves, disease in clinical perspective. *Frontiers in Bioscience-Landmark*. 2019 Jan 1;24(1):33-45.
- 7-Choi YJ, Lim HT, Lee SJ, Lee SY, Yoon JS. Assessing Graves' ophthalmopathy-specific quality of life in Korean patients. *Eye*. 2012 Apr;26(4):544-51.
- 8-Kendler DL, Lippa J, Rootman J. The initial clinical characteristics of Graves' orbitopathy vary with age and sex. *Archives of ophthalmology*. 1993 Feb 1;111(2):197-201.
- 9-Stan MN, Bahn RS. Risk factors for development or deterioration of Graves' ophthalmopathy. *Thyroid*. 2010 Jul 1;20(7):777-83.
- 10-Traisk F, Tallstedt L, Abraham-Nordling M, Andersson T, Berg G, Calissendorff J, Hallengren B, Hedner P, Lantz M, Nystrom E, Ponjavic V. Thyroid-associated ophthalmopathy after treatment for Graves' hyperthyroidism with antithyroid drugs or iodine-131. *The Journal of Clinical Endocrinology & Metabolism*. 2009 Oct 1;94(10):3700-7.
- 11- Vestergaard P. Smoking and thyroid disorders—a meta-analysis. *European Journal of Endocrinology*. 2002 Feb;146(2):153-61.
- 12- Smith, T. J., & Hegedüs, L. (2016). Graves' disease. *New England Journal of Medicine*, 375(16), 1552-1565.
- 13- Antonelli, A., Ferrari, S. M., Ragusa, F., Elia, G., Paparo, S. R., Ruffilli, I., ... & Fallahi, P. (2020). Graves' disease: Epidemiology, genetic and environmental risk factors and viruses. *Best Practice & Research Clinical Endocrinology & Metabolism*, 34(1), 101387.
- 14- Wémeau, J. L., Klein, M., Sadoul, J. L., Briet, C., & Vélayoudom-Céphise, F. L. (2018, December). Graves' disease: introduction, epidemiology, endogenous and environmental pathogenic factors. In *Annales d'endocrinologie* (Vol. 79, No. 6, pp. 599-607). Elsevier Masson.
- 15- Chin, Y. H., Ng, C. H., Lee, M. H., Koh, J. W. H., Kiew, J., Yang, S. P., ... & Khoo, C. M. (2020). Prevalence of thyroid eye disease in Graves' disease: A meta-analysis and systematic review. *Clinical endocrinology*, 93(4), 363-374.
- 16- Hiromatsu, Y., Eguchi, H., Tani, J., Kasaoka, M., & Teshima, Y. (2014). Graves' ophthalmopathy: epidemiology and natural history. *Internal Medicine*, 53(5), 353-360.
- 17- Lazarus, J. H. (2012). Epidemiology of Graves' orbitopathy (GO) and relationship with thyroid disease. *Best Practice & Research Clinical Endocrinology & Metabolism*, 26(3), 273-279.
- 18- Debnam, J. M., Koka, K., & Esmaeli, B. (2021). Extrathyroidal manifestations of thyroid disease: graves eye disease. *Neuroimaging Clinics*, 31(3), 367-378.
- 19- Colobran R, Armengol Mdel P, Faner R, Gärtner M, Tykocinski LO, Lucas A, Ruiz M, Juan M, Kyewski B, Pujol-Borrell R. Association of an SNP with intrathymic transcription of TSHR and Graves' disease: a role for defective thymic tolerance. *Hum Mol Genet*. 2011 Sep 1;20(17):3415-23. doi: 10.1093/hmg/ddr247. Epub 2011 Jun 3. PMID: 21642385.
- 20- Stefan M, Wei C, Lombardi A, Li CW, Concepcion ES, Inabnet WB 3rd, Owen R, Zhang W, Tomer Y. Genetic-epigenetic dysregulation of thymic TSH receptor gene expression triggers thyroid autoimmunity. *Proc Natl Acad Sci U S A*. 2014 Aug 26;111(34):12562-7. doi: 10.1073/pnas.1408821111. Epub 2014 Aug 13. PMID: 25122677; PMCID: PMC4151767.
- 21- Bahn RS. Graves' ophthalmopathy. *N Engl J Med*. 2010 Feb 25;362(8):726-38. doi: 10.1056/NEJMra0905750. PMID: 20181974; PMCID: PMC3902010.
- 22- Burch HB, Wartofsky L. Graves' ophthalmopathy: current concepts regarding pathogenesis and management. *Endocr Rev*. 1993 Dec;14(6):747-93. doi: 10.1210/edrv-14-6-747. PMID: 8119236.
- 23- Tellez M, Cooper J, Edmonds C. Graves' ophthalmopathy in relation to cigarette smoking and ethnic origin. *Clin Endocrinol (Oxf)*. 1992 Mar;36(3):291-4. doi: 10.1111/j.1365-2265.1992.tb01445.x. PMID: 1563082.
- 24- Wiersinga WM, Bartalena L. Epidemiology and prevention of Graves' ophthalmopathy. *Thyroid*. 2002 Oct;12(10):855-60. doi: 10.1089/105072502761016476. PMID: 12487767.
- 25- Douglas RS, Gupta S. The pathophysiology of thyroid eye disease: implications for immunotherapy. *Curr Opin Ophthalmol*. 2011 Sep;22(5):385-90. doi: 10.1097/ICU.0b013e3283499446. PMID: 21730841; PMCID: PMC3512192.
- 26- Stan MN, Garrity JA, Bahn RS. The evaluation and treatment of graves ophthalmopathy. *Med Clin North Am*. 2012 Mar;96(2):311-28. doi: 10.1016/j.mcna.2012.01.014. Epub 2012 Feb 22. PMID: 22443978; PMCID: PMC3898790.
- 27- Shan SJ, Douglas RS. The pathophysiology of thyroid eye disease. *J Neuroophthalmol*. 2014 Jun;34(2):177-85. doi: 10.1097/WNO.000000000000132. PMID: 24821101.

- 28- Papageorgiou KI, Hwang CJ, Chang SH, Jarullazada I, Chokron Garneau H, Ang MJ, King AJ, Mancini R, Douglas RS, Goldberg RA. Thyroid-associated periorbitopathy: eyebrow fat and soft tissue expansion in patients with thyroid-associated orbitopathy. *Arch Ophthalmol*. 2012 Mar;130(3):319-28. doi: 10.1001/archophthalmol.2011.1271. PMID: 22411661.
- 29- Barrio-Barrio J, Sabater AL, Bonet-Farriol E, Velázquez-Villoria Á, Galofré JC. Graves' Ophthalmopathy: VISA versus EUGOGO Classification, Assessment, and Management. *J Ophthalmol*. 2015;2015:249125. doi: 10.1155/2015/249125. Epub 2015 Aug 17. PMID: 26351570; PMCID: PMC4553342.
- 30- Antonelli A, Fallahi P, Elia G, Ragusa F, Paparo SR, Ruffilli I, Patrizio A, Gonnella D, Giusti C, Virili C, Centanni M. Graves' disease: Clinical manifestations, immune pathogenesis (cytokines and chemokines) and therapy. *Best Practice & Research Clinical Endocrinology & Metabolism*. 2020 Jan 1;34(1):101388.
- 31- Weiler DL. Thyroid eye disease: a review. *Clinical and experimental optometry*. 2017 Jan 1;100(1):20-5.
- 32- Li H, Wang T. The autoimmunity in Graves's disease. *Front Biosci (Landmark Ed)*. 2013 Jan 1;18:782-792.
- 33- Edith T, Starich GH, Mazzaferri EL. Sensitivity, specificity, and cost-effectiveness of the sensitive thyrotropin assay in the diagnosis of thyroid disease in ambulatory patients. *Archives of internal medicine*. 1989 Mar 1;149(3):526-32.
- 34- Furmaniak J, Sanders J, Miguel RN, Smith BR. Mechanisms of action of TSHR autoantibodies. *Hormone and Metabolic Research*. 2015 Sep;47(10):735-52.
- 35- Bradley EA. Graves ophthalmopathy. *Current Opinion in Ophthalmology*. 2001 Oct 1;12(5):347-51.
- 36- Ralls PW, Mayekawa DS, Lee KP, Colletti PM, Radin DR, Boswell WD, Halls JM. Color-flow Doppler sonography in Graves disease: "thyroid inferno". *American Journal of Roentgenology*. 1988 Apr 1;150(4):781-4.
- 37- Ruchała M, Szczepanek E. Thyroid ultrasound-a piece of cake? *Endokrynologia Polska*. 2010;61(3):330-44.
- 38- Dolman PJ. Evaluating Graves' orbitopathy. *Best Pract Res Clin Endocrinol Metabol* 2012; 26: 229–248.
- 39- Dolman PJ, Rootman J. VISA Classification for Graves orbitopathy. *Ophthal Plast Reconstruct Surg* 2006; 22: 319–324.
- 40- Menconi F, Marcocci C, Marino M. Diagnosis and classification of Graves' disease. *Autoimmun Rev* 2014; 13: 398–402.
- 41- Scruggs RT, Black EH. Thyroid eye disease with significant levator involvement and ptosis: a case report. *Ophthal Plast Reconstruct Surg* 2015; 31: e153-e154.
- 42- Bartalena L, Baldeschi L, Boboridis K et al. The 2016 European Thyroid Association/European Group on Graves' Orbitopathy Guidelines for the Management of Graves' Orbitopathy. *Eur Thyroid J* 2016; 5: 9–26.
- 43- Bhatti MT, Dutton JJ. Thyroid eye disease: therapy in the active phase. *J Neuroophthalmol* 2014; 34: 186–197.
- 44- Bartalena L. Diagnosis and management of Graves disease: a global overview. *Nat Rev Endocrinol* 2013; 9: 724–734.
- 45- Bartalena L. Diagnosis and management of Graves disease: a global overview. *Nat Rev Endocrinol* 2013; 9: 724–734.
- 46- Bartalena L, Marcocci C, Bogazzi F et al. Relation between therapy for hyperthyroidism and the course of Graves' ophthalmopathy. *New Engl J Med* 1998; 338: 73–78.
- 47- Thornton J, Kelly SP, Harrison RA et al. Cigarette smoking and thyroid eye disease: a systematic review. *Eye (Lond)* 2007; 21: 1135–1145.
- 48- Bartalena L. Prevention of Graves' ophthalmopathy. *Best Pract Res Clin Endocrinol Metab* 2012; 26: 371–379.

Fibromyalgia : A review

Yasir Al-Athari ¹, Mina Mahawish ²

(1) First author, M.B.Ch.B. , MRCGP UK, GP UK

(2) Second author, MPharm UK, Clinical Pharmacist NHS UK

Corresponding author:

Dr Yasir Al-Athari

Email: Yasir.alathari@gmail.com

Received: January 2024. Accepted: February 2024; Published: March 1, 2024.

Citation: Yasir Al-Athari, Mina Mahawish. Fibromyalgia : A review. World Family Medicine. March 2024; 22(3): 52-56.

DOI: 10.5742/MEWFM.2024.95257627

Abstract

This paper reviews guidelines of fibromyalgia. Fibromyalgia is a common medical condition which is still misdiagnosed with other rheumatological disorders. It can be complex and brings many challenges. Presentation can vary from patient to patient. It is estimated that around up to 5% of population may have fibromyalgia with more cases in women. Although there is no cure for this condition, more understanding of Fibromyalgia can contribute to a well-rounded effective treatment and therapy options via a multidisciplinary approach to help in relieving the symptoms.

Keywords : fibromyalgia, challenges, multidisciplinary approach, therapy, rheumatological disorders.

Definitions and epidemiology

Fibromyalgia is a medical condition presenting with widespread musculoskeletal pain, tiredness, poor sleeping patterns and tenderness in different points in the body (1). It can be associated with other symptoms such as headaches, brain fog and increased sensitivity to sensations such as light, noise, temperature and touch (2). The cause is still unclear and undiagnosed with a high number of patients. There is no evidence of muscle inflammation and it is thought to be a disorder of pain processing (3). The prevalence of fibromyalgia is more in females than males and the percentage can be increased by age. The number of consultations of fibromyalgia is increasing over time due to increased public awareness (4).

Aetiology

There is still no clear aetiology found that can cause fibromyalgia but some theories suggest there could be factors contributing in developing fibromyalgia such as:

- Genetic factors: this can run in families which can increase risk of fibromyalgia (5).
- Change in pain perception and threshold: Abnormal pain processing in the nervous system and hypersensitivity. However, the mechanism is still not clear. It seems that pain in fibromyalgia can mimic neuropathic pain and analgesia can be ineffective (6).
- Poor sleeping patterns which can affect healing process of muscles.
- Patients with history of rheumatic disorders such as arthritis, rheumatoid arthritis and ankylosing spondylitis.
- Triggers such as physical injuries, infections and emotional trauma.
- Mental health illnesses such as depression.

Symptoms of fibromyalgia

(see Figure 1):

- Widespread pain which can vary in intensity. It can be worse in certain areas such as back and neck. It can flare up and get worse at various times.
- Fatigue.
- Poor sleeping pattern and may not feel refreshed after sleeping all night.
- Headache, dizziness, forgetfulness and poor concentration.
- Achiness and stiffness.
- Stress, anxiety and low mood.
- Constipation, diarrhoea or stomach cramps. It can be diagnosed as Irritable Bowel Syndrome IBS.
- Irritable or overactive bladder.

Diagnosis

Diagnosis of fibromyalgia remains challenging due to the absence of definitive biochemical markers or imaging studies (8). However, physicians rely on the patient's reported symptoms by taking a detailed medical history and clinical assessment. The subjective nature of pain perception can make the diagnostic process complicated. The second challenge is that fibromyalgia shares symptoms with other medical conditions such as hypothyroidism, ankylosing spondylitis, systemic lupus erythematosus SLE, rheumatoid arthritis, multiple sclerosis, sleep apnea, chronic fatigue syndrome, depression and medications (high dose opioids, statins, letrozole). The diagnostic approach involves ruling out other medical conditions via tests such as urine, blood tests includes (FBC, ESR, CRP, CK, LFT, TFT, Glucose, U&E), x-rays and other scans. The American College of Rheumatology (ACR) has set up a criteria for fibromyalgia diagnosis (See Figure 2). This criteria included identifying duration and sites of pain with associated symptoms then giving a total score to aid diagnosis. Patients play an important aspect of diagnostic approach. Effective communication with patients can help build a full picture. Also, a symptoms diary can be very effective in tracking patterns to make a diagnosis.

Fibromyalgia is a common condition in primary care. However, it may need a holistic approach and involve other specialties when there is doubt in diagnosis, such as rheumatologists, pain management team and neurologists.

Figure 1 – Symptoms of fibromyalgia (7)

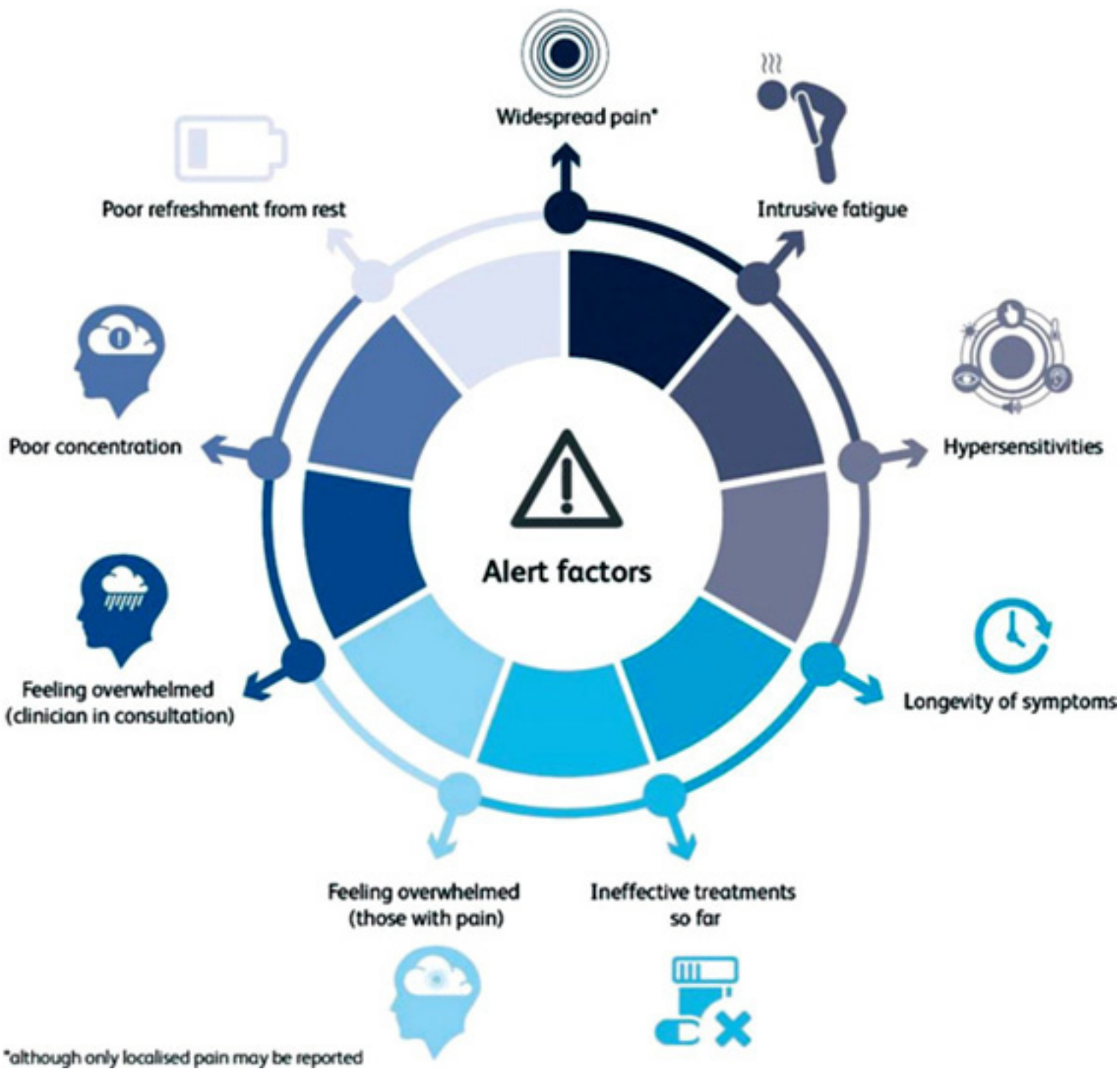


Figure 2 – Fibromyalgia diagnostic worksheet (7)

Fibromyalgia syndrome diagnostic worksheet

Symptom severity index (SSI)

Have your problems with the symptoms below been present for 3 months or more?

☐ Yes

☐ No

If yes, using the following scale, indicate the severity of each symptom over the past week by circling the appropriate number.

	No problem	Mild	Moderate	Severe
Fatigue	0	1	2	3
Trouble thinking or remembering	0	1	2	3
Waking up tired (unrefreshed)	0	1	2	3

During the past 6 months, have you had any of the following symptoms?

Pain or cramps in lower abdomen

☐ Yes

☐ No

Depression

☐ Yes

☐ No

Headache

☐ Yes

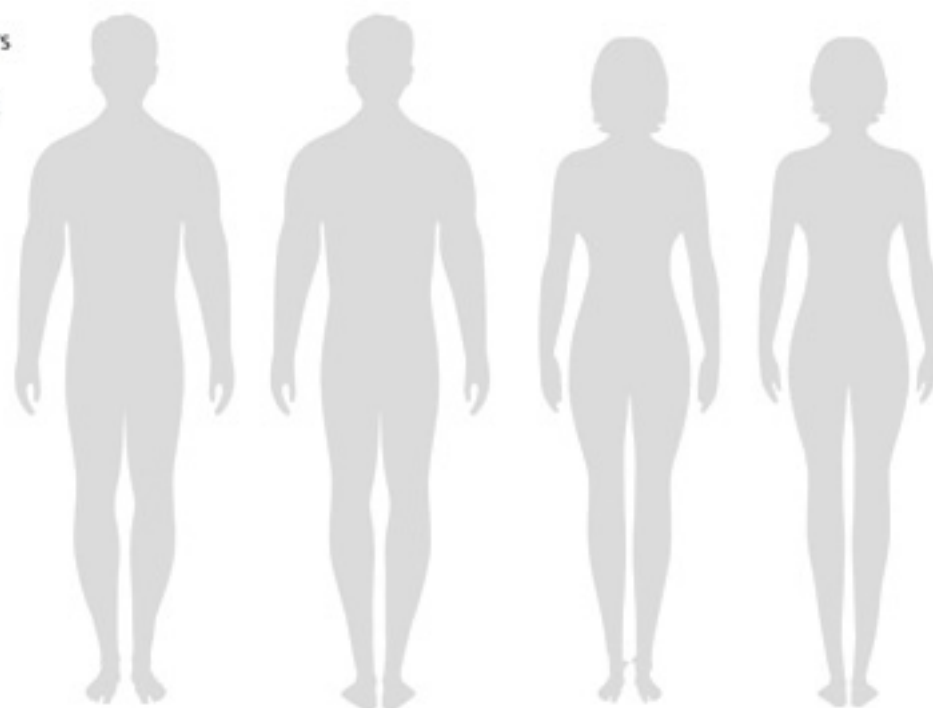
☐ No

Total score* for the SSI _____

*The sum of the three scaled symptoms plus one point each for the other symptoms (pain or cramps, depression, headache). The total will be between 0 and 12.

Body map

Use the figures to record where pain occurs in detail. Shade the areas of your body where you have felt persistent or recurrent pain for the past 3 months or longer (chronic pain).



Calculating the WPI score

Use this checklist to calculate the widespread pain index (WPI) score. Tick the areas where you have had chronic pain for 3 months or longer.

Region 1: left upper

- ☐ L jaw
- ☐ L shoulder girdle
- ☐ L upper arm
- ☐ L lower arm and/or L wrist/hand, L elbow

Region 2: right upper

- ☐ R jaw
- ☐ R shoulder girdle
- ☐ R upper arm
- ☐ R lower arm and/or R wrist/hand, R elbow

Region 3: left lower

- ☐ L hip and/or L buttock
- ☐ L upper leg and/or L groin
- ☐ L lower leg and/or L ankle/foot, L knee

Region 4: right lower

- ☐ R hip and/or R buttock
- ☐ R upper leg and/or R groin
- ☐ R lower leg and/or R ankle/foot, R knee

Region 5: axial

- ☐ Neck
- ☐ Upper back
- ☐ Lower back
- ☐ Chest (L and/or R)
- ☐ Abdomen

Total score* for the WPI _____

*The total will be between 0 and 19.

L=left; R=right

A diagnosis requires widespread pain > 3 months duration with currently either
i) widespread pain index (WPI) ≥ 7 and symptom severity scale (SSS) score ≥ 5 , or
ii) WPI 4–6 and SSS score ≥ 9 , with pain in 4/5 body regions.

Treatment

Fibromyalgia is a chronic condition which needs a multidisciplinary approach from primary or secondary care settings which involve an individualised care plan that focuses on improving symptoms and function with regular monitoring and follow up (9). Physicians and patients should agree on a treatment plan that focuses on goals to improve quality of life. The management plan can include pharmacological and non pharmacological treatments.

Non pharmacological treatment includes :

1- Exercise: Regular, low impact exercise can help improving symptoms and overall wellbeing. Activities that may help include aerobic activity (walking , swimming and cycling), strengthening training (using weights, rubber bands etc.), yoga, stretching and dance. They are recommended to promote flexibility, reduce stiffness and enhance mood. It is important to start slowly, tailor exercise as per individual capability and then gradually increase intensity by time.

2- Physiotherapy: physiotherapists can help patients to stay active and achieve desired goals. They will show patients different types of exercise in tailored treatment plan.

3- Occupational therapy: occupational therapists help patients to work out their usual daily activities without worsening of symptoms of fibromyalgia. They might suggest tools to cope with symptoms such as aids (mobility aids, rails, walkers) and home / work place adaptations.

4- Acupuncture: There is evidence that acupuncture can be used for a short term to improve symptoms.

5- Cognitive behavioural therapy CBT and counselling: Chronic pain of fibromyalgia can be a major factor which affects mood and behaviour. Physiological therapies used to manage symptoms of low mood, stress and pain. It helps patients to deal with symptoms in a different perspective and reduce the burden on overall health. It includes counselling, relaxation techniques and CBT.

6- Sleep hygiene: following practical strategies to address poor sleeping patterns, patients with fibromyalgia can experience improvement in quality of life like lowering pain reception and improve functionality.

7- Group therapy: Patients are encouraged to attend group therapy or support groups which may help them understand fibromyalgia by discussing it with other peers and professionals in a different environment setting. They may feel not alone and can share their experiences with others.

8- Education for patients and carers: It is important to explain and conduct information clearly to patients and their carers to increase chances of dealing effectively with fibromyalgia. This can be done by signposting patients to support groups, using leaflets, watching educational videos, listening to podcasts and reading self help books.

Pharmacological treatments:

It is recommended that non drug treatment should always be tried first. The pharmacological intervention of fibromyalgia includes a variety of medications to target

symptoms. Anti depressants particularly amitriptyline and duloxetine are most common medications used for pain, improve sleep and mood disturbance. Anti convulsants such as gabapentin and pregabalin which can target target nerve pain. Although, there is no definite evidence of efficacy and safety of anti convulsants in reducing pain, sleep problems and fatigue (10). According to NICE guidance analgesia such as NSAIDs and opioids no longer recommended in treating primary pain disorder including fibromyalgia. Patient who are already on analgesia and declares benefit from medication, a shared care plan needed by shared decision making explaining to patients risks and lack of evidence. If there is little benefit, using same process and gradual reduction of established analgesia is recommended (11).

References

- 1- Bhargava J, Hurley JA. Fibromyalgia. 2023 Jun 11. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. PMID: 31082018.
- 2-<https://www.nhsinform.scot/illnesses-and-conditions/brain-nerves-and-spinal-cord/chronic-pain/fibromyalgia/>
- 3- Clauw DJ, Arnold LM, McCarberg BH; FibroCollaborative. The science of fibromyalgia. *Mayo Clin Proc.* 2011 Sep;86(9):907-11. doi: 10.4065/mcp.2011.0206. PMID: 21878603; PMCID: PMC3258006.
- 4- Kocyigit BF, Akyol A. Fibromyalgia syndrome: epidemiology, diagnosis and treatment. *Reumatologia.* 2022;60(6):413-421. doi: 10.5114/reum.2022.123671. Epub 2022 Dec 30. PMID: 36683836; PMCID: PMC9847104.
- 5- Ovrom EA, Mostert KA, Khakhkhar S, McKee DP, Yang P, Her YF. A Comprehensive Review of the Genetic and Epigenetic Contributions to the Development of Fibromyalgia. *Biomedicines.* 2023 Apr 7;11(4):1119. doi: 10.3390/biomedicines11041119. PMID: 37189737; PMCID: PMC10135661.
- 6- Staud R, Domingo M. Evidence for abnormal pain processing in fibromyalgia syndrome. *Pain Med.* 2001 Sep;2(3):208-15. doi: 10.1046/j.1526-4637.2001.01030.x. PMID: 15102253.
- 7-<https://www.rcplondon.ac.uk/guidelines-policy/diagnosis-fibromyalgia-syndrome>
- 8- Siracusa R, Paola RD, Cuzzocrea S, Impellizzeri D. Fibromyalgia: Pathogenesis, Mechanisms, Diagnosis and Treatment Options Update. *Int J Mol Sci.* 2021 Apr 9;22(8):3891. doi: 10.3390/ijms22083891. PMID: 33918736; PMCID: PMC8068842.
- 9- Ram PR, Jeyaraman M, Jeyaraman N, Nallakumarasamy A, Khanna M, Gupta A, Yadav S. Beyond the Pain: A Systematic Narrative Review of the Latest Advancements in Fibromyalgia Treatment. *Cureus.* 2023 Oct 31;15(10):e48032. doi: 10.7759/cureus.48032. PMID: 38034135; PMCID: PMC10687844.
- 10- Üçeyler N, Zeller D, Kahn AK, et al. Small fibre pathology in patients with fibromyalgia syndrome. *Brain.* 2013 Jun;136(Pt 6):1857-67. doi: 10.1093/brain/awt053. Epub 2013 Mar 9. PMID: 23474848.
- 11-<https://www.nice.org.uk/guidance/ng193>

Insomnia in adults: a brief review

Jakir Hussain Ullah

Correspondence:

Dr Jakir Hussain Ullah
Consultant family physician
PHCC, Qatar
Email: jullah@phcc.gov.qa

Received: January 2024. Accepted: February 2024; Published: March 1, 2024.

Citation: Jakir Hussain Ullah. Insomnia in adults: a brief review. World Family Medicine. March 2024; 22(3): 57-61.

DOI: 10.5742/MEWFM.2024.95257628

Abstract

Insomnia is a common and debilitating condition in adults, especially in the elderly. **Keywords:** Insomnia, adults

It is associated with poor mental health and contributes to the development of a wide range of medical conditions, including obesity, cardiovascular disease, diabetes and dementia. The condition is frequently missed or underdiagnosed and poorly managed. This brief review summarises the aetiology, clinical features, diagnosis and latest management strategies.

Introduction

Sleep disturbance or insomnia is a common problem affecting around 10% of the adult population, and its prevalence increases dramatically with age [1]. Based on its duration, insomnia can be classified as acute (less than three months) or chronic (more than three months). According to the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5), chronic insomnia is defined as a sleep disturbance that occurs at least three nights a week for three months or more and causes clinically significant distress or functional impairment, e.g. fatigue, reduced cognitive performance or mood disturbance [2]. The International Classification of Sleep Disorders (ICSD-3) defines insomnia as a problem initiating or maintaining sleep that results in daytime consequences, e.g., fatigue and daytime somnolence [3].

Aetiology

The pathophysiology of insomnia is multifactorial, complex and not fully understood. Spielman et al. [4] proposed a three-factor model for the aetiology of insomnia disorders that has been widely adopted. The model consists of predisposing, precipitating and perpetuating factors as described below.

1. Predisposing factors: >45 years of age, female gender, menopause, being divorced, separated or widowed, lower levels of education, smoking, excess alcohol, reduced exercise and shift working. There also appears to be a genetic pre-disposition which may cause an imbalance in the sleep-wake system regulation in the brain [5], i.e., sleep-promoting neurotransmitters, including gamma-aminobutyric-acid (GABA), adenosine, melatonin and prostaglandin D2 are downregulated and wake-promoting mediators including orexin, norepinephrine and histamine are upregulated.
2. Precipitating factors include social stresses, physical and or mental illness, and medications, including beta-blockers, glucocorticoids and non-steroidal anti-inflammatory drugs.
3. Perpetuating factors: behavioural patterns that develop from insomnia, i.e., worrying about the inability to sleep, spending excessive time in bed trying to fall asleep and taking daytime naps to compensate.

Changes with sleep with ageing

Current thinking is that there are four stages to sleep. The first three are non-rapid eye movement stages, designated N1, N2 and N3, accounting for approximately 18, 48 and 16% of sleep time, respectively. N1 is light sleep and gets progressively deeper through N2 and then N3 stage. The latter stage is characterised by very slow brain waves, called delta-wave sleep. The fourth stage is rapid eye movement sleep, designated R sleep, accounting for roughly 18% of sleep. In the R stage, brain activity increases to levels similar to being awake. Dreaming occurs in this stage. Total sleep time reduces with age

from around 12 hours plus in children to 6.5-8.5 hours in young adults and 5-7 hours in older adults. Furthermore, as we age, the amount of time in N3 'deep' and R-stage sleep decreases [6].

Clinical features and associated morbidity

Sleep disturbance can present as difficulty falling asleep (sleep onset insomnia), poor sleep maintenance, i.e. frequently waking up and finding it difficult to get back to sleep, or early morning waking (early morning insomnia). The impact includes daytime sleepiness, poor concentration, fatigue and increased risk of accidents due to the features above. If left untreated, insomnia is strongly linked to the development of mental illness; e.g. older adults with insomnia have a 23% increased risk of depression [6]. However, It is important to note there is a bi-directional relationship between insomnia and mental illness [6].

Insomnia is associated with an increased risk of cardiovascular disease, including hypertension, myocardial infarction (MI), heart failure and possibly stroke [6]. The HUNT study reported a 27-45% increased risk of MI in patients with chronic insomnia [7]. Furthermore, the sleep heart study showed that middle-aged and older adults who slept 5 hours or less had a 2.5 times increased risk of diabetes compared to individuals who slept 7 to 8 hours per night [8]. Chronic insomnia is also thought to increase the risk of asthma symptoms and allergic rhinitis, although the mechanism is not well understood [9]. These comorbidities are thought to arise due to dysregulation of the hypothalamus-pituitary axis, leading to increased levels of adrenocorticotrophic hormone, sympathetic drive, and elevation of inflammatory mediators and c-reactive protein [5]. Shift work that involves night duty results in disrupted sleep patterns and has been linked to an increased risk of breast and prostate cancer [10]. Long-term insomnia is also associated with the development of dementia [11], and imaging studies have also shown a correlation between cortical atrophy and poor sleep [12]. Insomnia is also a common reason for sick leave, leading to reduced productivity in the workforce and work-related and motor vehicle accidents [1].

Diagnosis

Insomnia is a clinical diagnosis. A thorough history is required and can be aided by sleep diaries (for 14 days) and sleep questionnaires, e.g., the insomnia severity index (ISI), which is a widely used diagnostic tool [13]. Sleep environment, lighting, temperature, timing, partner sleep pattern and collateral history, snoring, use of electronic devices, caffeine, nicotine, alcohol intake, and medical/psychiatric conditions, e.g., cardiorespiratory disease, depression, anxiety and medications, can all contribute to the development of insomnia. Sleep studies using wrist actigraphy can help determine the quality of the patient's sleep. Polysomnography is not required for the diagnosis of insomnia but helps rule out alternative sleep disorders

Management

First-line management of insomnia involves the use of non-pharmacological methods such as sleep hygiene, cognitive behavioural therapy for insomnia (CBT-I) and brief behavioural treatment. Pharmacological options can be tried if first-line interventions fail or there is insufficient benefit.

Non-pharmacological therapy

Sleep hygiene

Patients should be advised to have a consistent bedtime routine, i.e. going to bed at the same time every night, limiting caffeine, nicotine and alcohol in the evening, avoiding exercise within 6 hours of bedtime, avoiding daytime naps and not using electronic devices in bed [5, 11].

Cognitive behaviour therapy for insomnia

This involves a course of cognitive behavioural therapy addressing perpetuating factors associated with chronic insomnia. It is designed to identify, challenge and change misconceptions regarding sleep. It can be delivered face-to-face or online, although evidence suggests the former is more effective. Numerous meta-analyses have shown positive and long-lasting effects in treating chronic insomnia, and hence, CBT-I is considered the gold standard treatment [11, 15]. However, in-person CBT-I is often limited by the availability of trained practitioners, cost and the time commitment required. Several mobile apps and online options are available, including SLEEPIO, and SHUTi [5, 16].

Brief behavioural treatment

- **Sleep restriction therapy:** this involves limiting the hours in bed to actual sleep time until sleep efficiency improves. For example, limiting time in bed to 5 hours for a patient who reports an average sleep time of 5 hours. If the actual time slept in this period is less than 85% of the time, further time restriction is done by reducing time in bed by 15-30 minutes. When actual sleep time exceeds 85% of the time in bed, sleep time is increased by 15 – 30 minutes [5, 11].
- **Stimulus control:** this therapy aims to re-associate going to bed with sleeping only. It involves going to bed only when tired and not using the bed for other reasons such as reading, working or watching TV. If unable to sleep after 15-20 minutes, the patient should get out of bed, sit or walk around and only return to bed if feeling sleepy [5, 11].
- **Relaxation techniques:** this may involve paced diaphragmatic breathing, meditation, yoga and mindfulness to reduce pre-sleep arousal and worry in patients with insomnia [11].

Pharmacological treatments

Pharmacological agents should be used as adjunct to non-pharmacological methods. The evidence base is generally weak, and the risks may outweigh the benefits; interestingly, several studies have reported that almost 60% of the effects of medications can be explained by the placebo effect [17]. Options include benzodiazepines, Z- drugs (zopiclone, zolpidem), anti-depressants, anti-histamines melatonin and orexin antagonists (Table 1).

Benzodiazepines and z-drugs are non-specific agonists of the GABA receptor. The former, in addition to causing sedation, has anxiolytic and muscle-relaxing effects. They are effective in treating short-term insomnia and have been shown to improve sleep latency and maintenance. However, they have significant side effects, including daytime drowsiness, cognitive impairment, reduced dexterity and increased risk of falls [18]. Furthermore, long-term use leads to tolerance, dependence, rebound insomnia and other withdrawal symptoms on cessation [18]. Benzodiazepines are contra-indicated in individuals with sleep apnoea and chronic respiratory disease due to the risk of respiratory drive suppression [18]. Based on the above, the Beers criterion for potentially inappropriate medication use in older adults advises avoiding benzodiazepines as a treatment for insomnia [19]. As a result, benzodiazepines and z-drugs are classed as controlled drugs or not available in many countries, including the Middle East.

Melatonin is widely used for insomnia and is available over the counter in many countries. It is a hormone released by the pineal gland, which is under the control of the hypothalamus and suprachiasmatic nucleus. Melatonin levels are higher at night than day and act as a feedback signal to the circadian rhythm [20]. The principle behind its use is that exogenous melatonin can be used to reset a disrupted circadian rhythm [21].

Dual orexin inhibitors, such as daridorexant, are a new class of medications that are effective and safe in treating chronic insomnia. Orexin A and Orexin B are neuropeptides that promote wakefulness. Inhibition of Orexin A and B receptors has been shown to reduce wakefulness and improve sleep latency and maintenance with little or no next-day functional impairment compared to placebo and z-drugs [22]. Adverse effects appear to be mild, and crucially, there seems to be little to no potential for abuse due to a lack of tolerance and withdrawal symptoms [22].

Table 1: Medications for the treatment of short-term and chronic insomnia [23].

Medication class	Examples	Indications
Benzodiazepines	Nitrazepam Flurazepam Loprazolam Diazepam Lormetazepam Lorazepam temazepam	Indicated in short term insomnia only, for 3-5 days use. Not beneficial in chronic insomnia
Z-drugs	Zopiclone Zolpidem	Licensed in the UK for short treatment of insomnia for up to 4 weeks
Tri-cyclic antidepressants	Doxepin Amitriptyline Mirtazapine trazadone	Doxepin is a tricyclic anti-depressant that has FDA approval for use in insomnia. Amitriptyline is not helpful except in treating insomnia in the context of neuropathic pain
Other classes of anti-depressants	Trazadone Mirtazapine	Indicated in treating insomnia in the context of co-existing depression only
Orexin inhibitors	Daridorexant	Indicated for treatment of chronic insomnia
Melatonin	Melatonin Ramelteon	In the UK, melatonin 2mg MR is licenced to treat insomnia in individuals over 55 for a period of up to 13 weeks. Ramelteon is a synthetic melatonin receptor agonist available in the USA.
Anti-histamines	Chlorphenamine Diphenhydramine Promethazine	These are recommended for use when sleep disturbance occurs in the context of eczema, hives, and other causes of itching.

Summary

Insomnia is a condition associated with significant morbidity that requires careful consideration and management. The current NICE guidelines, representing best practice, are summarised below [23].

Management of short-term insomnia (i.e. < 3 months duration)

- Refer to specialist services if suspecting sleep disorder other than insomnia, e.g. sleep apnoea, circadian rhythm disorders, narcolepsy or parasomnia.
- Address comorbid conditions if present, e.g. depression and anxiety
- Promote sleep hygiene techniques
- Insomnia due to an acutely stressful event or situation that would be expected to resolve within a few weeks but has failed to respond to sleep hygiene can be managed with a short course (3-7 days) of a z-drug, e.g. zolpidem

- Patients with insomnia that is likely to persist and is not due to an acutely stressful event or situation that has not responded to sleep hygiene techniques should be referred for CBT-I. In the meantime, a short-term Z drug (1-2 weeks) or prolonged release melatonin if over 55 can be tried as an adjunct

Management of chronic insomnia disorder (Insomnia for >3 months)

- Refer to specialist services if another sleep disorder is suspected other than insomnia, e.g. sleep apnoea, circadian rhythm disorders, narcolepsy or parasomnia.
- Address comorbid conditions, e.g. depression and anxiety if present
- Promote sleep hygiene techniques
- Offer CBT-I as the first line for all adults
- Short-term Z drug use may be indicated for one week or less to manage behavioural or cognitive symptoms due to lack of sleep
- If over 55, a 3-week trial of melato

References

- Shaha D. Insomnia Management: A Review and Update. *The Journal of Family Practice*; 72. Epub ahead of print 1 July 2023. DOI: <https://doi.org/10.12788/jfp.0620>.
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. *Diagnostic and Statistical Manual of Mental Disorders*; 5. Epub ahead of print 2013. DOI: <https://doi.org/10.1176/appi.books.9780890425596>.
2014. International Classification of Sleep Disorders – Third Edition (ICSD-3) (Online) - American Academy of Sleep Medicine. learn.aasm.org, <https://learn.aasm.org/Listing/a1341000002XmRvAAK>.
- Spielman AJ, Caruso LS, Glovinsky PB. A behavioural perspective on insomnia treatment. *The Psychiatric Clinics of North America* 1987; 10: 541–553.
- Bollu PC, Kaur H. *Sleep Medicine: Insomnia and Sleep*. Missouri Medicine 2019; 116: 68–75.
- Patel D, Steinberg J, Patel P. Insomnia in the elderly: A review. *Journal of Clinical Sleep Medicine* 2018; 14: 1017–1024.
- Krokstad S, Langhammer A, Hveem K, et al. Cohort Profile: The HUNT Study, Norway. *International Journal of Epidemiology* 2012; 42: 968–977.
- Gottlieb DJ, Punjabi NM, Newman AB, et al. Association of Sleep Time With Diabetes Mellitus and Impaired Glucose Tolerance. *Archives of Internal Medicine* 2005; 165: 863.
- Sundbom F, Malinovschi A, Lindberg E, et al. Insomnia symptoms and asthma control—Interrelations and importance of comorbidities. *Clinical & Experimental Allergy* 2019; 50: 170–177.
- Sigurdardottir LG, Valdimarsdottir UA, Mucci LA, et al. Sleep Disruption Among Older Men and Risk of Prostate Cancer. *Cancer Epidemiology Biomarkers & Prevention* 2013; 22: 872–879.
- Riemann D, Baglioni C, Bassetti C, et al. European guidelines for the diagnosis and treatment of insomnia. *Journal of Sleep Research* 2017; 26: 675–700.
- Sexton CE, Storsve AB, Walhovd KB, et al. Poor sleep quality is associated with increased cortical atrophy in community-dwelling adults. *Neurology* 2014; 83: 967–973.
- Insomnia Severity Index, https://www.ons.org/sites/default/files/InsomniaSeverityIndex_ISI.pdf.
- Gossard TR, Trotti LM, Videnovic A, et al. Restless Legs Syndrome: Contemporary Diagnosis and Treatment. *Neurotherapeutics* 2021; 18: 140–155.
- Muench A, Vargas I, Grandner MA, et al. We know CBT-I works, now what? *Faculty Reviews*; 11. Epub ahead of print 1 February 2022. DOI: <https://doi.org/10.12703/r/11-4>.
- Erten Uyumaz B, Feijs L, Hu J. A Review of Digital Cognitive Behavioral Therapy for Insomnia (CBT-I Apps): Are They Designed for Engagement? *International Journal of Environmental Research and Public Health* 2021; 18: 2929.
- Winkler A, Rief W. Effect of Placebo Conditions on Polysomnographic Parameters in Primary Insomnia: A Meta-Analysis. *SLEEP*. Epub ahead of print 1 June 2015. DOI: <https://doi.org/10.5665/sleep.4742>.
- Matheson E, Hainer BL. Insomnia: Pharmacologic Therapy. *American Family Physician* 2017; 96: 29–35.
- American Geriatrics Society. American Geriatrics Society 2019 updated AGS Beers criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society* 2019; 67: 674–694.
- Brown GM. Light, melatonin and the sleep-wake cycle. *Journal of Psychiatry and Neuroscience* 1994; 19: 345–353.
- Sletten TL, Magee M, Murray JM, et al. Efficacy of melatonin with behavioural sleep-wake scheduling for delayed sleep-wake phase disorder: A double-blind, randomised clinical trial. *PLOS Medicine* 2018; 15: e1002587.
- Jiang F, Li H, Chen Y, et al. Daridorexant for the treatment of insomnia disorder: A systematic review and meta-analysis of randomized controlled trials. *Medicine* 2023; 102: e32754.
- . NICE, <https://cks.nice.org.uk/topics/insomnia> (2024, accessed 22 February 2024).

The Prevention of Diabetic Ketoacidosis in Patients with Type 2 Diabetes on Sodium-Glucose Transport Protein 2 Inhibitors

Sara Elsheikh Ahmedana ¹, Musa Basheer Mansour ², Amr Musa Basheer ³

(1) Co-author Musa Basheer Mansour, MBBS, MD, MSc, Dip, Consultant at PHCC, Primary Health Care Corporation, Umm Ghuwailina Health Center- Doha-Qata

(2) Co-author Amr Musa Basheer, Medical Student at The Royal College of Surgeons in Ireland – Medical University of Bahrain, Adliya, Bahrain.

(3) Corresponding author, Sara Elsheikh Ahmedana, MBBS, MD, MSc, Dip, Consultant at PHCC, Primary Health Care Corporation, Abu Baker Al-Siddiq Health Center- Doha-Qatar

Corresponding author:

Sara Elsheikh Ahmedana, MBBS, MD, MSc, Dip,
Consultant at PHCC, Primary Health Care Corporation, Abu Baker Al-Siddiq Health Center
Doha-Qatar

Mobile: +97430188874. P.O. Box 26555.

Email: sahmedana@phcc.gov.qa, sararmusa97@yahoo.com

Received: January 2024. Accepted: February 2024; Published: March 1, 2024.

Citation: Sara Elsheikh Ahmedana, Musa Basheer Mansour, Amr Musa Basheer. The Prevention of Diabetic Ketoacidosis in Patients with Type 2 Diabetes on Sodium-Glucose Transport Protein 2 Inhibitors. World Family Medicine. March 2024; 22(3): 62-74. DOI: 10.5742/MEWFM.2024.95257631

Abstract

Background: Sodium-Glucose Transport Protein 2 Inhibitors (SGLT2Is) effectively control diabetes. Diabetic ketoacidosis (DKA) has been reported as a life-threatening adverse effect due to SGLT2Is use.

Aim: This study aims to review the current evidence of incidence, predisposing factors and the prevention of DKA in T2DM patients on SGLT2Is use.

Methods and Materials: Two reviewers have conducted a search strategy of studies published in English between August 2012 and November 2020, in EBSCOhost, Google Scholar, PubMed, Science Direct and Wiley. Two reviewers independently assessed the eligibility and quality of the studies and extracted the data.

Results: 85 studies were identified in the initial search; 75 records were removed and finally, 10 studies were included. Only studies discussing the prevention of DKA in T2DM patients on SGLT2Is were selected, extracted and categorized into main domains that included SGLT2Is use in T2DM patients and DKA (50%), SGLT2Is use in T2DM patients (20%), the clinical presentation of DKA (20%) and DKA prevention (10%). Six studies showed SGLT2Is increased the risk of DKA with very low rates in two studies. The precipitating factors of DKA in all included studies were revealed as

stopping or reducing insulin, trauma, infection, surgery, severe acute illness, vigorous exercise, dehydration, low carbohydrate intake and excessive alcohol intake. In two studies DKA can be prevented by wakefulness and education, in one study by closed follow-up, in one study by regular monitoring and adjustment of medications and in two studies by recognition of patients at risk.

Conclusions: This review summarized the prevention of DKA in T2DM patients on SGLT2Is use with consideration of incidence, a summary of evidence and predisposing factors. Physicians, health care providers and patients should be aware of SGLT2Is use, regular follow up, precipitating factors, symptoms, signs and prevention of DKA.

Keywords: Sodium-Glucose Transport Protein 2 Inhibitors SGLT2Is, Type 2 diabetes mellitus, Diabetic Ketoacidosis, Scoping Review.

Introduction

Type 2 Diabetes mellitus [T2DM] is an endocrine disorder of various causes, recognized by hyperglycemia resulting from a deficiency in insulin secretion, insulin action or both, and associated with abnormal metabolism of lipids, proteins, electrolytes, and carbohydrates [1]. T2DM is rapidly spreading globally because the estimated prevalence in 2019 was 9.3% (463 million people) and is expected to be 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045 [2]. Gliflozins or SGLT2Is are used for the treatment of T2DM [3-5] with an estimated glomerular filtration rate [eGFR] ≥ 20 mL/min/1.73 m² and urinary albumin ≥ 30 mg/g [6]. SGLT2Is reduce the glycated haemoglobin level (HbA1c), blood pressure, body weight and improve the renal and cardiovascular outcomes with low hypoglycaemic risk [7,8]. In 2013 they were approved by the Food Drugs and Administration (FDA) and included canagliflozin, dapagliflozin, empagliflozin and ertugliflozin [9]. SGLT2Is work at the kidneys by decreasing the reabsorption of glucose back in the blood during the filtration process. As a result, the decreased reabsorption of glucose at the kidneys means that excess glucose in the blood remains with the glomerular filtrate and is excreted as urine and causes glucose malabsorption in the gastrointestinal tract [7,10]. The adverse effects include DKA which is a life-threatening condition characterized by ketoacidosis, ketonuria, and hyperglycaemia [Ketonemia >3.0 mmol/L or significant ketonuria $>2+$ on standard urine sticks, blood glucose >11.0 mmol/L or known DM, Bicarbonate <15.0 mmol/L and/or venous pH <7.3 . Also fracture risk, amputation risk, diuretic effect, bladder cancer, increased risk of urinary tract infections, slight elevation in lipoprotein cholesterol, electrolytes imbalance, uric acid/chronic renal disease, Fournier's gangrene, and free fatty acid elevations [9,11] can occur.

The percentage of euglycemic DKA is 0.01% and associated with blood glucose levels (<14 mmol/L), relative insulin insufficiency and precipitated by surgery or trauma, acute illnesses, alcohol abuse and dehydration [7]. DKA was a consistent nearly 2-fold increased risk (HR 2.20, 95% CI 1.25 to 3.87, $p=0.006$), but the event rates were low (<1 per 1000 patient years) [3].

In 2015, the FDA warned that the treatment of T2DM using SGLT2Is could increase the risk for ketoacidosis among patients [12]. In 2016 the European Medicines Agency [EMA] reported that gliflozins can cause life-threatening DKA, but the advantages exceeding the disadvantages [7]. SGLT2Is impede the reabsorption of glucose in the kidneys by decreasing the threshold for the elimination of glucose, causing glycosuria and causing a shift in the utilization of substrates from carbohydrates to the oxidation of fats, a source of energy, and the accumulation of acid in the blood and hyperglucagonemia [13].

The study showed the estimated prevalence rate and evaluated the comparative risk of DKA among individuals with T2DM in standard clinical practice. The results of the study illustrated that growth in the risk of DKA

was more seen in new users of SGLT2Is than those individuals who use metformin, DPP-4 inhibitors, or GLP-1 receptor agonists [14]. With the increasing incidence of diabetes, statistics of patients with ketosis-prone diabetes also increases. There has been an increased rate of hospitalization for DKA among younger patients diagnosed with T2DM. Meanwhile, the prescription of SGLT2Is as an adjunctive medication for T2D has increased. The increase in prescription is linked with the high cases of DKA among T2DM patients [13].

This review aimed and used the available evidence to establish the relationship between DKA in patients with T2DM on SGLT2Is use. This is achieved through establishing the incidence of DKA, contributing factors, the prevention strategies of DKA for the patients and health care providers, for the appropriate use of gliflozins and best health care outcomes because DKA is life-threatening and causes long-term comorbidity and death [15,16].

Methods and Materials

This research uses scoping reviews to assess the incidence, contributing factors, and prevention strategies for DKA among patients diagnosed with T2DM using SGLT2Is. The research question included three parts; what is the incidence, the precipitating factors, and the prevention approaches of DKA in patients with long-standing T2DM on SGLT2Is?

Aims

This study reviewed the current evidence of prevention of DKA in adults' patients with T2DM on SGLT2Is use.

Objectives

The objectives were to determine the incidence, analyze the precipitating factors, and identify the prevention of DKA in patients with long-standing T2DM SGLT2Is usage.

Eligibility Criteria

The date, exposure of interest, geographical location of the study, language, participants, peer review, reported outcomes, setting, study design and type of publication were considered for eligibility. The inclusion criteria were long-standing T2DM patients over 18 years, management of T2DM with SGLT2Is and any other drugs or nonpharmacological method and DKA management. Eligible articles in this review were scholarly, peer-reviewed and were published in the English language, since 2012 to the search date. The exclusion criteria were confined to pregnant women, individuals under the age of 18 years, T1DM, and grey literature. Articles older than 10 years old were also excluded.

Study Design

This Scoping literature review considered only published studies with an aim to draw the key concepts of the studies in the broad scope of the field management of T2DM patients on gliflozins use and the occurrence of DKA. The principle of Arksey & O'Malley [17] was used and

included identifying clear research questions and aims, searching strategies, identifying appropriate research papers, studies selection, extracting and charting the data, and finally summarizing, analyzing, and presenting the outcomes on the report [17].

Literature Search Strategy

The databases EBSCOhost, Google Scholar, PubMed, Science Direct and Wiley were used, and the kinds of literature were written in English. To make the search effective, keywords [Type 2 diabetes mellitus, Diabetic ketoacidosis, Sodium-glucose transport protein 2 inhibitors], Boolean Operators, proximity, truncations were used to make the search more sensitive. Time restrictions were applied in the search, for instance the databases were restricted to provide articles published since 2012. Grey literature sources, commentary, broadcasting, editorials, conferences were excluded. The corresponding author/s might be involved and communicated with for further data details if needed.

Identification and Selection Relevant Articles/Source of Evidence Screening and Selection

Based on the eligibility criteria, aim and research question, firstly the titles and abstracts were assessed for screening and identification and secondly the full texts were assessed for eligibility. To avoid disagreement, the eligibility of the studies was discussed with two reviewers (Sara & Musa). A PRISMA flow chart was used for effective summarization of the evidence (Figure 1). Primary studies presented an opportunity to quantify the effect of the SGLT2Is on the patient and the risk of causing DKA while most recent studies provided the best opportunity for a reliable review.

Data Extraction (Charting) and Collection Process

The included studies were compiled and extracted in (Table 2). The extracted data were linked to the research questions and aims, and included citations, titles, country of study, the aims, population characteristics, designs, settings, sample size, sample techniques, data sources, measures, analysis, confounder variables, and key observations. The narrative review or descriptive-analytical method was used to extract contextual or process-oriented information from each study (Table 2).

Summarizing, Analyzing and Presenting the Findings

The included studies were categorized into five main domains i.e. SGLT2Is use for patients with T2DM and rate or risk of DKA, precipitating factors and prevention of DKA, and assessment of SGLT2Is.

The methodological studies characteristics were also evaluated in a table and each study was assessed for the design, sample size, the target of the study and the setting. Then the data were classified and presented in percentage

Results

Literature Search Results

The authors demonstrate in (Figure 1) a total of eighty-five studies were identified and involved in the initial search for this scoping review revealing thirty from PubMed, twenty from Science Direct, ten from EBSCOhost, five from Wiley and twenty from Google scholar. A total of thirty-five duplicated records was removed with a remaining fifty records. The remaining records after screening were twenty-six and the excluded records after the screening process was twenty-four. Full-text articles assessed for eligibility were twenty-six and sixteen full-texts were excluded in the eligibility process. Finally, ten studies were included in the synthesis.

Characteristics of Included Articles

The included studies were categorized (Table 1); (n 5, 50%) of the articles discussed Gliflozins use in T2DM and DKA, (n 2, 20%) discussed the gliflozins use in T2DM, (n 2, 20%) discussed the clinical presentation of DKA and (n 1, 10%) discussed DKA prevention. The countries of origin were (n 4, 40%) not available (N/A), (n 2, 20%) in United States, (n 1, 10%) in China, (n 1, 10%) in India, (n 1, 10%) in Syria and (n 1, 10%) in Greece. The population characteristics were the prevention of DKA in T2DM patients on SGLT2Is use. The design was (n 3, 30%) case report, (n 2, 20%) systematic review, (n 2, 20%) systematic review and metanalysis, (n 1, 10%) retrospective study, (n 1, 10%), prospective study and (n 1, 10%) literature review. The setting of the studies was (n 3, 30%) hospital and (n 7, 70%) N/A. Sample size was thirty-four individual case reports, seven trials, one patient, 60,580 patients, one patient, one N/A, sixty patients, 34,322 patients, 115 admissions and one patient.

Data Extraction of the Included Articles

The data were extracted in tables under the following subtitles citation number, citation, titles, country of origin, aims of the study, population characteristics, design, setting, sample size, sample technique, measures, analysis, confounders, and key observation (Table 2).

Table 1: Methodological Characteristic of The Included Articles(n=10)

Characteristics	Categories	n	%
Country of Origin	N/A	4	40
	USA	2	20
	China	1	10
	India	1	10
	Syria	1	10
	Greece	1	10
Study Design	Case report	3	30
	systematic review	2	20
	systematic review and meta-analysis	2	20
	retrospective study	1	10
	prospective study	1	10
	literature review	1	10
Sample size	60,580 patients	1	10
	34,322 patients	1	10
	60 patients	1	10
	One patient	3	30
	115 admissions	1	10
	34 individuals	1	10
	7 trials	1	10
	One N/A	1	10
Setting/Target	Hospital	3	30
	N/A	7	70
Study discussed specific title	Gliflozins use in T2DM and DKA relationship	5	50
	Gliflozins use in T2DM.	2	20
	Clinical presentation of DKA	2	20
	Prevention of DKA	1	10

Figure 1: PRISMA Flow Chart of Scoping Review

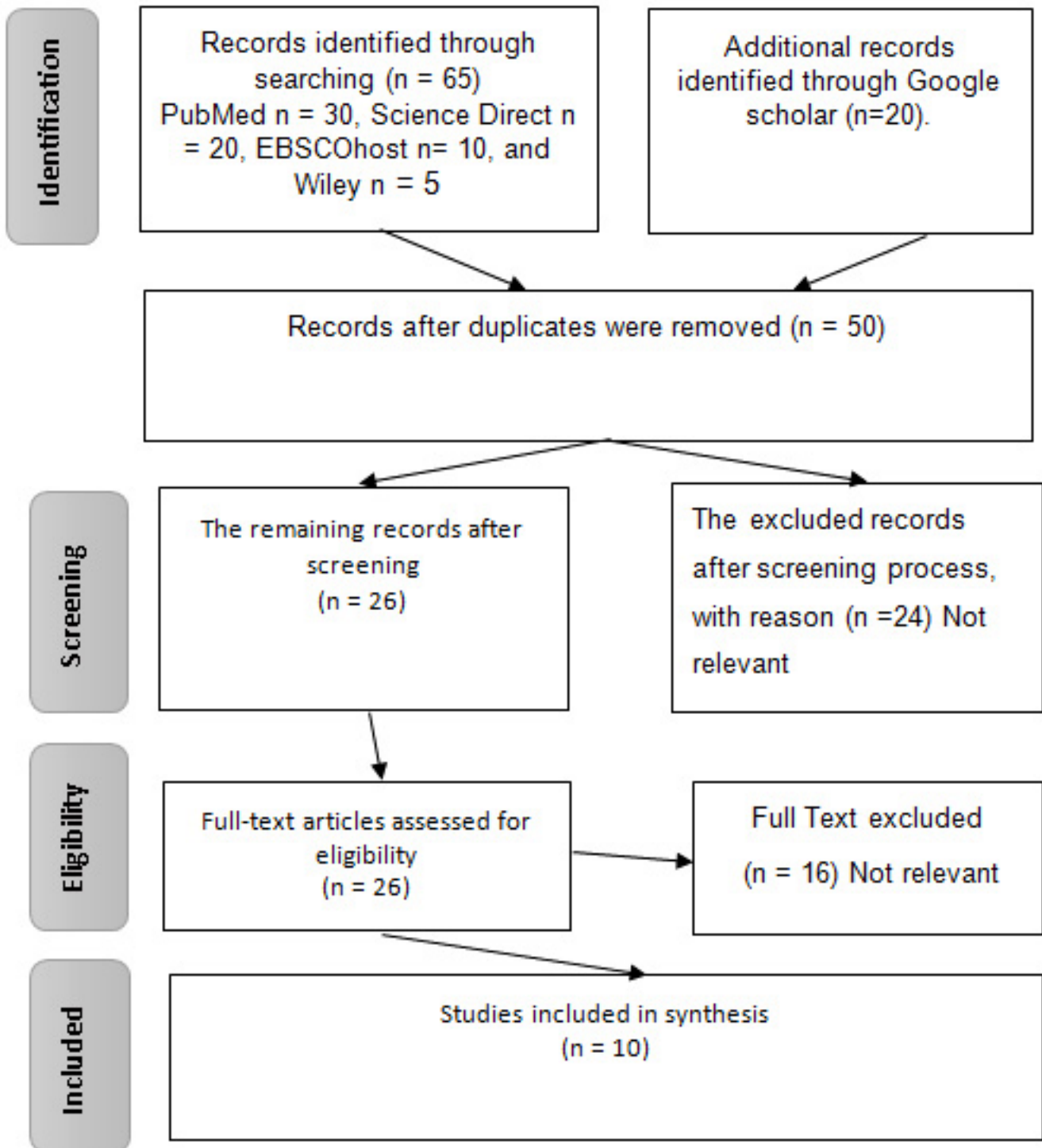


Table 2: Data Extraction of included articles

Citation	Title	Country of origin	Aim of study	Population characteristics	Design	Setting	Sample Size	Sample technique	Data source	Measures	Analysis	Confounder Variables	Key observation
Burke et al. 2017	SGLT2 Inhibitors: A Systematic Review of Diabetic Ketoacidosis and Related Risk Factors in the Primary Literature.	United States	Better understand the clinical presentation and characteristics of DKA caused by SGLT2 inhibitors.	Type 2 diabetes patients treated with SGLT2i and developed DKA	Systematic review of primary literature	NA	34 individual case reports	Search on numerous databases using the key words canagliflozin, dapagliflozin, empagliflozin, SGLT2, sodium glucose cotransporter2 inhibitor, diabetic ketoacidosis, ketoadicidosis, metabolic acidosis, and a cidosis.	Primary literature	Blood glucose levels on the presentation for SGLT2i-induced DKA	Descriptive analysis	NA	Canagliflozin was implicated in cases of DKA. There was no precise link between the occurrence of DKA and the interruption of SGLT2i that could be identified.
Clar et al. 2012	A systematic review of SGLT2 receptor inhibitors in dual or triple therapy in type 2 diabetes.	N/A	Assessing the clinical safety and effectiveness of the SGLT2 receptor inhibitors in dual or triple therapy in type 2 diabetes.	Adults of any ethnic origin above the age of 16 diagnosed with type 2 diabetes	Systematic review	NA	7 trials	Randomized control trials of SGLT2i compared to a placebo or active comparator among T2D patients in combination with dual therapy	MEDLINE, Embase, Cochrane Library	Quality assessment was done using the Cochrane risk of bias score	Metaanalysis was done	Costs of SGLT2i are not known. Lack of long-term data on the safety of SGLT2i	7 trials fully assessed and published dapagliflozin. Canagliflozin was assessed by one. Both canagliflozin and dapagliflozin resulted in the loss of weight but dapagliflozin appears to be more effective.

Elaisha et al. 2018	SGLT2 inhibition may precipitate euglycemic DKA after bariatric surgery.	N/A	To describe potential risk factors for DKA by identifying individual patient characteristics associated with cases of SGLT2i-related DKA.	An obese male patient with poor management of T2D using SGLT2i dapagliflozin	Case report	Hospital	1 patient	NA	Patient hospital records	Effectiveness of SGLT2 inhibition treatment plan	Case Study Analysis	The limited scope of the study	Precipitating factors included patients with T2DM, those who recently had major surgery, had latent autoimmune diabetes of adulthood and, had decreased or discontinued insulin
Liu et al. 2020	SGLT2 inhibitors and risk of diabetic ketoacidosis in patients with type 2 diabetes: systematic review and meta-analysis of randomized controlled trials.	China	Assessing the effects of SGLT2 inhibitors on DKA in patients with T2D.	T2D patients	A systematic review and meta-analysis	NA	60580 patients	Randomized Controlled Trials	Cochrane Central Register of Controlled Trials, EMBASE and PubMed	Peto's method Mantel-Haenszel method	Grade analysis	The difference in age has different treatment outcomes	SGLT2 inhibitors increase the risk of DKA in patients with T2D.

Gajjar et al. 2019	Euglycemic Diabetic Ketoacidosis in the Setting of SGLT2 Inhibitor Use and Hyperglycemic Demia: A Case Report and Review of Literature	N/A	To discuss the diagnosis, pathophysiology, prevention, and management of DKA induced by the use of SGLT2 inhibitors.	A 28-year-old female with T2D	A case report and literature review of eDKA among patients using SGLT2 inhibitors.	NA	1 patient	NA	Patients medical history and literature review	Predisposition to the eDKA risk factors	Case report and descriptive analysis	The patient diagnosis did not check c-peptide, glutamic acid decarboxylase antibodies, and islet cell antibodies which are relevant for diabetes diagnosis	Risk factors for eDKA include the reduction or omission of insulin, dehydration, severe acute illness, surgery, extreme physical activity, low carbohydrate diets, or excessive alcohol intake. EDKA caused by SGLT2 inhibitors is rare. This is largely reported in the setting of known precipitants.
Gosmanov et al. 2014	Management of adult diabetic ketoacidosis	N/A	Providing an overview on DKA from its pathophysiology to clinical presentation with a depth focus on up-to-date therapeutic management.	N/A	Literature review on DKA.	NA	NA	NA	NA	Effective management of Diabetic ketoacidosis (DKA) measures including up-to-date therapeutic interventions	Descriptive analysis	The study assumed that timely adjustment of insulin dose, fluids, electrolytes frequent monitoring of blood glucose levels, patient and provider education can effectively prevent DKA.	DKA management based on its pathophysiology is complex and requires carefully selected approaches that aim to restore deficiencies in insulin, fluids, and electrolytes. Therefore, individualized management is recommended due to the varying and unique patient characteristics.

Seth et al. 2015	Clinical Profile of Diabetic Ketoacidosis: A Prospective Study in a Tertiary Care Hospital.	India	Looking into the precipitating factors, and clinical profile and outcome in DKA patients in the emergency room of tertiary care hospital.	Diabetes patients diagnosed with DKA	A prospective study	Hospital	60 patients	NA	Patients medical history and current diagnosis	Diagnostic criteria for DKA Blood glucose more than 250, arterial pH less than 7.3, serum bicarbonate less than 15 mEq/l	Calculation of percentages	Did not involve patients using SGLT2i	Early diagnosis and treatment can reduce mortality and morbidity.
Zelniker et al. 2019	SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials.	United States	To assess the magnitude of the effect of SGLT2i on particular renal and cardiovascular outcomes and whether key baseline characteristics determine heterogeneity.	T2D patients	A meta-analysis and systematic review	NA	34322 patients	randomized, placebo-controlled, cardiovascular outcome trials of SGLT2i in patients with T2D.	3 Trials	NA	NA	Poor data analysis	SGLT2i have moderate benefits on atherosclerotic major adverse cardiovascular events. They are vital in reducing the progression of renal disease and hospitalization for heart failure irrespective of a history of heart failure or existing atherosclerotic cardiovascular disease.

Aloufi, 2015	Precipitating factors, outcomes, and recurrence of diabetic ketoacidosis at a university hospital in Damascus.	Syria	Studying the precipitation factors, outcome, and recurrence of diabetic ketoacidosis (DKA).	T2D patients with DKA	This was a retrospective study	Hospital	115 admissions	100 DKA patients that fulfilled the American Diabetic Association DKA diagnostic criteria	Medical records	NA	Statistical package for social science Chi-square	The limited scope of the study	Infections followed by insulin-related problems were the predominant precipitating factors for DKA patients in all admissions, which was similar to other studies. But the mortality rate was higher due to the severity of underlying precipitating illness.
Papadokosta et al. 2019	Euglycemic Diabetic Ketoacidosis Secondary to Dapagliflozin in a Patient with Colon Malignancy.	Greece	To assess the negative effects, in this case, euglycemic diabetic ketoacidosis, of using SGLT2 even though its use has increased.	64-year-old-man with a 3-day history of abdominal pain, nausea, and vomiting.	A case report	NA	1 patient	NA	Patients medical records and history	NA	NA	The limited scope of the study	Euglycemic diabetic ketoacidosis is a likely effect of using SGLT2 inhibitors. Clinicians must identify patients with the risk of euglycemic DKA and provide the relevant advice.

The Domains of the Review

SGLT2Is use for patients with T2DM and risk of DKA

Ten studies were included in this review; six out of them show that the use of SGLT2Is in T2DM patients increases the risk of DKA [3,4, 15, 18-20,22]

SGLT2Is use for patients with T2DM and rates of DKA

Two out of the ten studies show that the rates of DKA are very low [3,4].

SGLT2Is use for patients with T2DM and precipitating factors of DKA

The precipitating factors are many, and all the included studies revealed that stopping insulin, or reducing insulin dose, trauma, infection, surgery, severe acute illness, vigorous exercise, low fluids intake and dehydration, low carbohydrate intake, excessive alcohol intake play a major role in the occurrence of DKA [3,4,15,18-23].

SGLT2Is use for patients with T2DM and prevention of DKA

In two included studies, it was shown that DKA can be reduced and prevented by wakefulness and education [3,22], by a closed follow-up in one study [4], by regular monitoring and pre-emptively adjustment of medications in one study [14] and by recognition of patients at risk in two studies [18,19].

Assessment of SGLT2Is (Table 3):

The development and application of the eligibility criteria were appropriately used throughout the selection of the studies. The assessment of SGLT2Is causing DKA among T2DM patients was adequately determined in two studies [18,19], the adverse effects were mentioned in four studies [3,20-22] and the risk factors for DKA among T2DM patients using SGLT2Is were highlighted in two studies [4,15] and one study determined the prevention strategies [23].

Discussion

The included studies of this review used various designs to manage and prevent DKA in patients with T2DM on SGLT2Is.

Incidences and Risk of DKA and summary of evidence

DKA is an issue of concern among T2DM patients using SGLT2Is. This is because DKA is a rare occasion among patients with T2DM. Although there is no precise link between using SGLT2Is and DKA development, it is evident from the results that SGLT2Is increase the risk for DKA [15]. SGLT2Is are designed for individuals with T2DM [23]. SGLT2Is prevent the reabsorption of glucose from the primary urine at the proximal renal tubes, reduce body weight and are accompanied by pleiotropic effects that are attributable to weight loss. These pleiotropic effects might include non-alcoholic fatty liver disease, amelioration of insulin resistance, and dyslipidemia. In

relevance to recent evidence, it has been suggested that individuals on SGLT2Is are at more risk of developing the condition. In EMPA-REG OUTCOME trial [Empagliflozin] Cardiovascular Outcome Event Trial in T2DM Patients [7,020 patients], five events of DKA were occurred and the treatment events per 1000 patients/year was 0.10. In CANVAS Program Canagliflozin and Cardiovascular and Renal Events in T2DM [10,142 patients], 18 events of DKA were occurred and the treatment events per 1000 patients/year was 0.60. In DECLARE-TIM 58 (Dapagliflozin Effect on Cardiovascular Events) [17,143 patients], 48 events of DKA were occurred and the treatment events per 1000 patients/year was 0.90 [3]. Very few SGLT2Is users have a risk of developing DKA which is associated with an increased level of glucagon [15]. DKA influenced by the amalgamation of ketosis and metabolic acidosis in euglycemic patients with low intake of food, dehydration, decreased insulin doses, vomiting, loss of weight, infection, surgical procedure or operation, or poorly controlled diabetes [15,23,24]

The incidence of DKA in T2DM patients on SGLT2Is is 0.1% in 1000 patients/year [21]. For DKA there was a consistent nearly 2-fold increased risk (HR 2.20, 95% CI 1.25 to 3.87, p=0.006), but the event rates were low (<1 per 1000 patient years) [3]. From March 2013 to May 2015 FDA reported forty-four cases of euglycemic DKA. In 2015 May EMA reported 101 cases of life-threatening conditions worldwide in EudraVigilance with an estimated exposure above 0.5 million patient-years [25]. Eighty-five DKA events were registered as an outcome of thirty-nine RCTs that involved 60580 participants [18].

Predisposing factors of DKA in T2DM patients use SGLT2Is

The exact mechanism in which SGLT2Is increase the risk of DKA among T2DM patients is yet to be established. Several factors might increase the risk of developing DKA among patients diagnosed with T2DM taking SGLT2Is. The risk factors include a history of alcohol abuse which generally promotes hypoglycemia, and increased demand for insulin due to an acute illness, restricted intake of carbohydrates, stress, dehydration, surgery, or a sudden decrease or loss in insulin levels in the body [15,22].

Prevention of DKA among T2DM patients using SGLT2Is.

Early detection and management of DKA can avoid complications and mortality [23].

Since DKA has fatal consequences, the primary prevention strategy is effective communication, proper patient education on the symptoms, effects, and consequences of DKA. During patient education, it is important to enlighten the patients on the early signs and symptoms which include polyuria, polydipsia, nausea, vomiting, weakness, dehydration, hypotension, abdominal pain, feeling or being sick, fast, and deep breathing [15,23]. Stopping SGLT2Is before surgery and repetition postponement until patients are fit to preserve evenness of diet, adequate carbohydrate intake and fluids without prolonged catabolic

Table 3: Assessment of SGLT2Is in the included articles

Citation	The assessment of SGLT2Is causing DKA among T2DM patients,	Addressing Side Effects associated with SGLT2Is.	The risk factors for DKA among T2DM patients using SGLT2Is.	Failure to adequately address the topic	Prevention strategies for DKA	Incomplete Follow up
Burke et al., 2017	+	+	+	+	-	-
Clar et al. 2012	+	+	-	-	?	?
Elasha et al. 2018	+	+	-	?	+	?
Liu et al. 2020	+	+	-	+	-	?
Gajjar et al. 2020	+	+	+	+	-	-
Gosmanov et al. 2014	+	+	-	-	+	?
Seth et al. 2015	+	+	-	+	?	?
Zelniker et al. 2019	+	+	-	-	-	?
Alourfi, 2015	-	+	+	?	-	-
Papadokostaki et al. 2019	?	+	+	+	+	?

Low risk (+), high risk (-) and unclear (?).

state [20]. Additionally, follow the sick day rule includes frequent testing of blood sugar and urine for ketones, increased state [20]. Additionally, follow the sick day rule includes frequent testing of blood sugar and urine for ketones, increased carbohydrate and fluids and never stop insulin but considerably increase the dose, during illness even without eating. Also, patients and family's education about symptoms and signs reduces DKA [15, 26].

Limitations

This review includes papers published in the English language that may exclude some studies. Also, this review provided a broad scope of T2DM patients on SGLT2Is use, predisposing factors, the incidence, and prevention of DKA. Furthermore, the number of included papers is occasionally small because some published papers require purchase, and the fund was not available. The quality assessment and critical appraisal of the 10 studies consists of sex elements for each study; high risk was 18, unclear was 12 and low risk was 30. Moreover, the included studies did not include or mention biases that can affect internal or generalized validity. In four studies the country of origin was not determined, seven studies were without a setting, one did not specify the sample size, five did not specify sample technique and two studies were without analysis. Additionally, grey literature was not included due to many reasons that included the time factor to find articles, the multiple search engines, hand searching and the need for communications with the corresponding authors. Finally, due to the lack of sufficient literature and the inclusion of few studies in this review, this limits the scope and the extensiveness in highlighting the consequences of using SGLT2Is among T2DM patients.

Conclusion

This scoping review summarized the use of SGLT2Is among T2DM patients, the incidence, the summary of the evidence, the predisposing factors, and the prevention of DKA. DKA among SGLT2Is users, is rare and life-threatening, has unclear mechanisms/ pathophysiology and can be intractable to diagnose. Clinicians should be aware of T2DM on SGLT2Is users with hemodynamic stability, normal vital signs, asymptomatic and comparatively normal blood glucose levels and should check the ketones levels in suspected patients. SGLT2Is users should be observed closely and advised regarding symptoms such as nausea, vomiting, abdominal pain, tachypnea, and lethargy. In addition to DKA triggers factors such as alcohol abuse, infections, trauma, and reduced fluids intake. Physicians, clinicians, health care providers, pharmacists, pharmacological companies, and policymakers could consider the results of this review to manage and guide the people with T2DM who use SGLT2Is. Patients should look out for and recognize DKA symptoms, avoid the factors that precipitate DKA and follow the physician's advice and guidance. Safety could be an essential area of future research.

Implications of the findings for research

The future conduct of primary research, or systematic review may be appropriate based on gaps in knowledge identified from the results of the review.

Acknowledgements

I appreciate the Teaching Staff of Master of Science in Diabetes Care at The University of Warwick in UK for The Continuous Support and Great Co-Operation and Assistance.

Funding

There was no funding source for this research.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

References

1. Alotaibi A, Perry L, Gholizadeh L, Al-Ganmi A. Incidence and prevalence rates of diabetes mellitus in Saudi Arabia: An overview. *J Epidemiol Glob Health*. 2017;7(4):211-8.
2. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9(th) edition. *Diabetes Res Clin Pract*. 2019;157:107843.
3. Zelniker TA, Wiviott SD, Raz I, Im K, Goodrich EL, Bonaca MP, et al. SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. *Lancet*. 2019 Jan 5;393(10166):31-9.
4. Gajjar K, Luthra P. Euglycemic Diabetic Ketoacidosis in the Setting of SGLT2 Inhibitor Use and Hypertriglyceridemia: A Case Report and Review of Literature. *Cureus*. 2019 Apr 4;11(4):e4384.
5. Nauck MA. Update on developments with SGLT2 inhibitors in the management of type 2 diabetes. *Drug Des Devel Ther*. 2014;8:1335-80.
6. *Diabetes Care* 2023;46(Suppl. 1):S191-S202 <https://doi.org/10.2337/dc23-S011>
7. Morris D. The SGLT2 inhibitors – where are we now? *Journal of Diabetes Nursing*. 2017; 21: 162-7
8. Fleming N, Hamblin PS, Story D, Ekinici EI. Evolving Evidence of Diabetic Ketoacidosis in Patients Taking Sodium-Glucose Cotransporter 2 Inhibitors. *J Clin Endocrinol Metab*. 2020;105(8).
9. Simes BC, MacGregor GG. Sodium-Glucose Cotransporter-2 (SGLT2) Inhibitors: A Clinician's Guide. *Diabetes Metab Syndr Obes*. 2019;12:2125-36.
10. Peene B, Benhalima K. Sodium glucose transporter protein 2 inhibitors: focusing on the kidney to treat type 2 diabetes. *Ther Adv Endocrinol Metab*. 2014;5(5):124-36.
11. Chen J, Fan F, Wang JY, Long Y, Gao CL, Stanton RC, et al. The efficacy and safety of SGLT2 inhibitors for adjunctive treatment of type 1 diabetes: a systematic review and meta-analysis. *Sci Rep*. 2017 Mar 9;7:44128.
12. Vellanki P, Umpierrez GE. Increasing Hospitalizations for DKA: A Need for Prevention Programs. *Diabetes Care*. 2018;41(9):1839-41.
13. Rajeev SP, Cuthbertson DJ, Wilding JP. Energy balance and metabolic changes with sodium-glucose co-transporter 2 inhibition. *Diabetes Obes Metab*. 2016;18(2):125-34.
14. Wang, L., Voss, E. A., Weaver, J., Hester, L., Yuan, Z., DeFalco, F., ... & Rosenthal, N. (2019). Diabetic ketoacidosis in patients with type 2 diabetes treated with sodium-glucose co-transporter 2 inhibitors versus other antihyperglycemic agents: An observational study of four US administrative claims databases. *Pharmacoepidemiology and drug safety*, 28(12), 1620-1628.
15. Burke KR, Schumacher CA, Harpe SE. SGLT2 Inhibitors: A Systematic Review of Diabetic Ketoacidosis and Related Risk Factors in the Primary Literature. *Pharmacotherapy*. 2017 Feb;37(2):187-94.
16. Ogawa W, Sakaguchi K. Euglycemic diabetic ketoacidosis induced by SGLT2 inhibitors: possible mechanism and contributing factors. *J Diabetes Investig*. 2016;7(2):135-8.
17. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2007 Feb 23;8:19e32.
18. Liu J, Li L, Li S, Wang Y, Qin X, Deng K, et al. Sodium-glucose co-transporter-2 inhibitors and the risk of diabetic ketoacidosis in patients with type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials. *Diabetes Obes Metab*. 2020 Sep;22(9):1619-27.
19. Papadokostaki E, Liberopoulos E. Euglycemic Diabetic Ketoacidosis Secondary to Dapagliflozin in a Patient with Colon Malignancy. *Case Rep Endocrinol*. 2019;2019:3901741.
20. Elasha, H, Elsheikh AM, Wafa W, Meeran K. SGLT2 inhibition may precipitate euglycemic DKA after bariatric surgery. *Clin Diabetes Res*. 2018;2(1), 40-42.
21. Clar C, Gill JA, Court R, Waugh N. Systematic review of SGLT2 receptor inhibitors in dual or triple therapy in type 2 diabetes. *BMJ Open*. 2012;2(5).
22. Alourfi Z, Homsy H. Precipitating factors, outcomes, and recurrence of diabetic ketoacidosis at a university hospital in Damascus. *Avicenna J Med*. 2015 Mar;5(1):11-5.
23. Seth P, Kaur H, Kaur M. Clinical Profile of Diabetic Ketoacidosis: A Prospective Study in a Tertiary Care Hospital. *J Clin Diagn Res*. 2015 Jun;9(6):OC01-04.
24. Evans K. Diabetic ketoacidosis: update on management. *Clin Med (Lond)*. 2019 Sep;19(5):396-8.
25. Rosenstock J, Ferrannini E. Euglycemic Diabetic Ketoacidosis: A Predictable, Detectable, and Preventable Safety Concern With SGLT2 Inhibitors. *Diabetes Care*. 2015 Sep;38(9):1638-42.
26. Gosmanov AR, Gosmanova EO, Dillard-Cannon E. Management of adult diabetic ketoacidosis. *Diabetes Metab Syndr Obes*. 2014;7:255-64.

A case of sleep apnoea

Yasir Al-Athari ¹, Mina Mahawish ²

(1) General Practitioner, United Kingdom.

(2) Clinical pharmacist, Viaduct Care, NHS, United Kingdom.

Corresponding Author:

Yasir Al-Athari

General practitioner in United Kingdom

Email: yasir.alathari@gmail.com

Received: January 2024. Accepted: February 2024; Published: March 1, 2024.

Citation: Yasir Al-Athari, Mina Mahawish. A case of sleep apnoea. World Family Medicine. March 2024; 22(3): 75-77

DOI: 10.5742/MEWFM.2024.95257629

Abstract

This case report represents a comprehensive overview of the assessment, diagnosis, and subsequent management of a 60 year old patient who sought medical attention due to debilitating fatigue. Despite displaying atypical symptoms and an absence of characteristic signs, polysomnography revealed significant degree of obstructive sleep apnea. This case highlights the importance of considering sleep-related disorders in the differential diagnosis of fatigue and the remarkable efficacy of continuous positive airway pressure (CPAP) therapy in improving the patient's quality of life.

Keywords: obstructive sleep apnea, fatigue, continuous positive airway pressure, case report

Background

Sleep apnea is a sleep disorder characterised by interruptions in breathing during sleep. These interruptions, called apneas, can be caused by relaxation of throat muscles, leading to reduced airflow or complete blockage. This disrupts the regular cycle and can result in poor sleep quality and daytime fatigue. Excessive daytime fatigue is a common complaint encountered in clinical practice. It is estimated that one billion people around the world are affected by obstructive sleep apnea and there can be more than 50 % prevalence of the condition in some countries (1). While various aetiologies can underlie this symptom, it is essential to consider sleep-related disorders, particularly obstructive sleep apnea, in the diagnostic evaluation of fatigue. Untreated and undiagnosed obstructive sleep apnea can have major health complications such as cardiovascular disease, stroke, metabolic disease, excessive daytime sleepiness, work-place errors, traffic accidents and death (2).

Case Report

A 60 year old female of Middle Eastern origin presented to the family physician with severe tiredness for about six months despite obtaining what she believed was adequate nighttime sleep (7-8 hours). Notably, the patient did not express the typical symptoms of loud snoring or excessive daytime sleepiness. There were no other symptoms noted by patient from history taking. She denied any unexplained weight loss. She used to be active in the past; now even simple tasks feel like a huge effort. It started affecting her work and she had to cut down on her social activities. Her medical history was notable for mild hypertension, was on anti hypertensive medication and she reported no family history of sleep disorder. She does not smoke and she has a balanced diet. Her mood was stable but she feels down when she cannot do her usual daytime activities.

Upon a thorough examination her vital signs including her blood pressure, heart /respiratory rate and oxygen saturation were all within normal ranges. The patient revealed no signs of respiratory distress. Cardiovascular and neurological examinations yielded unremarkable findings. Her BMI was 32.

Given the severity of fatigue coupled with absence of apparent comorbidities or other significant symptoms, extensive investigations for the cause of tiredness were carried out. These included blood tests such as HbA1c, FBC, Ferritin, B12/Folate, ESR, Liver function test, Renal function test, Thyroid function test, IgA tissue transglutaminase and Vitamin D. All tests were back normal apart from folic acid level which was low. It had been thought symptoms of fatigue may be related and she was given supplements accordingly.

Symptoms were not improved and the patient came back to her family physician with the same symptoms. This time she mentioned while on holiday a friend mentioned weird noises while she was sleeping. Subsequently an assessment was carried out in the medical practice which includes a questionnaire called Epworth Sleepiness Scale to assess daytime sleepiness and likelihood of obstructive sleep apnea. The result was 8 which suggested mild symptoms. STOP-BANG score result suggested mild to moderate obstructive sleep apnea. Due to unexplained symptoms of tiredness and results of both questionnaires, referral was made to a sleep clinic to carry out sleeping studies.

The patient had polysomnography which revealed a significantly elevated apnea-hypopnea index AHI of 30, indicative of moderate to severe obstructive sleep apnea. Initiation of continuous positive airway pressure (CPAP) therapy was promptly organised. Following an initial period, the patient reported a substantial improvement in daytime alertness and energy levels. Subsequent polysomnography demonstrated a notable reduction in the AHI to 3, signifying the remarkable effectiveness of CPAP therapy in relieving obstructive sleep apnea.

Discussion

Obstructive sleep apnea can be a challenge to healthcare professionals, and it may need more awareness in the clinical setting to the complications of this condition. It can be life threatening, however it is a preventable condition with a proper treatment (5). Unfortunately, it is still underdiagnosed around the world and it is predicted that the life expectancy of patients with obstructive sleep apnea is less than the general public (6).

This case demonstrated the critical importance of maintaining a high index of suspicion for atypical presentations of obstructive sleep apnea, even in the absence of classic symptoms like prominent snoring or daytime sleepiness (7). The common symptoms of sleep apnea include unrefreshing sleeping, morning headaches, feeling of choking while sleeping and memory deficit (3). Careful assessment of risk factors is quite important to determine chances of sleep apnea. It is crucial to address these factors which can have a positive impact on a patient's life. A patient could be considered as a high risk of developing sleep apnea with any of the following: obesity, uncontrolled hypertension, type 2 diabetes mellitus, stroke and TIA, heart failure, asthma and COPD, thyroid related conditions and atrial fibrillation (4). There are two ways to assess patients with suspected sleep apnea that can aid diagnosis; they are Epworth Sleepiness Scale and STOP-Bang questionnaires (8). Prompt referral and rigorous diagnostic evaluation, including polysomnography, is imperative for accurate diagnosis. Polysomnography is the gold standard test to diagnose sleep apnea (9). The demonstrable efficacy of CPAP therapy in normalising sleep patterns and ameliorating symptoms further underscores its significance as a frontline intervention for OSA (10).

Conclusion

This case report serves as a poignant reminder of the necessity for vigilance in recognising and addressing atypical presentation of obstructive sleep apnea, particularly in patients presenting with severe fatigue. Early diagnosis and intervention with CPAP therapy can lead to a profound enhancement in the patient's quality of life and overall well-being.

References

1. Benjafield AV, Ayas NT, Eastwood PR, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. *Lancet Respir Med* 2019; 7: 687–698. doi:10.1016/S2213-2600(19)30198-5.
2. Kanuert M, Naik S, Gillespie M, Krygera M. Clinical consequences and economic costs of untreated obstructive sleep apnea syndrome. *World J Otorhinolaryngol Head and Neck surgery* Sep 2015; 1(1):17-27. doi: 10.1016/j.wjorl.2015.08.001.
3. Obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s NICE guideline [NG202] Published: 20 August 2021.
4. Mitra A, Bhuiyan A, Jones E. Association and Risk Factors for Obstructive Sleep Apnea and Cardiovascular Diseases: A Systematic Review. *Diseases* Dec 2021;9(4):88.doi: 10.3390/diseases9040088.
5. Lavie P. Mortality in sleep apnoea syndrome: a review of the evidence. *European Respiratory Review* 2007 16: 203-210; DOI: 10.1183/09059180.00010610.
6. Slowik J, Sankari A, Colleen J. Obstructive sleep apnea. *Statpearls* Dec 2022
7. Saaresranta T, Anttalainen U, Polo O. Sleep disordered breathing: is it different for females? *ERJ Open Research* 2015 1: 00063-2015; DOI: 10.1183/23120541.00063-2015.
8. Amra B, Rahmati B, Soltaninejad F, et al. Screening Questionnaires for Obstructive Sleep Apnea: An Updated Systematic Review. *Oman Med J*. 2018 May; 33(3): 184–192. doi: 10.5001/omj.2018.36.
9. Cook J. Oximetry data affect the quality of gold standard polysomnography. *J Clin Sleep Med*. 2021 Jun 1; 17(6): 1329. doi: 10.5664/jcsm.9216.
10. Liu T, Li W, Zhou H, et al. Verifying the Relative Efficacy between Continuous Positive Airway Pressure Therapy and Its Alternatives for Obstructive Sleep Apnea: A Network Meta-analysis. *Front. Neurol.*, 28 June 2017 Sec. Sleep Disorders Volume 8 - 2017 | <https://doi.org/10.3389/fneur.2017.00289>.