The Egyptian Journal of Internal Medicine

REVIEW

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Pneumococcal vaccination in diabetic patients: review from clinical practice

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Abstract

The Middle East and North Africa (MENA) region has the second-highest rate of increase in diabetes, especially in KSA, Egypt, and UAE. Diabetes accounts for a significant economic burden in terms of the cost of treatment, the management of complications, disability, and the loss of productivity. Diabetic adults have an increased susceptibility to infections due to the presence of hyperglycemia. The risk of pneumonia is higher in patients with diabetes. Pneumonia caused by *Streptococcus pneumoniae* (pneumococcal infections) is the most frequent cause of hospitalization in KSA, which also increases the risk of mortality in diabetic patients. The annual planned pilgrimage to Mecca, KSA, is one of the largest frequent religious gatherings globally, and outbreaks of infectious diseases are of great concern. This review will discuss the pneumococcal infection outbreak and prevention in patients with diabetes in KSA. Also, it will gather information discussed by a scientific advisory board held in Riyadh in 2020 covering the current understanding of pneumococcal disease prevention in diabetic patients and recommendations to overcome barriers facing vaccination.

Keywords Diabetes, T2DM, *S. pneumoniae*, Pneumonia, Pneumococcal vaccination

Background

Diabetes mellitus (DM) is a metabolic disorder characterized by abnormally high blood glucose levels. It results from two main reasons, a defect in insulin secretion called type 1 diabetes mellitus (T1DM) or a defect in insulin action called type 2 diabetes mellitus (T2DM) [1]. T1DM affects children and adolescents, whereas T2DM affects middle-aged and older adults [2]. DM is a complicated, chronic, and heterogeneous disorder associated with a significant burden on the economy in terms of treatment costs, management of complications, and loss of productivity [3].

The region of the Middle East and North Africa (MENA) has the second-highest rate of increase in diabetes, especially in the Kingdom of Saudi Arabia (KSA), Egypt, and the United Arab Emirates (UAE) [4]. In a previous study conducted in KSA at the Department of Primary Care at King Fahd Armed Forces Hospital, of 6024 patients, DM was present in 1792 (30%) patients. The prevalence of diabetes was 34.1% in males and 27.6% in females [5]. The reasons behind uncontrolled diabetes in the Gulf Cooperation Council (GCC) region are the poor-quality management systems implemented in some institutions, patients' poor education, and patients' noncompliance to medications [6].

A substantial risk factor for the onset of diabetes in a patient is their age. Nearly half of all patients with DM are older adults (aged ≥ 65 years) [7]. Also, diabetes prevalence has been rising recently due to obesity [8].

Mortality rates and medical costs are both increased by diabetes. The International Diabetes Federation (IDF) estimates 418,900 deaths among persons aged between 20 and 79 in the MENA area were caused by diabetes and its complications in 2019. Additionally, the cost of diabetes-related health care exceeded 24.9 billion USD [9].

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T2DM is the most common type of diabetes and accounts for 90% of diabetic patients [10]. Females make up the vast majority of T2DM patients [11], and they are prone to develop more severe complications than males [12].

It has been reported that pneumococcal disease increased the risk of mortality in diabetic patients [13]. Therefore, here, we aim to discuss the pneumococcal infection outbreak and prevention in patients with diabetes in KSA.

In this review, we will give an overview of the relationship between pneumococcal infection and diabetes in KSA and highlight the importance of pneumococcal vaccination. Also, we will summarize a very interesting scientific advisory board held in Riyadh in 2020, where a panel of leading endocrinologists from different institution sectors across KSA was invited to discuss pneumococcal disease prevention in diabetic patients, and give professional recommendations to overcome vaccination-related barriers.

Main text

Hyperglycemia and increased risk of pneumococcal infection

Diabetic adults have an increased susceptibility to infections due to hyperglycemia [14]. The risk of pneumonia is high in patients with diabetes and is among the most frequent causes of hospitalization [15]. The risk of death in diabetic patients rises following hospitalization for pneumonia [13].

Several biological mechanisms underlie the increased risk of pneumococcal, most of which are mediated through hyperglycemia's harmful effects [14, 16].

Of note, the risk rate of pneumonia is higher in diabetic patients compared to non-diabetic patients [15, 17]. In diabetic patients, pneumonia is among the most frequent causes of hospitalization due to infection. Nearly one in three patients with diabetes hospitalized for infection had pneumonia [13]. There is substantial evidence that diabetes is linked to a 25–75% increase in the risk ratio (RR) of pneumonia-related hospitalization. The risk of hospitalization due to pneumonia rises with a longer duration of diabetes and poor glycemic management [18].

Because diabetes is a chronic condition, patients with it are at risk of pneumococcal disease all year, not only in the winter, unlike seasonal influenza [17]. The planned annual Hajj in Mecca, KSA, is recognized as one of the largest recurring religious mass gatherings globally, and the outbreak of an infectious disease is of considerable concern. Therefore, the number of cases infected with pneumococci increases more in this highly crowded season [19].

It is noteworthy that the most commonly at-risk conditions in diabetes include chronic kidney disease (CKD) and chronic obstructive pulmonary disease (COPD) [20, 21]. Accordingly, this risk of pneumonia increases with the rise in these comorbidities [22].

In a retrospective cohort study using clinical data of all pilgrims whose diagnosis of pneumonia was confirmed during Hajj days (2004–2013), the major risk factors of pneumonia were COPD, bronchial asthma, diabetes mellitus, and chronic heart failure. Eighty-four percent of patients involved in this study were diabetic [23]. Also, in the same study, the mortality rate of pneumonia cases admitted to the intensive care unit (ICU) was 21.45%. In parallel, internationally, the mortality rate of pneumonia cases admitted to ICU was approximately 35% [23].

Pneumonia is a major cause of critical illness during the Muslim pilgrimage (Hajj) in Mecca. A study performed in 1986 reported a mortality rate in ICU of 34%, while in 1994, the reported mortality rate in ICU was 17% [24]. In 2009 and 2010, 452 people (from 40 different countries) had serious disease during the Hajj, with pneumonia being the main reason for 123 (27.2%) of all ICU admissions and a death rate of approximately 19.5%. Smoking (22.8%), diabetes (32.5%), and COPD (17.1%) were the most prevalent pre-existing comorbidities [25]. Likewise, in a study conducted in 2016, 266 patients with community-acquired pneumonia (CAP) were enrolled. 70.6% of them were hospitalized, with diabetes accounting for more than 36% of the cases. The ICU mortality rate was more than 10% [26].

Diabetic patient and vaccination

In KSA, the government obligates the vaccination to all pilgrims of Hajj in which influenza and meningococcal vaccines were recently added to the required immunization list [27, 28]. Currently, pneumococcal vaccines are highly recommended. On the other hand, the Saudi Thoracic Society guidelines recommended influenza and pneumococcal vaccination for diabetic patients [29].

The following discussion summarizes the main points of a scientific advisory board that took place in Riyadh (2020).

The Saudi Ministry of Health (SMOH) has yearly established Key Performance Indicators (KPIs) and provides pneumococcal immunization vaccines to various diabetic centers. In some institutions, as part of their regulations, it is noted that anyone under 50 years old should receive at least one pneumococcal vaccine followed by another activation dose at the age of 55. Sometimes, pneumococcal vaccines are not prescribed due to the lack of awareness among physicians. Besides, a higher percentage of patients who have had influenza and pneumococcal vaccines might result from combining these awareness

initiatives. Pneumococcal vaccination is FDA-approved above the age of 50. However, the Advisory Committee on Immunization Practices (ACIP) and the Center for Disease Control and Prevention (CDC) recommended giving vaccination above the age of 65.

Accessibility, availability, adverse effects, high cost of the vaccine, lack of understanding about the vaccine, fear of site of injection discomfort, and lack of time for doctors to suggest vaccination are the most often encountered hurdles to patients receiving vaccinations.

Of note, when patients come to diabetes care, they notice that the only role of such institutions is to control and monitor their blood glucose. Hence, the majority of patients do not search for recommendations regarding immunization against pneumococcal disease.

Importantly, the family physician is the primarily responsible specialty that recommends the pneumococcal vaccine to T2D patients, as they are more concerned about the pneumococcal disease than other specialties. Furthermore, discussing the need for vaccination with patients still in the diagnostic phase, treatment beginning phase, or in the case of patients with complications is not advisable. However, the follow-up stage (6 months and more) is the perfect time to discuss pneumococcal vaccination with patients.

It is recommended that immunization must be a shared goal among different stakeholders and not only physicians. Also, the campaigns should focus on educating the public as well as physicians. However, it is part of the physician's responsibility to monitor whether high-risk patients are vaccinated.

Conclusion and recommendations

Many practitioners are not satisfied with the diabetes management care provided in the institutions, although many institutions are well equipped in addition to the multidisciplinary team involved to ensure the optimum diabetes control provided. Sharing more specific and detailed statistics regarding the risk of pneumonia in patients with diabetes in addition to comorbidities is completely useful. Unless the practitioner himself makes it part of his practice, patients will not take the initial step in seeking recommendations regarding pneumococcal vaccination. Importantly, the follow-up (6 months and beyond) stage was the most appropriate time to discuss pneumococcal vaccination with patients.

Merging pneumococcal vaccination awareness campaigns, along with the influenza vaccine campaigns, could yield a better percentage of immunized patients. Besides, pharmaceutical companies were recommended to conduct educational meetings, lectures, and campaigns to provide more awareness of pneumococcal vaccination. Also, they were recommended to conduct local campaigns in the institutions while scaling and collaborating with the patient's education department.

Interestingly, the following results were concluded in a quantitative analysis of the scientific advisory board (Riyadh, 2020).

The experts fully agreed that approximately 85% of diabetic patients are T2D, and only 15% are T1D. They also agreed that most T2D patients are females (54.2%). About 67% of the advisors mentioned that more than 70% of T2D patients were adults (18–65 years old). Out of seven advisors, four agreed that the majority (> 70%) of T2D patients are adults, one advisor mentioned that adults account for < 15%, and another advisor said that they account for 51–70% of the total number of T2D patients.

Additionally, 33% of the advisors indicated that the rate of the overall T2D patients hospitalized due to pneumonia during the year 2019 was 6–15%.

About 71% of the advisors mentioned that, in 2019, less than 5% of immunized T2D patients are hospitalized for pneumonia. Likewise, 88% of the advisors indicated that their T2D patients do not seek their recommendation for immunization against pneumococcal disease, whereas only one advisor stated the opposite.

Approximately half of the advisors stated that the family physician is the primarily responsible specialty that usually informs and recommends the pneumococcal vaccine to T2D patients in their institute/clinic. Also, out of seven advisors, four mentioned that the family physician is the responsible specialty, two stated that it was the responsibility of primary care physicians, and one noted that it was the responsibility of other specialties.

The advisors agreed that it is not wise to discuss vaccination importance with patients who are still in the diagnosis or even treatment initiation phase. However, Hajj, according to the advisors' insights, was the best time to talk to patients about vaccinations. On the contrary, 43% of the advisors indicated that their institution/clinic did not allow them to prescribe vaccines automatically inside its system for their T2D patients, and 57% indicated that they were allowed.

About half of the advisors agreed that immunization guidelines were applied to their T2D patients, while 29% mentioned that they were not applied, and 20% stated that they were well applied. Also, about the extent to which advisors, institution/clinic implements the MOH immunization campaigns regarding pneumococcal vaccines, approximately half of the advisors (43%) stated that it is not at all implemented, while 29% of the advisors mentioned that it was not implemented, but 29% of the advisors stated that it was well implemented.

The advisors also showed that the lack of vaccination importance knowledge was the main leading reason

Table 1 Vaccine accessibility barriers and enlisting limitations identification in KSA

Leading barriers	Recommended management
Institutions infrastructure	Build a particular room facilitated for the vaccination procedures
	Increase human resources
	Provision of vaccines in all centers
	Prevention must be a goal in all institutes
Inclusion procedure	Clearly specified and established rules
	Reduce the need to vaccinate just certain groups
	Create a plan for including vaccination in the treatment of diabetes
	The majority of doctors have to be able to order the vaccination
Medical facilities regulations	Availability of vaccine
	Conduction of small campaigns specific to each institution to increase awareness
	Shorten the vaccination processes held by the vaccination committee
Insurance policies	Expand the coverage by insurance to all patients

why their T2D patients normally refuse pneumococcal immunization.

Finally, the professional recommendations made by counselors for managing barriers related to vaccination were (1) availability in diabetes centers, (2) raising public and HCPs' awareness about the importance of vaccination, (3) presence of vaccines at reasonable prices, (4) providing adequate training to the vaccinating staff, and (5) informing patients about the disease's mortality risk and the value of vaccination in lowering that risk.

Endocrinologists in KSA are still mostly unaware of the value of the pneumococcal vaccination. The architecture of institutions, inclusion policies, medical facility rules, and insurance policies are the top four accessibility obstacles (Table 1).

Abbreviations

ACIP	Advisory Committee on Immunization Practices
CKD	Chronic kidney disease
CAP	Community-acquired pneumonia
COPD	Chronic obstructive pulmonary disease
DM	Diabetes mellitus
GCC	Gulf Cooperation Council
ICU	Intensive care unit
IDF	International Diabetes Federation
KPIs	Key performance indicators
KSA	Kingdom of Saudi Arabia
MENA	Middle East and North Africa
RR	Risk ratio
SMOH	Saudi Ministry of Health
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus

Acknowledgements
Not applicable.

Author's contributions
AG collected the data and drafted the manuscript. The author read and approved the final manuscript.

Funding
Not applicable.

Availability of data and materials
All data are available upon request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The author declares that there are no competing interests.

Received: 4 December 2022 Accepted: 20 February 2023
Published online: 27 February 2023

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