



RSSDI update on vaccination in people with diabetes

Sanjay Agarwal¹ · Jothydev Kesavadev² · Banshi Saboo³

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Abstract

Background and Aim People with diabetes are at increased risk for infections, and vaccine-preventable diseases such as pneumococcal and influenza infections pose serious complications, including increased mortality rates. Despite the benefits of vaccinations in preventing such infections and their complications, vaccine uptake among individuals with diabetes remains suboptimal, particularly in countries like India. This article aims to address the importance of vaccinations in people with diabetes, discuss various vaccine-preventable diseases, and present harmonized vaccine recommendations tailored to the Indian context.

Methods A review of current guidelines from international health organizations such as the American Diabetes Association (ADA), Centers for Disease Control and Prevention (CDC), and Advisory Committee on Immunization Practices (ACIP) was conducted. Vaccination recommendations for pneumococcal, influenza, hepatitis B, Tdap, shingles, and respiratory syncytial virus (RSV) were evaluated, with a focus on their applicability to people with diabetes in India.

Results Vaccines including pneumococcal polysaccharide vaccine (PPSV23) and pneumococcal conjugate vaccine (PCV13) have proven efficacy in preventing pneumococcal infections among people with diabetes. Influenza vaccines are shown to reduce all-cause mortality and prevent cardiovascular events during flu seasons. Hepatitis B, Tdap, and shingles vaccines are recommended for adults with diabetes. However, evidence reveals low vaccination coverage, particularly in India, where awareness and education regarding vaccination are lacking. The article provides harmonized vaccination recommendations specifically for the Indian context, aiming to address gaps in vaccine coverage and accessibility. The need for culturally sensitive education campaigns and healthcare provider engagement to improve vaccination rates is emphasized.

Conclusion Vaccinations play a key role in preventing serious infections in people with diabetes, yet hesitancy and limited awareness persist, especially in India. By providing clear, country-specific guidelines and increasing education efforts, vaccine uptake can be improved, ultimately reducing the burden of preventable diseases.

Keywords Vaccination · Diabetes · Vaccine-preventable diseases · Influenza · Pneumococcal vaccine · Hepatitis · Tdap vaccine

Introduction

In the past 2 years there were significant changes in the vaccine recommendations in diabetes in view of emerging evidence and new formulations. People with diabetes are at an increased risk of complications from most of the common vaccine preventable diseases. Even with proper

management, diabetes can weaken the immune system, making it more difficult to fight infections and increase the risk of contracting certain diseases. Prevention among people with diabetes is important to improve their quality of life and longevity. These diseases pose a great threat to people with diabetes, causing severe complications and fatal outcomes.

Pneumococcal and Influenza infections can be fatal in people with diabetes, with mortality rates up to 50% [1]. Also, influenza epidemics may increase the death rates by 5–15% among people with diabetes during the flu season [2]. Thus, vaccination is the safest and cost-effective way to prevent infections such as; influenza, pneumonia, hepatitis, shingles, varicella, tetanus, diphtheria, and pertussis among the vulnerable population. Vaccinations not only help prevent infections, but also helps in reducing hospitalizations, and its adverse complications.

✉ Sanjay Agarwal
agarwalclinic@gmail.com

¹ Aegle Clinic, Pune, India

² Jothydev's Diabetes Research Centre, Trivandrum, Kerala, India

³ DiaCare, Ahmedabad, Gujarat, India

Even though people with diabetes show reduced immune responses to infections, vaccines are effective in creating an adequate immune response. Also, people with diabetes can reap similar benefits with the help of vaccinations, to those without diabetes.

In India, evidence shows poor vaccine uptake and a lack of awareness on vaccines and their importance among people with diabetes. Specific guidelines on vaccination for people with diabetes, based on Indian standards are also lacking. In this position statement, we endeavor to shed light on the important vaccinations and their schedule for individuals with diabetes.

Infections & vaccinations

Pneumococcal infection

Pneumococcal infections are caused by the bacteria, *Streptococcus pneumoniae* [3]. Disease manifestations include fever and chills, cough, rapid or difficulty in breathing, and chest pain [4]. Pneumococcal infections also have been found to increase mortality and hospitalization in people with Type 1 diabetes (T1D) and Type 2 Diabetes (T2D) compared to people without diabetes [5]. People with diabetes (both T1D & T2D) also have 1.4 times the risk of getting community-acquired pneumonia (CAP) [6].

Immunization is the best economical approach to prevent and counter pneumococcal infections [7]. There are two types of pneumococcal vaccines; the pneumococcal polysaccharide vaccine (PPSV) and the pneumococcal conjugate vaccine (PCV).

Pneumococcal polysaccharide vaccine (PPSV)

Approved in 1983, the 23 valent pneumococcal polysaccharide vaccine (PPSV23) contains 23 of the more than 90 serotypes of pneumococci. Serotypes of PPSV23 include 4, 6B, 9 V, 14, 18C, 19F, 23F, 1, 5, 7F, 3, 19A, 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, and 33F [8]. The vaccine consists of a polysaccharide capsule, to stimulate an immune response [9].

Pneumococcal conjugate vaccine (PCV)

The pneumococcal conjugate vaccine (PCV) has a polysaccharide conjugated to a carrier protein, helping create a better immune response [9]. PCVs are distinguished by the number of serotypes they provide protection against [10]. The original 7-valent conjugate vaccine (PCV7) was replaced by the manufacturer with PCV10 and PCV13 in 2009 [11]. Currently, PCV13, PCV15, and PCV20 are used for vaccination [12, 13]. PCV13 is the only vaccine available in India among the PCV series.

PCV13

PCV13 effectively immunizes individuals against a range of serotypes, including 1, 3, 4, 5, 6B, 6A, 7F, 9 V, 14, 18C, 19A, 19F, and 23F [12, 14]. The vaccine has high efficacy among people with diabetes [15, 16]. The U.S. Food and Drug Administration (USFDA) approved PCV13 for adults aged 50 years or older on December 30, 2011 [17].

Vaccination schedule

Even though vaccines have proven efficacy, the uptake of pneumococcal vaccine among individuals with diabetes remains suboptimal [18, 19]. Pneumococcal vaccination is still a grey area, even among the high-risk groups. This may be due to lack of awareness on vaccinations. India also lacks studies on pneumococcal vaccination and its efficacy among people with diabetes.

Influenza infections

Influenza infection affects individuals of all age groups, including children [20]. High-risk individuals for influenza include those with pre-existing diabetes, cardiovascular disease, people on immunosuppressors, and other chronic illnesses. This group of individuals experiences more severe clinical courses, worse health outcomes, and higher influenza-related complications [21]. The influenza virus can infect the same individual repeatedly as the virus undergoes rapid evolution, avoiding immune memory cells [22]. Therefore, the yearly updated influenza vaccine remains the most effective preventative measure against influenza and associated infections.

Influenza vaccine

Flu shots do not provide complete protection from influenza, but it helps reduce the chances of infection as well as protect against serious adverse outcomes including hospitalization and death. There are two types of influenza vaccine- a live attenuated vaccine administered nasally and an inactivated vaccine administered intramuscularly. While both vaccines are safe and effective, the attenuated vaccine is not recommended for people with diabetes [15].

In addition to protecting from the flu, the vaccine has proven to reduce all cause death, cardiovascular death, and death from Acute Myocardial Infraction (AMI) or stroke among people with diabetes during the flu season [23]. The influenza vaccine helps prevent cardiovascular and cerebrovascular events, especially among people with cardiovascular risk, or previous history of cardiovascular events, primarily by preventing influenza infection and its associated complications. While the

vaccines primary purpose is to prevent influenza, its cardiovascular benefits are significant and well-documented, particularly in high-risk populations [24, 25].

The flu vaccine is well-tolerated [26], and is also effective in reducing the incidence rate of infection [27] among people with diabetes. Literature reveals statistically significant increase of antibody titre and an increased percentage of B-lymphocytes 1 week after influenza vaccination in people with T1D, and a significant reduction in interleukin-2 receptor carrier cells were observed in T2D patients after 72 h, marking valid protection against the influenza virus. Upon further observation, none of the vaccinated patients were affected with the virus the following year [28]. Even though evidence state that vaccines are safe and effective, the coverage, acceptance, and knowledge of vaccines are very low in various regions.

Knowledge of flu vaccines and the uptake rate is very low among people with diabetes in India [29] [30]. Healthcare professionals (HCPs) are also lacking awareness about the vaccine, and its importance, especially in high-risk groups [31]. Awareness, attitude, and practices towards flu vaccines must be improved among HCPs and people with diabetes.

Multiple infections of influenza on a single person is possible due to antigenic drift. Every year the global antigenic drift of the flu vaccine is reviewed and the vaccine is updated accordingly [32]. India every year witnesses two peaks of seasonal influenza. One is from January to March and the other in post-monsoon season [33]. Getting vaccinated during any of this season is recommended to get the maximum efficacy. HCPs should also suggest their patients to get vaccinated during the peak infection period.

Quadrivalent flu vaccines include vaccine viruses or viral proteins from four viruses: one influenza A (H1N1) virus, one influenza A (H3N2) virus, one influenza B/Victoria lineage virus and one B/Yamagata lineage virus. Trivalent flu vaccines only include three vaccine viruses, instead of four [34].

According to the recommendations from ADA, every person with diabetes ≥ 50 years should take a flu shot each year [35]. The CDC, recommends the minimum age to receive the influenza vaccine is two years for the live vaccine and six months for the inactivated vaccine. One dose annually is recommended for all individuals above nine years old [32].

It is also important to note that according to the ACIP, individuals experiencing moderate to severe acute illness, regardless of the presence of fever, should typically postpone receiving the influenza vaccine until they have fully recovered. This recommendation is intended to prevent any potential confusion between the symptoms of the illness and possible side effects of the vaccine, as well as to ensure that the immune system mounts the most effective response to the vaccination once the individual is in optimal health [36].

Hepatitis B infections

Hepatitis B virus (HBV) is a major global health concern, and infection can lead to liver fibrosis, resulting in an elevated risk of cirrhosis and hepatocellular carcinoma [37]. HBV is transmitted from infected mother to child, sexual contact with the infected, and sharing of contaminated needles, syringes, insulin pens, and glucometers [13].

Based on available data, there may be a direct correlation between the development of insulin resistance and T2D and chronic hepatitis B [38]. T2DM is associated with an increased risk of liver fibrosis [39], cirrhosis, decompensation, and hepatocellular carcinoma (HCC) in patients with chronic hepatic biopsy (CHB) [38]. Furthermore, in this population, T2DM raises the risk of non-liver cancers and overall mortality. Additionally, T2DM plays a significant role in the metabolic dysfunction-related steatotic liver disease that many CHB patients experience [38]. Studies also show that Chronic HBV infection could also increase the risk of gestational diabetes [40, 41].

Extensive glycemic control may help CHB patients with their prognosis, despite the lack of precise guidelines for managing T2DM in this patient population [38].

Hepatitis B vaccine

Hepatitis B (HB) vaccines are safe, affordable, and effective, and are the only means to fight the virus and its infection [42]. Vaccination is proven to be effective in preventing HB infections, especially in high-risk group people, including people with diabetes [43, 44]. In a phase IV study from China among people with T2D, HB vaccine was proven to induce good immunogenicity [45], and is safe for use [46, 47]. Precautions and timely vaccination are mandatory to avoid complications of the infection.

Tdap vaccine

Tdap (Tetanus, Diphtheria, and Pertussis) vaccines are vaccines that can prevent tetanus, diphtheria, and pertussis infections [48]. Tetanus enters the body through cuts and wounds whereas diphtheria and pertussis spread from individual to individual, through airborne droplets [49, 50]. Tetanus can cause painful stiffening of muscles. Diphtheria causes difficulty in breathing, heart failure, or even death. Pertussis infections, also known as “whooping cough” can cause violent and uncontrollable cough, making it hard to breathe eat, or drink [48].

Studies state that Tdap vaccines are effective and safe in preventing infections among people with gestational diabetes, protecting the mother and fetus, infant (during the first months of life), and the mother (during postpartum)

[51, 52]. But evidence on T2D and T1D is scant. There are no Indian studies as of now on the efficacy of the Tdap vaccine among people with diabetes. However, multiple organizations have recommended Tdap for people with diabetes, to be safe from the risk of infection (Table 1.).

Zoster (shingles) vaccine

Varicella-zoster virus (VZV) is the causative agent of chickenpox (varicella) and herpes zoster (shingles) [60]. Following primary infection with chickenpox, shingles develop at a later stage due to the reactivation of latent VZV [61]. The disease causes symptoms such as neuropathic pain (peripheral and postherpetic neuralgia (PHN)) and dermatomal vesicular rash [60, 62]. PHN is a type of neuropathic pain characterized by persistent or intermittent intense pain and hyperalgesia [63]. Shingles causes fewer than 100 deaths annually; however, it causes significant morbidity due to the associated pain. Deaths are usually found in older or immunocompromised people [64].

Multiple meta-analysis studies have shown that people with diabetes are at risk for Herpes Zoster (HZ) [65–67]. This makes it important to discuss zoster vaccine uptake among people with diabetes.

Vaccination is the only method to achieve protection against shingles [68]. Live attenuated zoster vaccine (LZV), and a recombinant zoster vaccine (RZV) (Shingrix) are licensed for use in adults for the prevention of and HZ [60]. The RZV is superior compared to LZV in real-world practice among people with diabetes [69, 70]. One can receive Shingrix vaccine even if in the past they had Shingles, received Zostavax, and received varicella (chickenpox) vaccine [71].

Respiratory syncytial virus

The respiratory syncytial virus (RSV) is a virus that causes lower respiratory tract infections in adults and children. In India, hospital-based studies have reported RSV detection rates ranging from 5 to 54%, while community-based studies have shown rates between 8 and 15%. RSV peaks in winter in North India [72]. The FDA approved the vaccine for use among adults aged ≥ 60 years in 2023. ADA and CDC recommend adults with diabetes aged ≥ 60 years to take a single shot of vaccine with shared decision-making with healthcare providers, as they are at high risk for RSV infections (Table 1.) [73].

In India, the vaccine against RSV is not yet approved. Even though infections are reported, evidence among people with diabetes and India is lacking. However, we recommend taking the vaccine once available in clinical settings for completing the immunization schedule for adults.

Vaccination in India

In a country like India, where rapid urbanization, changes in lifestyle, diet, and pollution occurs, vaccination is mandatory to prevent adverse events and even mortality [74]. Even though vaccines have been proven to be effective via various clinical trials, there are still people who hesitate towards vaccinations. Vaccine hesitation, education, affordability and reach are the factors that affects Indian population from being vaccinated. Vaccination in India, especially among people with diabetes is poorly promoted and educated [75].

WHO launched the Expanded Program of Immunization (EPI) in 1974, which India adopted in 1978, and was later called the Universal Immunization Program (UIP). Vaccination programs in India have found improvement, four decades after the launch of EPI and UIP [76]. But as all these programs were targeting the general population, vaccination programs or schedules specific for people with diabetes are lacking in India.

The urban population in India have access to education, financial stability, and comprehensive healthcare, through which they also get access to vaccines, while compared to the rural population [56].

Awareness of Vaccine-Preventable Diseases (VPD) is much needed in India. Epidemiological studies, collaborations between hospitals, patient education camps and awareness classes can create a much bigger change in the numbers of vaccination in India, especially among older people [57].

Harmonised recommendations

Raising awareness among health planners and healthcare providers about the crucial aspects surrounding the implementation of adult vaccines on a national scale is imperative, despite lingering uncertainties regarding effectiveness, safety, and financial implications. Although many prominent health societies in India have initiated adult vaccine programs, the absence of a standardized schedule for adults remains a notable gap [77].

Aligning with the above recommendations, we attempt to suggest a vaccination schedule for people with diabetes, specific to the Indian population (Table 1.).

While the benefits of vaccination are unequivocal, vaccination coverage remains low in many parts of the world, including in many developed countries. Vaccine hesitancy, which can be defined as a delay in accepting or refusing vaccines despite the availability of vaccine services, can be the reason to blame for the overall drop in vaccination coverage [78].

Education on vaccination is important to create awareness among the public about the necessity of taking vaccines. A strong recommendation from the doctor is found to be effective in building confidence and acceptance of vaccination

Table 1. Harmonised recommendations for the use of vaccines among people with diabetes in India

Disease	Available vaccines in India	Age group	Recommendation	Revaccination/schedule	Dose	Reference(s)
Pneumonia	Pneumovax 23 Prevenar 13	19–64 years	PCV13 if taken previously, vaccinate with PPSV23 one year later Already vaccinated with PPSV23 and PCV13* Vaccinate with PCV13. One year [†] later vaccinate with PPSV23	Schedule complete PPSV23 booster dose after 5 years [§]	0.5 mL	American Diabetes Association (ADA) [20] (2024) Centers for Disease Control Prevention (CDC) [53] (2024) Advisory Committee on Immunisation Practices (ACIP) [54] (2024)
Influenza	Influvac tetra (2024) FluLaval FluQuadri	≥ 6 months	Routine annual vaccination	Annual revaccination with the latest vaccine available	0.5 mL	Advisory Committee on Immunisation Practices (2023) [55] American Diabetes Association (ADA) (2024) [20]
Hepatitis B vaccine	Genevac B	≥ 20 years [^]	3 dose series; Dose 1 to be followed with dose 2 after a month. Dose 3 after 6 months	Schedule complete	1.0 mL	Advisory Committee on Immunisation Practices (2022) [56] American Diabetes Association (ADA) (2024) [20]
Tetanus, Diphtheria & Pertussis	Diphtheria-Tetanus-Pertussis vaccine adsorbed	All adults	Single dose	Every 10 years	0.5 mL	American Diabetes Association (ADA) (2024) [20] Advisory Committee on Immunisation Practices (2023) [57]
Herpes zoster	Shingrix vaccine	≥ 50 years	Single dose	2 doses at an interval of 2–6 months	0.5 mL	Advisory Committee on Immunisation Practices (2018) [58] American Diabetes Association (ADA) (2024) [35]
Respiratory Syncytial Virus infections	Respiratory Syncytial Virus vaccine	≥ 60 years	Single dose with shared decision-making with HCP [§]		0.5 mL	American Diabetes Association (ADA) (2024) [35] Centers for Disease Control and Prevention (CDC) (2024) [59]

*Review pneumococcal vaccine recommendations again when your patient turns 65 years old †Consider minimum interval (8 weeks) for adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak (CSF) leak §For adults with an immunocompromising condition, cochlear implant, or CSF leak, the minimum interval for PPSV23 is ≥ 8 weeks since last PCV13 dose and ≥ 5 years since last PPSV23 dose; for others, the minimum interval for PPSV23 is ≥ 1 year since last PCV13 dose and ≥ 5 years since last PPSV23 dose ^Hepatitis B vaccine may be administered at the discretion of the treating clinician based on the person's likelihood of acquiring hepatitis B infection §Single shot of vaccine to be taken once available in India, with shared decision making PPSV23 Pneumococcal Polysaccharide Vaccine 23, PCV13 Pneumococcal Conjugate Vaccine 13, PCV20 Pneumococcal Conjugate Vaccine 20, PCV15 Pneumococcal Conjugate Vaccine 15, HCP Health Care Professional

among patients. Appropriate management of electronic records, and vaccination cards, will help in the quick management of vaccination details of patients. A team approach can be utilized for monitoring and recommending vaccines. Partnering with local hospitals and community pharmacies will help in improving vaccination rates [79].

For the vaccination of younger children, parental knowledge about the vaccines is important. Motivational Interviews and face-to-face interactions with healthcare professionals were found to be effective in improving parental knowledge of vaccination. The reminder/recall method is the method by which a patient is communicated via messages, emails, and calls about their vaccination status. Such a method was found to be effective in childhood influenza, and adulthood vaccinations [79]. School-based vaccination camps and student interactions were found to be effective in improving vaccination rates [79, 80].

In India, vaccine hesitancy is common. Reasons for hesitancy include cultural and religious factors, co-existence of western (modern) medicine and indigenous medicine, lack of education on the role of vaccination, concerns on vaccine potential, and side effects are the major factors affecting vaccination rates [74].

Along with other strategies, vaccine education provided in a culturally responsive and sensitive way, has proven to improve vaccination among the people of India. An example to this statement was made by WHO during their polio campaign in India, where they involved religious leaders in its promotion. India was later (in 2014) declared polio-free by WHO [74, 81].

The goal of vaccination is the herd immunity that it provides. Vaccine promotion is important in a community, and community nurses should promote and ensure each individual is vaccinated in the community [82].

Conclusion

Diabetes stands as a pressing global health issue, necessitating vaccines such as Influenza, Pneumonia, HBV, and HZ to stave off associated infections. Despite the proven safety and efficacy of vaccines, widespread hesitancy poses a significant threat to global health. Vaccines play a pivotal role in preventing numerous diseases, annually saving 3–5 million lives worldwide. However, adolescents and adults often harbor concerns about vaccines, highlighting the importance of enhanced education regarding vaccine-preventable illnesses to assuage fears.

Encouragingly, vaccination rates have seen improvement globally, including in India, where uptake of DTP, Hepatitis, and Influenza vaccines has risen over the past five years. Nonetheless, certain regions in developing countries still

face challenges in accessing vaccines. Therefore, raising awareness about the importance of vaccination remains crucial, particularly in diabetes clinics, where individuals should be informed about recommended vaccinations alongside their diabetes management.

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