# Suggested use of vaccines in diabetes

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### ABSTRACT

Diabetes has emerged as a disease of major public health importance in India affecting the rich and the poor alike. Conventionally, comprehensive diabetes management is aimed at preventing micro and macro vascular complications. However, morbidity and mortality due to infections are also significant. In developing countries like India, the concept of adult immunization is far from reality. Recently the H1N1 pandemic has triggered the necessity for considering immunization in all age groups for the prevention of vaccine-preventable fatal infectious diseases. Considering the economics of immunization in a developing country, providing free vaccines to all adults may not be a practical solution, although the free universal immunization program for children is in existence for several decades. There is no consensus on the use of vaccines in diabetes subjects in India. However, there are some clinics offering routine pneumococcal, influenza and other vaccinations. Patients with diabetes have a deranged immune system making them more prone for infections. Hospitalization and death due to pneumococcal disease and influenza are higher in diabetes patients. They, like other healthy individuals, have a normal humoral response to vaccination with clinically significant benefits. The American Diabetes Association, Advisory Committee on Immunization Practices, Centers for Disease Control and Prevention, World Health Organization, United Kingdom Guidelines and a number of other scientific organizations have well defined guidelines for vaccination in diabetes. In this article we make some suggestions for clinicians in India, regarding use of vaccines in subjects with diabetes.

Key words: Diabetes, vaccination, immunization

# INTRODUCTION

According to the International Diabetes Federation (IDF) Diabetes Atlas, in 2011 India is already home to 61.3 million diabetes subjects and this number is predicted to reach 101.2 million by 2030.<sup>[1]</sup> Diabetes complications are looming large and 65% of the reported deaths are

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due to the cardiovascular complications.<sup>[2]</sup> Diabetes also confers an increased risk of developing and dying from infectious diseases and it is now considered an important complication of diabetes.<sup>[3]</sup> Indeed, the morbidity and mortality associated with infectious diseases like influenza and pneumonia, which are preventable by appropriate vaccination, are also very high. Although people of all ages are prone to infectious diseases like pneumonia and influenza, extremes of age and certain underlying medical conditions such as diabetes, asthma, and cardiovascular disease (CVD) aggravate the risk.<sup>[4]</sup>

Recommendations for vaccines assume great significance due to the increased prevalence of drug-resistant influenza and pneumococcal disease, and related complications in the elderly. The increased susceptibility

**Corresponding Author:** Dr. Jothydev Kesavadev, CEO and Director Jothydev's Diabetes and Research Centre, Kerala, India. E-mail: jothydev@gmail.com of diabetes subjects to pneumonia is mainly due to hyperglycemia, poor long-term diabetes control, longer duration of diabetes, decreased immunity, impaired lung function, pulmonary micro angiopathy, increased risk of aspiration and coexisting morbidity.<sup>[5]</sup> Longer duration of diabetes and poor glycemic control causes a 25–75% increase in the relative risk of pneumoniarelated hospitalizations in diabetes subjects emphasizing the increased importance of immunization in diabetes subjects.<sup>[6]</sup>

The Centers for Disease Control's (CDC's) Advisory Committee on Immunization Practices recommends influenza and pneumococcal vaccines for all individuals with diabetes.<sup>[7]</sup> A recent publication from India addresses the specific issue of Pneumococcal vaccination.<sup>[8]</sup>

In this article we review the role of all vaccinations in relation to diabetes. A systematic literature review was done and 52 studies were identified with particular focus on pneumonia and influenza vaccinations. Thirty-two Medline indexed studies are referenced along with Immunization Schedules and Morbidity and Mortality Week Reports (MMWR) by the CDC.

## **P**REVALENCE OF INFECTIONS IN **D**IABETES

### **Pneumococcal infections**

According to the World Health Organization (WHO), the mortality rate due to pneumococcal infections averages 10–20% while it may exceed 50% in high risk groups.<sup>[9]</sup> It is estimated that people with diabetes are almost three times at higher risk of death due to pneumonia-related complications.<sup>[10]</sup> Patients with Type 1 diabetes and type 2 diabetes have a 4.4- and 1.2-fold risk of pneumonia-related hospitalizations, respectively. Diabetes subjects with a HbA1c  $\geq$ 9% are at 60% increased risk of pneumonia-related with an A1c <7% have 22% increased risk in comparison to nondiabetic subjects.<sup>[6]</sup> There is increasing evidence which suggest that diabetes is one of the most common co-morbidities associated with pneumococcal infections.<sup>[11]</sup>

Diabetes mellitus is an independent risk factor for developing respiratory tract infections due to alterations of host defenses.<sup>[10,12]</sup> This is attributed to several factors such as

- Poor antibody response
- Cell mediated abnormalities
- Decreased CD4/CD8 lymphocyte ratios
  - Changes in natural killer cell function
  - Reduced lymphocyte blastogenesis
  - Defects in interleukin-2 function

- Reduced phagocytic function of monocytes
- Impaired leukocyte function
- Predisposition to colonization and pneumonia

A recent study shows that patients with preexisting diabetes are at increased risk of community-acquired pneumonia, mainly due to the worsening of existing cardiovascular and kidney disease.<sup>[13]</sup> Unfortunately there is no published data from India on the prevalence of pneumonia or influenza in diabetes patients.

### **Influenza Infection**

Mortality due to influenza is around 10,000–30,000 annually and people with diabetes are six times more likely to be hospitalized during an influenza epidemic<sup>[5]</sup> report that people with diabetes are six times more likely to be hospitalized during an influenza epidemic than those without diabetes, with the mortality varying between 5% and 15%. Evidence that influenza can trigger coronary complications, when taken in the context of diabetic subjects, gains more significance since the risk for CVD is already 2- to 4-fold higher in this sub group.<sup>[14]</sup> Sub group analysis and subsequent studies have shown vaccination to be efficacious as well as cost-effective in reducing hospital admissions as well as its associated complications.

A prospective study on the effects of a large-scale intervention with influenza and 23 valent pneumococcal vaccines in adults aged 65 years or older revealed that in general, vaccination leads to substantial health benefits and to a reduction of mortality from all causes in this age group.<sup>[15]</sup>

### **Hepatitis B infection**

Hepatitis B virus (HBV) causes a life-threatening liver infection that often leads to chronic liver disease and puts people at high risk of death from cirrhosis of the liver and hepato-cellular carcinoma.

Patients with diabetes are at a 2.1 times increased risk of infection by the HBV than nondiabetics.<sup>[16]</sup> HBV can be transmitted by medical equipment that is contaminated with blood that is not visible to the unaided eye.<sup>[17]</sup> Exposures to HBV may occur as a result of assisted monitoring of blood glucose and other procedures involving multi-patient use of finger stick devices designed for single-patient use and inadequate disinfection and cleaning of blood glucose monitors between patients.<sup>[18]</sup>

# **R**ECOMMENDATIONS FOR VARIOUS VACCINATIONS

### **Pneumococcal vaccination**

There are currently two types of pneumococcal vaccines:

Pneumococcal conjugate vaccine (PCV7 and PCV13) and pneumococcal polysaccharide vaccine (PPV). PCV13 is slowly replacing PCV7.<sup>[7]</sup> The minimum age for administration of PCV and PPV are 6 weeks and 2 years, respectively.

### Pneumococcal polysaccharide vaccine

Pneumococcal vaccine is a polyvalent, sterile, liquid vaccine for intramuscular or subcutaneous injection consisting of a mixture of highly purified capsular polysaccharides from the 23 most prevalent or invasive pneumococcal types of Streptococcus pneumoniae. The polyvalent polysaccharide vaccine contains 25 micrograms of purified capsular polysaccharide (0.5 ml per dose) from each of the 23 capsular types of Streptococcus pneumoniae, which is responsible for 90% of serious pneumococcal disease. The serotypes included in the vaccine are 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F. The six serotypes that cause invasive drug resistant pneumococcal infections (6B, 9V, 14, 19A, 19F, and 23F) are represented in the 23 valent vaccine.

### Pneumococcal conjugate vaccine

These are pneumococcal vaccines based on the conjugation of selected capsular polysaccharides to a protein carrier. The conjugate vaccine is supposed to be more efficient than the polysaccharide vaccine for the prevention of pneumococcal disease in children on account of immunological considerations and based on safety, immunogenicity, and efficacy trials.

Recommendations for vaccinations are based on the main risk factors for infectious diseases such as age, presence of chronic diseases, immuno-suppression, smoking status, alcohol use, and ethnic group. The organizations that have issued guidelines for pneumococcal vaccination include:

- American Diabetes Association (ADA)
- Advisory Committee on Immunization Practices (ACIP), USA.
- The Australian Technical Advisory Group on Immunization(ATAGI)
- The Canadian National Advisory Committee on Immunization
- · The United Kingdom Department of Health, and
- The Geriatric Society of India

Recommendations by different organizations on Pneumococcal Vaccination are listed in Table 1.

General indications for administration of Pneumococcal Polysaccharide Vaccination (PPV)<sup>[23]</sup> are enumerated in Table 2.

### Influenza vaccination

Influenza vaccine is recommended for all persons aged  $\geq 6$  months who do not have any contraindications to vaccination. Trivalent inactivated influenza vaccine (TIV) can be used for any person aged  $\geq 6$  months, including those with high-risk conditions. Live, attenuated influenza vaccine (LAIV) may be used for healthy nonpregnant persons aged 2-49 years. Since the safety or effectiveness of LAIV has not been established in persons with underlying medical conditions like chronic pulmonary (including asthma), cardiovascular (except hypertension) or metabolic (including diabetes mellitus) disorders that confer a higher risk for influenza complications, these persons should be vaccinated only with TIV. TIV contains inactivated viruses and thus cannot cause influenza. Only subvirion and purified surface antigen preparations of TIV (often referred to as "split" and subunit vaccines, respectively) are available. LAIV is administered intranasally, whereas TIV is administered intramuscularly.<sup>[24]</sup>

ACIP provides yearly guidelines on the prevention and treatment of influenza.<sup>[24]</sup> Pediatric guidelines from the American Academy of Pediatrics (AAP) are consistent with the ACIP recommendations for the 2011–2012 flu season.<sup>[25]</sup> According to the ACIP recommendations, vaccinating individuals at high risk before the influenza season each year is the most effective measure for reducing the impact of influenza. Annual influenza vaccination is recommended for all diabetes patients, both type 1 and type 2. On account of the change in circulating strains (antigenic drift) and waning immunity, yearly revaccination is required.

Recommendations by different organizations for Influenza vaccination is listed in Table 3.

General indications for Influenza vaccination.<sup>[24]</sup> is enumerated in Table 4.

Fluzone high dose is an approved inactivated vaccine for subjects  $\geq 65$  years. People in this age group are at highest risk for seasonal influenza complications, which may result in hospitalization and death.<sup>[24]</sup> In clinical studies, Fluzone High-Dose demonstrated an enhanced immune response compared with Fluzone in individuals aged 65 years and older.<sup>[29]</sup>

### **Hepatitis B vaccination**

On the basis of available information about HBV risk, morbidity and mortality, available vaccines, age at diagnosis of diabetes, and cost-effectiveness, ACIP 2012 recommends Hepatitis B vaccination for all unvaccinated adults with diabetes younger than 60 years as soon as feasible after

Organization	Recommendation	Revaccination
1. American Diabetes Association. <sup>[19]</sup>	All diabetic subjects $\ge$ 2 years of age.	<ul> <li>a. A onetime revaccination is recommended for individuals &gt;64 years of age if the vaccine was administered &gt;5 years ago.</li> <li>b. Other indications for repeat vaccination include nephrotic syndrome, chronic renal disease, and other immunocompromised states, such as posttransplantation.</li> </ul>
2. Advisory Committee on Immunization Practices. <sup>[7]</sup>	<ul> <li>a. All persons at age 65 years.</li> <li>b. Adults aged 19-64 years with chronic medical conditions like chronic heart disease, chronic lung disease, diabetes mellitus, asthma, etc.</li> <li>c. PPV is recommended for children aged 2 years or older with certain underlying medical conditions, including diabetes mellitus.</li> </ul>	<ul> <li>a. Those who received PPV before age 65 years for any indication should receive another dose at age 65 years or later if at least 5 years have passed since their previous dose. Those who receive PPV at or after age 65 years should receive only a single dose.</li> <li>b. A second dose of PPV is recommended 5 years after the first dose for persons aged 19–64 years with functional or anatomic asplenia and for persons with immunocompromising conditions</li> <li>c. Single revaccination should be administered after 5 years to children with functional/ anatomic asplenia or immunocompromising condition.</li> </ul>
3. Australian Technical Advisory Group on Immunization. <sup>[20]</sup>	<ul> <li>a. All persons aged ≥ 65 years</li> <li>b. People aged ≥ 10 years who have underlying chronic illnesses predisposing them to including, acute nephrotic syndrome chronic cardiac, renal or pulmonary disease, diabetes, etc.</li> <li>c. Tobacco smokers.</li> <li>a. Children ≤ 9 years of age who have underlying chronic illnesses.</li> </ul>	
4. Canadian National Advisory Committee on Immunization. <sup>[21]</sup>	<ul> <li>a. All individuals ≥ 65 years of age</li> <li>b. Children ≥ 5 years of age and adults who have not previously received pneumococcal vaccines should be vaccinated with Pneu-P-23. Pneu-C-7 is not contraindicated in children ≥ 5 years of age with high-risk conditions.<sup>[21]</sup></li> </ul>	
5. The United Kingdom Department of Health. <sup>[22]</sup>	<ul> <li>a. All adults over the age of 65</li> <li>b Children under the age of 5 who have previously had invasive pneumococcal disease.</li> <li>a. Consider all patients over the age of 2 months with increased risk for the following including type I diabetes mellitus, or type 2 diabetes requiring oral hypoglycemic drugs. It does not include diabetes that is diet-controlled.</li> </ul>	
6. The Geriatric Society of India. <sup>[23]</sup>	Persons aged 50 years and above.	

Table 1: Recommendations by different organizations on pneumococcal vaccination
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# Table 2: General indications for administration of pneumococcal polysaccharide vaccination<sup>[7]</sup>

Individuals aged 65 years or older. Subjects with diabetes aged 2 years and above. Other medical conditions Chronic lung disease (including asthma) and who smoke cigarettes Chronic cardiovascular diseases Immunocompromising conditions (including chronic renal failure or nephrotic syndrome) Chronic liver diseases, Cirrhosis, Chronic alcoholism Functional or anatomic asplenia (e.g., sickle cell disease or splenectomy) Cochlear implants Cerebrospinal fluid leaks.

diagnosis. Hepatitis B vaccination may be administered at the discretion of the treating clinician to unvaccinated adults with diabetes who are aged  $\geq 60$  years.<sup>[30]</sup> This may be based on likelihood of acquiring the infection at chronic care facilities (assisted blood glucose monitoring, insulin injections). Patients with Chronic Kidney Disease including those on hemodialysis should also be vaccinated.<sup>[31]</sup>

The vaccine is made from the inactivated (dead) hepatitis B virus. Two single-antigen recombinant hepatitis B vaccines are available. Hepatitis B vaccination usually consists of three doses of vaccine administered intramuscularly at 0, 1, and 6 months.<sup>[32]</sup>

# **EFFICACY AND SAFETY OF PNEUMOCOCCAL** AND INFLUENZA VACCINATIONS

The efficacy and safety of pneumococcal vaccine have been shown in multiple case control studies as ranging from 56% to 81%.<sup>[33]</sup> In an indirect cohort analysis,<sup>[34]</sup> the efficacy of PPV23 was found to be 84% in diabetic patients and the efficacy of the vaccine did not decline with increasing interval after vaccination. In a retrospective

Organization	Vaccination
1. American Diabetes Association, Immunization Guidelines 2012. <sup>[19]</sup>	a. Influenza vaccine is recommended annually for all diabetic patients $\geq$ 6 months of age.
1. CDCs ACIP 2011–12 Influenza Vaccination Guidelines. <sup>[24]</sup>	a. Routine immunization (annual vaccination) is now recommended for anyone $\geq$ 6 months as soon as vaccine is available.
	b. Children aged 6 months to 8 years whose vaccination status is unknown or who have never received seasonal influenza vaccine before as well as children who did not receive at least 1 dose of influenza A (H1N1) 2009 monovalent vaccine regardless of previous influenza vaccine history should receive 2 dose of 2010-2011 seasonal influenza vaccine (minimum interval 4 weeks) during the 2010-2011 season.
2. Australian Technical Advisory	a. All individuals aged 65 years and over.
Group on Immunization. <sup>[26]</sup>	b. All Aboriginal and Torres Strait Islander peoples aged 15 years and over c. Pregnant women.
	d. Individuals aged 6 months and over with medical conditions predisposing to severe influenza including cardiac disease, chronic respiratory disease, diabetes and other metabolic disorders, renal disease, etc.
4. Canadian National Advisory Committee on Immunization for	a. Influenza vaccine may be administered to people of any age who are residents of nursing homes and other chronic care facilities, people $\geq 65$ years of age and healthy children 6–23 months of age. <sup>[32]</sup>
the 2011-2012 Season. <sup>[27]</sup>	<ul> <li>Adults (including pregnant women) and children with the following chronic health conditions are recommended recipients of Influenza Vaccine like cardiac or pulmonary disorders, diabetes mellitus and other metabolic diseases, renal disease, etc.</li> </ul>
5. The United Kingdom	a. All individuals aged 65 or over.
Department of Health. <sup>[28]</sup>	b. All those aged 6 months or over in a clinical risk group like chronic respiratory disease, heart disease, renal disease, liver disease, diabetes including Type 1 diabetes, Type 2 diabetes requiring insulin or oral hypoglycemic drugs and diet-controlled diabetes.

## Table 3: Recommendations by different organizations for influenza vaccination

#### Table 4: General indications for influenza vaccination

All diabetic patients ≥6 months of age Other medical conditions (compelling indications) Age≥ 50 years Chronic pulmonary diseases (including asthma) Cardiovascular diseases (except hypertension) Renal, hepatic, neurologic, hematologic disorders Metabolic disorders

study of a large cohort of 47,365 subjects aged 65 years or older, evidences suggest a vaccine effectiveness of 44% against pneumococcal bacteremia and hence its cost effectiveness for this indication.<sup>[35]</sup> There are a few studies claiming cost-effectiveness of pneumococcal vaccine and the most notable is a study from the US showing the vaccine to be highly cost effective in preventing pneumococcal bacteremia in people aged >65 years.<sup>[36]</sup> Pneumococcal vaccine is considered a safe and time-tested vaccine where moderately severe systemic reactions like fever and myalgia are uncommon while severe anaphylactic reactions are extremely rare.<sup>[37]</sup>

The newly licensed conjugate vaccine holds promise as a novel way of improving the immunogenicity of pure polysaccharide antigens and also of polysaccharides converted to T-cell dependent forms by protein conjugation.<sup>[38]</sup>

Literature search reveals statistically significant increase of antibody titer and an increased percentage of B-lymphocytes 1 week after influenza vaccination in diabetic subjects marking valid protection against the influenza virus. In a nested case-control study conducted during the 1999–2000 influenza A epidemic which was part of the Prevention of Influenza, Surveillance and Management (PRISMA) study, it was observed that adults with type 2 diabetes benefited considerably from influenza vaccination. Vaccination was associated with a 56% reduction in any complication (95% CI 36–70%), a 54% reduction in hospitalizations (26–71%), and 58% reduction in deaths (13–80%).<sup>[39]</sup>

### **Other vaccinations**

According to the Diabetes Public Health Resource of the Centers for Disease Control and Prevention, the following vaccinations are recommended for diabetes patients<sup>[40]</sup> In the Indian scenario there is a lack of evidence supporting the routine use of all the vaccines listed by CDC. Patients can be counseled on the necessity for Pneumococcal and Influenza vaccines, but other vaccines may be considered optional. It is quite obvious that immunization against vaccine preventable infections will be of considerable benefit in diabetes but their long-term cost effectiveness needs to be evaluated.

Recommended vaccines for diabetes patients<sup>[41]</sup> are given in Table 5.

# STRATEGIES TO IMPROVE THE RATE OF VACCINATION

Maintaining a diabetes registry, systemic tracking system, and reminder system serve as tools for improvising the acceptance to vaccination.<sup>[42]</sup> Standing Orders Programs (SOPs) that allow nonphysician medical staff to assess eligibility and administer vaccines without an individualized physician's order are a proven method to increase vaccination rates.<sup>[43]</sup> However, recent data on their use are not available.<sup>[44]</sup> Close follow-up by the

Vaccines	Doses
Pneumococcal	1 or 2 doses
(polysaccharide)	
Influenza	1 dose TIV annually
Tetanus diphtheria Pertussis	Substitute 1- time dose of Tdap; then
(Td/Tdap)	boost with Td every 10 years
Measles Mumps Rubella	1 or 2 doses, 4 week interval
(MMR)	
Varicella	2 doses, at least 4 weeks apart
Zoster	1 dose, ≥ 60 yrs
Hepatitis B	3 doses
Human Papillomavirus (HPV) Female.	3 doses through age 26 years. The second dose should be
Temale.	administered 1–2 months after the
	first dose; the third dose should be
	administered 6 months after the first
	dose (at least 24 weeks after the
	first dose).
Human Papillomavirus (HPV) Male.	3 doses through age 21 years

### Table 5: Recommended vaccines for diabetes patients

diabetes treatment team of the subjects especially with those aged  $\geq$ 65 years would help achieve the vaccination goals in the most vulnerable groups. Communication with the subjects about the need for vaccination and initiatives like educational packages on immunization, etc., will help generate awareness on the importance of immunization. Setting up a vaccine-only clinic as adjunct or making provision for vaccination during routine visits to the clinic and strictly following the ADA and ACIP recommendations, are some of the strategies for effective immunization. According to the ADA position statement, benchmarking organizations and national policy should emphasize guideline implementation strategies for improving the rate of immunization.<sup>[45]</sup> Successful implementation of standing orders for vaccination and immunization are essential for increasing vaccination rates. Periodic training of the staff accompanied by ongoing assessment of immunization rates, work flow, and missed opportunities to immunize patients are critical to sustain and enhance improvements.<sup>[46]</sup> There should be a detailed plan for the program's infrastructure, key service delivery components and quality assurance.[47]

In the Indian clinic set up, the diabetologist, dietitian, diabetes educator, pharmacist, psychologist, and other members of the diabetes care team may take over the responsibility of counseling the patients on the availability and requirement of routine vaccinations. Use of educational material in local language, discussion on vaccination during diabetes education and the use of vaccination cards will boost confidence among the patients. Some of the strategies that may improve the rate and outcomes of vaccination include:

- Identification of eligible candidates for vaccination.
- Informing the patients and caregivers regarding the benefits and risks of the vaccination and documenting the delivery of that information.
- Documenting refusal to take vaccination or presence of

a contraindication like allergy to egg, a recent episode of Guillain–Barre syndrome, etc.

- Recording the administration of a vaccine and records of revaccination or postvaccination adverse events.
- Providing a documentation of vaccine administration to subjects like vaccination card with full information regarding the vaccines.

The standing order protocols should be implemented such that the health care professionals should be trained to:

- screen patients who are most likely to benefit from and identifying those with contraindications to vaccinations
- administer vaccines
- monitor patients for adverse events.

The standards for adult immunization practice established by the National Coalition for Adult Immunization recommend a standard personal and institutional immunization record to verify the immunization status of patients and thus avoid the risk of inappropriate revaccination. Also a close followup with the vaccinee or his care giver by the treatment team or health care professional is highly beneficial in minimizing the risk of inappropriate re-vaccinations. The protocols should also aim at implementing a quality assurance process so that the standards of care are maintained.

## **EXPERIENCE WITH VACCINATION IN INDIA**

In India, till date there is lack of consensus or published guidelines on vaccination in diabetes. There are some clinics offering routine pneumococcal and influenza vaccinations while other clinics do not recommend any vaccinations. From the available evidence, the two vaccinations which will be of profound clinical benefit and cost effective in diabetes subjects would be influenza and pneumococcal vaccines.

We present experiences with vaccination at two diabetes centers in India–one from south and one from north India.

In a Diabetes Research Center located in Trivandrum, south India, pneumococcal vaccine has been routinely administered to all consenting subjects with diabetes since 2005. Influenza vaccination has also been similarly practiced since 2009. During clinic visits, patients and their caregivers, are briefed on the availability of pneumococcal and influenza vaccines, its advantages in diabetes and long-term safety and efficacy. They are also provided with vaccination cards.

Affordability, willingness, and attitude toward the procedure are taken into consideration before vaccinating each subject. On analysis of the electronic data of subjects on regular follow up with the Diabetes Tele Management System (DTMS<sup>®</sup>) at Jothydev's Diabetes and Research Centre JDC,<sup>[48]</sup> of the 2057 subjects who underwent pneumococcal vaccinations, only 17 reported mild pain and redness at the

site of injection which subsided in a day or two with oral paracetamol tablet. A total of 908 patients underwent flu shots since 2009 and none of them reported any injection side reactions or allergic responses. We found that 73% of the subjects aged >65 years had been administered the vaccine during one of their routine consultation visits. Of the subjects who received the pneumococcal vaccine 23% of the subjects were suffering from various diabetes-related complications like CVD, renal disease, retinopathy, etc. Age, gender, marital status, geographic area, educational level, occupation, type, duration and therapy of diabetes, and co-morbidities did not have a statistically significant effect on vaccination acceptance.

In a diabetes clinic at Kolkata, 1568 patients (duration >5.3 years) with diabetes were vaccinated against pneumonia and flu till December 15, 2010. The only side effects observed were aches or pain in joints or muscles, fever, local rash, or swollen glands. No severe allergic reactions were reported. Incidence of flu was drastically less with reduction of symptoms and absenteeism from flu when compared with the mean event rate as observed in the past 6 years.

# Suggested Recommendations for Vaccination in India

Based on our experience we make some recommendations

### Table 6: The suggested criteria for vaccination

- i. All adult diabetes subjects should be educated about administering pneumococcal and influenza vaccine and those above the age of 60 years should be strongly advised to be vaccinated.
- ii. Children with diabetes ≥ 2 years of age can be given pneumococcal polysaccharide vaccine and children above 6 months of age, influenza vaccine.
- iii. Other vaccines may be administered in diabetes subjects based on need.
- iv. Patients with renal failure in any age group can be immunized.
- v. People with diabetes and immunocompromised state due to concomitant conditions can be immunized irrespective of their age.
- vi. Patients with diabetes and chronic lung diseases like chronic obstructive pulmonary disease (COPD), bronchial asthma may be immunized irrespective of their age.
- vii. People of any age with diabetes who smoke may be immunized.

### Table 7: Contraindications to vaccination

- i. Hypersensitivity to the active substances or to any of the excipients of the vaccine.
- ii. History of chicken egg allergy particularly when considering flu shot. In these patients, chemoprophylaxis with amantadine/rimantadine or immunization using a protocol as reported by Murphy and Strunk need to be considered.<sup>[49]</sup> According to this protocol, egg-allergic patients with positive skin-test results could be safely administered the influenza vaccine through multiple, graded injections.
- iii. Recent history of Guillain-Barre syndrome within 6 weeks of a previous influenza vaccination in the case of flu shot.<sup>[50]</sup>
- iv. In addition, immunization should be postponed in patients with febrile illness or any acute infection.

for the use of pneumococcal and influenza vaccinations in patients with diabetes in India.

The suggested criteria for vaccination are listed in Table 6.

Contraindications to vaccination are listed in Table 7.

### CONCLUSION

Apart from considering conventional micro and macro vascular events as diabetes complications, infections due to influenza and pneumococci should also be regarded as having significant public health importance. All clinics where vaccinations are being advocated for diabetes should keep records of it so that efficacy of the vaccination may be assessed in relation to occurrence of fever, pneumonia, or hospitalization in vaccinated individuals compared with nonvaccinated subjects. Vaccination strategies in diabetes should evolve as part of routine care and a central registry need to be maintained. Long-term studies and research aimed at evaluating the cost-effectiveness of vaccination among diabetes patients in India would provide more evidence and support for the suggested vaccination guidelines.<sup>[50]</sup>

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