

Pneumococcal Vaccine in Diabetes : Relevance in India

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Abstract

Currently we have more than 65 million Diabetes patients in India with estimated 80 million prediabetics. Diabetes is a immunologically vulnerable population to develop all types of microbial infections. Pneumococcal infections do have a substantial morbidity and mortality burden in the community. India has a large geriatric pool now which has substantially increased pneumococcal disease burden. Diabetes is a well-known risk factor for pneumococcal infection and predisposes individuals to nasopharyngeal colonization with the pneumococcus which is associated with invasive infection. In diabetics who are elderly, with chronic kidney or pulmonary disease and long standing duration of the disease with poor glycemic control are the highest risk group susceptible to invasive pneumococcal disease. With now availability of Pneumococcal vaccine in India, now it may be an preventive option which can be offered. Most global organisations recommend pneumococcal vaccination to diabetics.

Introduction

India has the second largest diabetes population in the world with 65 million diabetics and over 80 million prediabetics. Diabetes mellitus is a heterogeneous group which has essentially four major types of which Type 1 is autoimmune and Type 2 is insulin resistance. Host defence of each diabetic however is compromised and thus they are prone to all microbial colonisation, infection and invasion. With the dual jeopardy of large diabetes pool especially in the elderly the role of pneumococcal disease become relevant in the Indian context.

Diabetes and Immune Vulnerability and Infection Proneness

Diabetics have a poor antibody response with a host of cell mediated immune abnormalities. They have decreased CD4/CD8 lymphocyte ratios which lead to changes in natural killer cell function, reduced lymphocyte blastogenesis, defects

in interleukin-2 function, and reduced phagocytic function of monocytes. Diabetic have classically impaired leukocyte function and thus are predisposed to colonization and pneumonia. Patients with diabetes have a high risk for microbiological infections (fungal, viral and bacterial) leading to complications with high morbidity and mortality. Clinically, most important infections are fungal and bacterial infections of the skin, urinary tract, respiratory tract. Other factors associated with diabetes (age, renal disease, and cardiovascular disease) have been shown to be significant co-morbid factors that can increase the risk of sequel of certain infections.

People with diabetes are susceptible to pneumococcal infection and are at increased risk

for the morbidity and mortality. Additional risk is associated with being age ≥ 65 years and having chronic cardiovascular, pulmonary, and renal disease. Diabetes mellitus has been identified as an independent risk factor for developing respiratory tract infections. There are no data on the burden of lower respiratory infections in India. World Health Organization data from low and middle income countries suggest that lower respiratory tract infections remain the third leading cause of death. *Streptococcus pneumoniae* remains the major cause of pneumonia. Apart from pneumonia and its complications, viz., empyema and lung abscess, the pneumococcus also causes other clinical syndromes such as sinusitis, otitis media, tracheobronchitis, bacteremia, meningitis and peritonitis, some of which have high case fatality rates. Diabetes is a well-known risk factor for pneumococcal infection and predisposes individuals to nasopharyngeal colonization with the pneumococcus which is associated with invasive infection. Pneumococcal pneumonia is the most common form of acute bacterial community acquired pneumonia. Bacteremia is seen in nearly 30% (8-50%) of individuals with pneumococcal infections, and of these, 15-20% are fatal despite treatment with antibiotics. Also, there are several studies which show that diabetes is one of the most common co-morbidities

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in patients with pneumococcal infection.¹

Preventive Strategies of Pneumococcal Disease

Assessment of the burden of disease due to vaccine-preventable disorders clearly shows that pneumococcal disease is the leading cause of death in all age groups with elderly population being the most affected. The high case fatality rate from bacteremic pneumococcal disease demands effective preventive strategies including immuno-prophylactic measures and vaccines. However in diabetic populations such strategies may be challenging due to immune abnormalities seen with diabetics. The antibody response of diabetics especially in high risk groups needs to be studied with various vaccination strategies. 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 which include diabetes. The organizations that have issued guidelines for pneumococcal vaccination in diabetes 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, The Geriatric Society of India among several others.

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. The minimum age for administration of PCV

and PPV are 6 weeks and 2 years, respectively.

Efficacy and Safety of Pneumococcal Vaccination

The efficacy and safety of pneumococcal vaccine have been shown in multiple case control studies as ranging from 56% to 81%.¹² In an indirect cohort analysis, 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 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.¹⁰ 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.¹¹ 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.²

Suggested Recommendations for Vaccination in India

Adult immunization in India is in its infancy. Currently based on global guidelines, it seems prudent to vaccinate all diabetics for both pneumococcal and influenza both. Based on our experience we make some recommendations for the use of pneumococcal and influenza vaccinations in patients with diabetes in India. Pneumococcal vaccination is most useful in diabetics above 65 yrs (geriatric population, diabetics with chronic kidney disease, diabetics with chronic cardio pulmonary diseases (COPD, Asthma, CCF) and diabetics under going transplantation. All

long standing diabetics more than 10 years as well as one with complications need vaccination. Diabetics with poor Glycemic control (glycosylated Hb > 7) need strong immune surveillance and thus become vaccine candidates.

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