

Short Communication

Adult Pneumococcal Vaccination: The place of PPSV23 after Launch of PCV20

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ABSTRACT

Adult vaccination for pneumococcal pneumonia and invasive pneumococcal disease has faced challenges of low awareness and vaccination rates in India. Both the pneumococcal polysaccharide 23-valent vaccine (PPSV23) and 13-valent conjugate vaccine (PCV13) have been available in India and are part of guidelines and recommendations for elderly adults. Recently PCV20 has also been introduced for adults in India. Given India's diverse socioeconomic profile, as well as generally lower drive among adults for appreciating the need, and spending on vaccines for themselves as compared to their children, it is imperative to use all available vaccines appropriately in adult pneumococcal vaccination practice. Current and evolving pneumococcal serotype epidemiology in Indian adults, availability of real-world data, cost and access of these vaccines, will determine the future pneumococcal vaccination landscape in our country.

KEYWORDS

• Pneumococcal • PPSV23 • PCV13 • PCV20 • Serotype • Adult Vaccination

INTRODUCTION

Pneumococcal vaccination is indicated for elderly adults and all adults with medical comorbidities and immunosuppressive conditions. Despite advances in antibiotics and vaccines, community-acquired pneumonia

(CAP) remains the most persistent cause of infection-related mortality globally. *Streptococcus pneumoniae* (pneumococcus), is the most common bacterial cause of CAP, particularly to the non-immune elderly, due to their propensity to develop invasive

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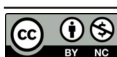
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pneumococcal disease (IPD), together with the predilection of the pathogen for the heart, leading to cardiovascular events (CVEs), particularly during the first seven days of acute infection, which is now recognized as a relatively common complication of IPD.¹ CVEs are seen in 20-25% pneumococcal CAP cases, and this greatly steps-up in-hospital mortality rates by almost 2-3 times, along with increasing duration of hospital stay and re-hospitalization rates.²

In India, Pneumococcal disease is a major health burden causing approximately 1.6 million pneumonia cases and 160,000 deaths annually. 65-70% cases occur in adults, with those 60 years and older (contributing to 32%), at-risk populations with compromised immune systems, and rural communities with limited healthcare facing particularly high rates of severe infection and mortality (up to 28%).^{3,4}

Adult Pneumococcal Vaccination

Clinical consensus guidelines have advised offering the pneumococcal polysaccharide vaccine PPSV23 vaccination in the Indian population (≥ 50 years) and emphasizing PPSV23 vaccination for the elderly (≥ 60 years) due to the higher risk of IPD.⁵ For adults with coexisting conditions like diabetes, smoking, COPD, high risk/severe asthma, and chronic lung, heart, kidney or liver disease, pneumococcal vaccination should be offered at the time of diagnosis or early in the course of management. For those adults with significant medical comorbidities or immunosuppressive conditions/treatment, both the pneumococcal

conjugate vaccines PCV13, followed by PPSV23 are recommended.

A systematic review and meta-analysis of 32 studies reported PPSV23 vaccine effectiveness (VE) against IPD that ranged from 50% (cohort studies) to 54% (case-control studies) and was found to align with the estimates reported by the CAPiTA study for PCV13 (48.5%).⁶ Sequential PCV13/PPSV23 vaccination had a high vaccine effectiveness (80.3%) against CAP in the hospitalized elderly (≥ 65 years).⁷ A study from Vellore, India revealed that serotype coverage offered by the pneumococcal conjugate vaccines PCV13, and pneumococcal polysaccharide vaccine PPSV23 were 64%, and 73%, respectively.⁸ This study also found 30% of the isolates were of non-vaccine serotypes among patients ≥ 50 yr of age with CAP.

Pneumococcal vaccination covers a dismal less than 1% adult population in India. Lack of awareness, understanding and of course cost remain main reasons.⁹ While adults from mid-upper socio-economic class show high awareness and willingness to vaccinate their children even at higher cost, but when it comes to themselves, adults often show ignorance and lack of willingness to spend on vaccines.

Pneumococcal Adult Serotypes and Vaccines

Figure 1 shows the pneumococcal serotypes in adults in India for CAP, and also shows the coverage by PPSV23 and the recently introduced PCV20.¹⁰ In IPD, the strains 3, 22F and 9N contributed to 15, 10.5 and 7% of infections in adults.¹¹

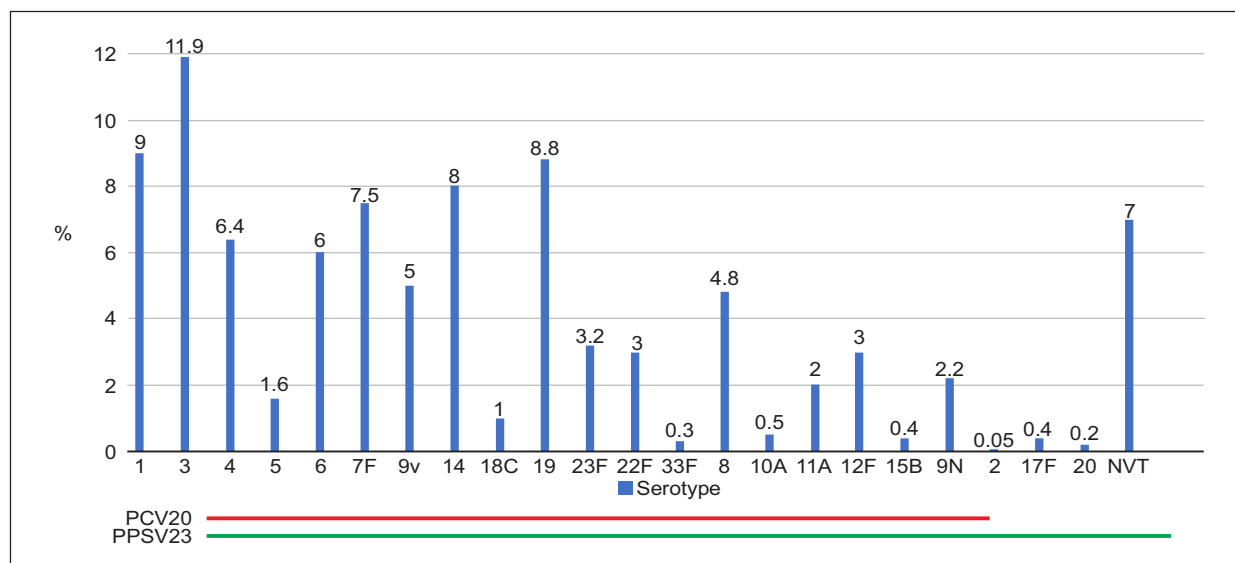


Figure 1: Pneumococcal Pneumonia serotypes in Adults

On comparing the strain coverage of different adult pneumococcal vaccines (Figure 2), PPSV23 followed by PCV20 show high rates.¹²

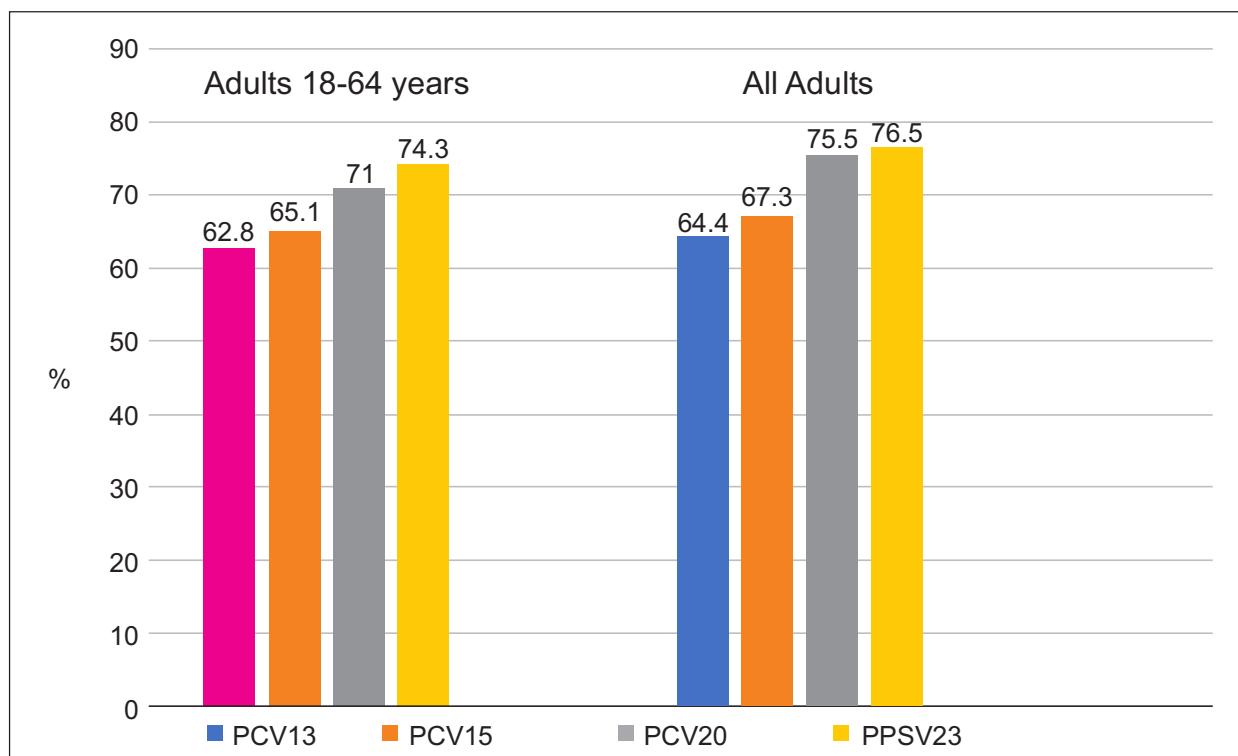


Figure 2: Serotype coverage by Pneumococcal Vaccines in Adults

In India, a study found that the predominant non-vaccine serotypes in adults were 13, 34, 35B, 31 and 16F.¹³ PPSV23 gives additional cover of serotype 2, 9N, 17F and 20 as compared to PCV20. Serotype 9N covered only by PPSV23, has been seen to cause 2.2% of adult pneumococcal CAP but up to 7% adult IPD, while serotype 2, 17F and 20 account for less than 1% infections, however serotype 17F is among the serotypes found in carriage and some invasive cases, especially in older adults aged 45–65 in India.¹⁴

Unlike cross protection in adults seen with the 6A and 6B strains, this is not true with 9V and 9N. At postimmunization, the geometric mean opsonic indices (OIs) for 6B and NVTs (6A, 6C, and 6D) significantly increased in both elderly and younger adults.¹⁵ The geometric fold increases of OIs were >3 times for all 4 serotypes, and >18 times for 6A and 6B. This demonstrated that 6B in PPSV23 induced cross-functional immune responses against serotypes 6A, 6C, and 6D. Serotypes 9N and 9V comprise about 90% of the group 9 disease isolates, and type 9N is more common than type 9V in adults, and type 9V predominates in infants and children. However, there is no

conclusive evidence of cross-protection from serotype 9V (included in current PCVs) to serotype 9N.^{16,17}

PCV20 was launched in India in August 2025. A pivotal phase 3 trial showed that PCV20 immune response was noninferior to PCV13 for the 13 shared serotypes and to PPSV23 for 6 of the 7 additional serotypes, demonstrating strong immune responses and a safety profile similar to both existing vaccines.¹⁸ In the cohort of patients from US and Sweden, statistical noninferiority criteria were met for 6 of 7 additional serotypes between PCV20 and PPSV23 (Serotype 8 did not meet noninferiority).¹⁹ The same was seen with the study in the cohort from Japan, South Korea, and Taiwan.²⁰ Serotype 8 has emerged as one of the prevalent serotypes causing IPD in adults. Morphologically, serotype 8 strains can exhibit increased adhesion and biofilm formation.²¹ While local and systemic adverse events (AEs) were similar between PCV20 and PCV13/PPSV23, the AE rate in those aged ≥60 years causing withdrawal from the study, was 30% higher in PCV20 group due to redness or swelling with or without pruritus at the injection site, palpitations, and anxiety. No AEs

led to withdrawal with PPSV23.^{19,22} The data with the Indian cohort is yet to be published.

PCV vaccines rely on a T-cell independent immune response, so like PCV13, PCV20 also induces a T-cell-dependent response, resulting in robust immunological memory by the activation of memory B cells and mucosal immunity, both providing longer-lasting and more effective protection against pneumococcal disease.²³ Polysaccharide-based vaccines can lead to hyporesponsiveness, where repeated vaccinations produce lower levels of antibodies, while PCV, which chemically links purified polysaccharides to a carrier protein, promotes consistent and increasing antibody levels with each dose. PCV20 has demonstrated efficacy comparable to PCV13, while offering broader serotype coverage by including seven additional serotypes (8, 10A, 11A, 12F, 15B/15C, 22F, 33F) beyond PCV13, which could help prevent 25–35 % more IPD cases and a substantial number of non-bacteremic pneumonia cases particularly in immunocompromised or comorbid elderly populations. Another critical advantage of PCVs is its ability to reduce nasopharyngeal Pneumococcal carriage, a key factor in achieving herd immunity and reducing community transmission.

Current Place of Different Pneumococcal Vaccines in Adults

In India, factors like access, price, availability, and real-world clinical experience are all determining points in adult vaccination. As mentioned, the most important point currently is to increase the rate of adult pneumococcal vaccination in India that is at a dismal <1%, and for this all the available vaccines should be utilized judiciously and appropriately. Vaccination with PCV13 and PPSV23 have been ongoing for many years in India. Recently PCV20 has also been introduced, which is currently at a 40% higher cost as compared to PPSV23, with its access, availability, and clinical experience expected to grow with time. Therefore, the following is suggested to accord a rightful place to all these pneumococcal vaccines.

- a) Elderly population above 50 years without significant comorbidities, and no evidence of immunosuppression who have not received any pneumococcal vaccine in adulthood, can be given a shot

of PPSV23, or PCV20 which has recently become available in India, depending on access, and practical clinician's experience and preference.^{5,24,25}

- b) Adult population with significant medical comorbidities or immunosuppression, are being given PCV13 followed by PPSV23 at a minimum gap of 8 weeks due to widest coverage and experience with this combination. These patients instead can also be given a single shot of PCV20 which is now available in India.
- c) Many patients with comorbidities have already received one of these vaccines (PCV13 or PPSV23) at or soon after their diagnosis. If PCV13 has already been given, PPSV23 is being given for both coverage and cost effectiveness, any time after 8 weeks or up to 1 year after PCV13. These patients can now also receive a single dose of PCV20 instead.
- d) If PPSV23 has already been given, depending on the type and severity of the comorbidity, the doctor can decide to give PCV20 or PCV13 at a gap of 1 year on a case-to-case basis.^{3,25}
- e) For revaccination, patients with high risk who have received both PCV13/PPSV23, can be given PCV20, 5 years after the last vaccine.²⁴

CONCLUSION

As India has a diverse socioeconomic profile, as well as variable pneumococcal immunization status in adults, both the tried and tested PPSV23 with widest coverage, as well as the newly introduced PCV20 have their place in adult pneumococcal vaccination practice based on patient factors, doctor's experience and access/availability. More and recent data on serotype epidemiology in Indian adults, and availability of real-world data for these vaccines, will shape the future pneumococcal vaccination adult guidelines, and clinician's practice, as well as pave the way to rapidly and robustly increase adult pneumococcal vaccination rates in our country.

Conflicts of interest: None

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Ethical declaration: Not Applicable

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