Indian J Med Res 142, September 2015, pp 241-243
DOI:10.4103/0971-5916.166528

Commentary

Knowledge of serotype prevalence & burden of invasive pneumococcal disease: a prerequisite to vaccine introduction in the country

Estimating the exact pneumococcal disease burden in India continues to be challenging, while morbidity and mortality rates remain high. Vaccination to prevent invasive pneumococcal infections has not yet been introduced in the Universal Immunization Programme (UIP), even as paediatricians advocate its use. Studies on serotype prevalence are still relevant in the Indian context. Some multicentric and single centre studies on serotypes involved in invasive pneumococcal disease (IPD) have been published[1,2]. Unlike other bacterial infections, burden of IPD continues to pose a problem worldwide by its varied epidemiological pattern, changing cellular and virulence characters and complex detection methods. World Health Organization in 2008 estimated high burden of pneumonia in Asia with most cases in India (43 million), China (21 million) and Pakistan (10 million), and additional high numbers in Bangladesh and Indonesia[3]. An ideal pneumococcal vaccine which is a preventable cause of morbidity and mortality in children and high risk adults, has eluded immunization programmes. Prato *et al*[4] has highlighted a changing scenario of the disease since the introduction of 23 valent polysaccharide vaccine. Studies on pneumococcal disease and its epidemiology are compounded by problems associated with establishing an aetiological diagnosis to determine serotype prevalence. Although several single site and a few multi site reports have been published, these have not been collated to get a nationwide comprehensive data in India.

The article by Balaji *et al*[5] in this issue is a report of a single centre with 114 *Streptococcus pneumoniae* isolates from IPD, over a period of six years (with an average of 19 per year). The magnitude of projected pneumococcal disease burden and serotype prevalence in a geographic area is not reflected by laboratory data, and therefore, it cannot be extrapolated to reflect the actual situation. One of the major challenges to serotype prevalence studies in India has been the meager laboratory data generated by a few centers only. This is understandable due to the complex laboratory procedures to isolate and serotype the organism. The authors have shown a 64 and 74.6 per cent coverage of pneumococcal conjugate vaccine-10 (PCV-10) and PCV-13 serotypes, respectively in contrast to only 48.2 per cent coverage of PCV-7. This has already been well documented in the West[6,7], hence it is not surprising that the same should be observed in Indian children. An earlier multicentric study (IBIS) from the same centre had shown serotype prevalence in children less than five years from several hospitals across India, representing a wider geographic distribution[1]. It is to be noted that serotypes reported in the IBIS study[1] and 25.4 per cent of the isolates from the present study were non-vaccine serotypes. The implications of the non-vaccine serotypes in the prevention of IPD remain a challenge. Despite its small numbers, a positive outcome of the present study is the data on serotypes detected over a period of time indicating a wide range involved in invasive disease. Predominance of some serotypes in any particular year has not been commented upon, possibly due to small numbers isolated per year.

A potential source of non-vaccine serotypes in the nasopharynx must be considered in the preventive strategy for IPD. Changing serotype pattern has been described in nasopharyngeal colonization studies which are presumed to be prelude to invasive infections[8]. There are several reports from India on serotype prevalence in nasopharyngeal colonizers in children ranging between 6.5 to 24 per cent, from the first six months of life to 10 yr of age[9,10]. Common serotypes encountered were 6, 19,14,15,2,3 and 4 in children between three

months to three years old in Vellore, while Coles *et al*[11] have reported the most prevalent serogroups/types during the first six months of life to be 6, 9, 10, 11, 14, 15, 19, 23 and 33, which accounted for 76.7 per cent of all serotyped isolates in Madurai. A study from Delhi reported the carriage rate to be 6.5 per cent with serotypes 1, 6, 14 and 19, of which serotype 19 was the most common in children between three months to three years[12]. These studies have shown substantial non-vaccine serotypes among the colonizers. Knowledge of drug resistance among the colonizers is also important to monitor circulating resistant serotypes.

Balaji *et al*[5] have reported decreased susceptibility to penicillin and cefotaxime among the non-vaccine serotypes. With macrolides, azithromycin and clarithromycin being widely used in respiratory tract infections, it would have been prudent to test these also. Erythromycin resistance along with high level of co-trimoxazole (which is no longer used in respiratory infections) has also been documented in other studies from India[13,14]. Unlike in some European countries[15] antibiotic resistance in pneumococci has not posed a challenge in India, except extremely high level of resistance to co-trimoxazole. With high disease burden and mortality in children due to IPD, it is not out of place to monitor for emergence of multidrug resistant strains. The easiest way to do so is to survey nasopharyngeal colonization in healthy children in the community[14,16.] Reports of unique mechanisms of resistance in pneumococci have been emerging in literature from the West[17]. A close watch on antibiotic resistance of *S. pneumoniae* among nasopharyngeal colonizers in hospitalized children would help monitor the changing pattern under antibiotic pressure in the hospital. Millennium Development Goal 4 to reduce mortality in children less than five year old between 1990 to 2015 has moved forward in some countries by introducing vaccines with expanded serotype coverage. PCV-13 has achieved significant success in this endeavour. Further broadening the scope by including prevalent serotypes needs to be explored as well[4]. There is a need for research on non-serotype based, or novel conjugate vaccines with conserved pneumococcal protein antigens, to overcome the problems associated with existing polysaccharide vaccines. Meanwhile, serotype prevalence in invasive diseases must continue to be documented to monitor occurrence of non-vaccine serotypes and serotype switching among existing strains responsible for invasive pneumococcal disease. Documentation of serotype prevalence across the country, including high disease burden States and vulnerable child population, is necessary to guide policy makers towards introducing an effective vaccine and researchers to explore newer possibilities of novel vaccine production.

Reba Kanungo
Department of Microbiology
Pondicherry Institute of Medical Sciences
Puducherry 605 014, India
reba.kanungo@gmail.com

References

1. Invasive Bacterial Infection Surveillance (IBIS) Group, International Clinical Epidemiology Network (INCLEN). Prospective multicentre hospital surveillance of *Streptococcus pneumoniae* disease in India. *Lancet* 1999; *353* : 1216-21.
2. Kanungo R, Rajalakshmi B. Serotype distribution & antimicrobial resistance in *Streptococcus pneumoniae* causing invasive & other infections in south India. *Indian J Med Res* 2001; *114* : 127-32.
3. Igor Rudan, Cynthia Boschi-Pinto, Zrinka Biloglav, Kim Mulholland, Harry Campbelle. Epidemiology and etiology of childhood pneumonia. *Bull World Health Organ* 2008; *86* : 408-16.
4. Prato R, Tafuri S, Fortunato F, Martinelli D. Why it is still important that countries know the burden of pneumococcal disease. *Hum Vaccin* 2010; *6* : 918-21.
5. Balaji V, Jayaraman R, Verghese VP, Baliga PR, Kurien T. Pneumococcal serotypes associated with invasive disease in under five children in India & implications for vaccine policy. *Indian J Med Res* 2015; *142* : 286-92.
6. Pilishvili T, Lexau C, Farley MM, Hadler J, Harrison LH, Bennett NM, *et al*. Sustained reductions in invasive pneumococcal disease in the era of conjugate vaccine. *J Infect Dis* 2010; *201* : 32-41.
7. O'Brien KL, Wolfson LJ, Watt JP, Henkle E, Deloria-Knoll M, McCall N, *et al*. Burden of disease caused by *Streptococcus pneumoniae* in children younger than 5 years: global estimates. *Lancet* 2009; *374* : 893-902.
8. Bogaert D, de Groot R, Hermans PWM. *Streptococcus pneumoniae* colonisation: the key to pneumococcal disease. *Lancet Infect Dis* 2004; *4* : 144-54.
9. Jebaraj R, Cherian T, Raghupathy P, Brahmadathan KN, Lalitha MK, Thomas K, *et al*. Nasopharyngeal colonization of infants in southern India with *Streptococcus pneumoniae*. *Epidemiol Infect* 1999; *123* : 383-8.
10. Kanungo R, d'Lima D, Rajalakshmi B, Natarajan MK, Badrinath S. Throat carriage of pneumococci in healthy school children in the Union Territory of Pondicherry. *Indian J Med Res* 2000; *112* : 100-3.
11. Coles CL, Kanungo R, Rahmathullah L, Thulasiraj RD, Katz J, Santosham M, *et al*. Pneumococcal nasopharyngeal

colonization in young South Indian infants. *Pediatr Infect Dis J* 2001; *20* : 289-95.

12. Wattal C, Oberoi JK, Pruthi PK, Gupta S. Nasopharyngeal carriage of *Streptococcus pneumoniae*. *Indian J Pediatr* 2007; *74* : 905-7.
13. Coles CL, Rahmathullah L, Kanungo R, Thulasiraj RD, Katz J, Santosham M, *et al*. Nasopharyngeal carriage of resistant pneumococci in young South Indian infants. *Epidemiol Infect* 2002; *129* : 491-7.
14. Lalitha MK, David T, Thomas K. Nasopharyngeal swabs of school children, useful in rapid assessment of community antimicrobial resistance patterns in *Streptococcus pneumoniae* and *Haemophilus influenzae*. *J Clin Epidemiol* 2013; *66* : 44-51.
15. Schrag SJ, Beall B, Dowell S. *Resistant pneumococcal infections: the burden of disease and challenges in monitoring and controlling antimicrobial resistance*, WHO/CDS/CSR/DRS/2001.6. Geneva: World Health Organization; 2001. p. 3-9 .
16. Devi U, Ayyagari A, Devi KR, Narain K, Patgiri DK, Sharma A, *et al*. Serotype distribution & sensitivity pattern of nasopharyngeal colonizing *Streptococcus pneumoniae* among rural children of eastern India. *Indian J Med Res* 2012; *136* : 495-8.
17. Stanek RJ, Maher MB, Norton NB, Mufson MA. Emergence of a unique penicillin-resistant *Streptococcus pneumonia* serogroup 35 strain. *J Clin Microbiol* 2011; *49* : 400-4.