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Commentary

Pneumococcal disease in India: The dilemma continues

This issue carries a study by Ravi Kumar *et al*[1] on the *Streptococcus pneumoniae* nasopharyngeal carriage in a convenience sample of 190 apparently healthy infants and children[1]. They have also described the antimicrobial sensitivity pattern of the isolated bacteria. There are some methodological limitations in their study (such as small sample size, unclear recruitment criteria, hospital-based enrolment, recruitment of children presenting for vaccination, incomplete description of serotypes searched for, unclear cut-off for penicillin susceptibility, *etc.*). There are also some flaws in analysis and interpretation. For example, the point-prevalence in the age group 3-12 months (21/96) has been interpreted as 49.2 per cent giving the erroneous impression that there is an inverse correlation between age and pneumococcal carriage. Despite these limitations, the study adds to the Indian literature already available on the subject[2-8]. Against this backdrop, what additional value does this study provide?

Such a study could have clinical and public health significance since nasopharyngeal colonization with *S.pneumoniae* is an initial step leading to infection[9-13] and its clinical outcomes. It is also well known now that nasopharyngeal carriage may be associated with acquisition of viral upper respiratory infections[14]. Further, recent data from India[15] also suggest that early colonization at two months of age could be associated with growth faltering (detected at 6 months). If this observation is true (and not merely a statistical artefact), it is possible that *S. pneumoniae* carriage has implications wider than being one of the aetiologies for upper or lower respiratory tract infection.

Given this background, several important issues emerge. First, colonization is not synonymous with infection or invasive disease. Therefore, what could be the cause and mechanism whereby asymptomatic carriage results in clinically important outcomes (including pneumonia, meningitis, growth failure, *etc.*) in some infants? Second, is there a way to predict which individual infant/child could (or would) experience such adverse outcomes? Third and perhaps more important, unless these aspects are investigated satisfactorily, is it sensible to advocate universal infant pneumococcal vaccination? Fourth, if pneumococcal vaccination is considered an important tool to reduce childhood morbidity/mortality, should the goal be elimination of nasopharyngeal carriage or restricted to reduction in clinically significant disease as envisaged presently?

The latter issues gain importance because much of the current scientific discourse on *S. pneumoniae* is coloured by the hype around available (note emphasis) vaccines[16]. Traditionally, three prongs are used to advocate vaccination, *viz. (i)* estimated/extrapolated burden of invasive disease, *(ii)* penicillin (and sometimes other antibiotic) resistance rates, and *(iii)* nasopharyngeal carriage rate. Kumar *et al*[1] have also used their limited data to argue in favour of vaccination along these lines.

Targeting the elimination of nasopharyngeal carriage of vaccine serotypes may not be an appropriate strategy. Among Alaskan infants, vaccination with the 7-valent pneumococcal conjugate vaccine was highly efficacious in reducing invasive disease caused by vaccine serotypes[17] but had limited effectiveness in decreasing disease burden owing to serotype replacement[18,19]. Serotype replacement and invasive disease caused by the non-vaccine serotypes, have raised significant issues in most developed countries also[20,21]. This raises the additional issues of whether Indian research should focus more on clinical aspects such as identifying infants/children at high(er) risk of adverse outcomes from pneumococcal infection, and managing them; or whether to 'go with the flow' and target universal vaccination.

This study also suggests that there is emerging penicillin resistance among pneumococcal isolates[1]. This is an interesting finding because most Indian studies and the recent pan-Asian ANSORP study[22]

do not corroborate this. It is unclear whether Kumar *et al*[1] used the recently prescribed minimum inhibitory concentration break points for penicillin resistance[23] which has resulted in the downward revision of penicillin resistance estimates. However, the more pertinent issue is not merely the potential for emerging penicillin resistance, but the causes thereof. In other words, we need to address rampant antibiotic (mis)use (including the empiric therapy of 'pneumonia' recommended by global agencies) and thereby decrease the potential for emergence of antimicrobial resistance.

To summarize, although this study by Kumar and colleagues[1] adds little additional information on pneumococcal carriage, it provides food for thought in various other directions.

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References

1. Ravi Kumar KL, Vandana A, Ganaie F, Ramesh AC. Nasopharyngeal carriage, antibiogram & serotype distribution of *Streptococcus pneumoniae* among healthy under five children. *Indian J Med Res* 2014; *140* : 216-20.
2. Devi U, Borah PK, Mahanta J. The prevalence and antimicrobial susceptibility patterns of beta-hemolytic streptococci colonizing the throats of schoolchildren in Assam, India. *J Infect Dev Ctries* 2011; *5* : 804-8.
3. Dhakal R, Sujatha S, Parija SC, Bhat BV. Asymptomatic colonization of upper respiratory tract by potential bacterial pathogens. *Indian J Pediatr* 2010; *77* : 775-8.
4. Wattal C, Oberoi JK, Pruthi PK, Gupta S. Nasopharyngeal carriage of *Streptococcus pneumoniae.Indian J Pediatr* 2007; *74* : 905-7.
5. Jain A, Kumar P, Awasthi S. High nasopharyngeal carriage of drug resistant *Streptococcus pneumoniae* and *Haemophilus influenzae* in North Indian schoolchildren. *Trop Med Int Health* 2005; *10* : 234-9.
6. 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.
7. 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.
8. 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.
9. Rupa V, Isaac R, Manoharan A, Jalagandeeswaran R, Thenmozhi M. Risk factors for upper respiratory infection in the first year of life in a birth cohort. *Int J Pediatr Otorhinolaryngol* 2012; *76* : 1835-9.
10. Syrjanen RK, Auranen KJ, Leino TM, Kilpi TM, Makela PH. Pneumococcal acute otitis media in relation to pneumococcal nasopharyngeal carriage. *Pediatr Infect Dis J* 2005; *24* : 801-6.
11. Garcia-Rodriguez JA, Fresnadillo Martinez MJ. Dynamics of nasopharyngeal clonization by potential respiratory pathogens. *J Antimicrob Chemother* 2002; *50* (Suppl S2) : 59-73.
12. Bogaert D, de Groot R, Hermans PW. *Streptococcus pneumoniae* colonization: the key to pneumococcal disease. *Lancet Infect Dis* 2004; *4* : 144-54.
13. Hill PC, Cheung YB, Akisanya A, Sankareh K, Lahai G, Greenwood BM, *et al*. Nasopharyngeal carriage of *Streptococcus pneumoniae* in Gambian infants: a longitudinal study. *Clin Infect Dis* 2008; *46* : 807-14.
14. Sleeman KL, Daniels L, Gardiner M, Griffiths D, Deeks JJ, Dagan R, *et al*. Acquisition of *Streptococcus pneumoniae* and nonspecific morbidity in infants and their families: a cohort study. *Pediatr Infect Dis J* 2005; *24* : 121-7.
15. Coles CL, Rahmathullah L, Kanungo R, Katz J, Sandiford D, Devi S, *et al*. Pneumococcal carriage at age 2 months is associated with growth deficits at age 6 months among infants in South India. *J Nutr* 2012; *142* : 1088-94.
16. Mathew JL. Pneumococcal vaccination in developing countries: Where does science end and commerce begin? *Vaccine* 2009; *27* : 4247-51.
17. O'brien KL, Moulton LH, Reid R, Weatherholtz R, Oski J, Brown L, *et al*. Efficacy and safety of seven-valent conjugate pneumococcal vaccine in American Indian children: group randomised trial. *Lancet* 2003; *362* : 355-61.
18. Hanage WP. Serotype-specific problems associated with pneumococcal conjugate vaccination. *Future Microbiol* 2008; *3* : 23-30.
19. Singleton RJ, Hennessy TW, Bulkow LR, Hammitt LL, Zulz T, Hurlburt DA, *et al*. Invasive pneumococcal disease caused by nonvaccine serotypes among alaska native children with high levels of 7-valent pneumococcal conjugate vaccine coverage. *JAMA* 2007; *297* : 1784-92.
20. Steens A, Bergsaker MA, Aaberge IS, Rønning K, Vestrheim DF. Prompt effect of replacing the 7-valent pneumococcal conjugate vaccine with the 13-valent vaccine on the epidemiology of invasive pneumococcal disease in Norway. *Vaccine* 2013; *31* : 6232-8.
21. Mehtälä J, Antonio M, Kaltoft MS, O'Brien KL, Auranen K. Competition between *Streptococcus pneumoniae* strains: implications for vaccine-induced replacement in colonization and disease. *Epidemiology* 2013; *24* : 522-9.
22. Kim SH, Song JH, Chung DR, Thamlikitkul V, Yang Y, Wang H, *et al*. ANSORP Study Group. Changing trends in antimicrobial resistance and serotypes of *Streptococcus pneumoniae* isolates in Asian countries: an Asian Network for Surveillance of Resistant Pathogens (ANSORP) study. *Antimicrob Agents Chemother* 2012; *56* : 1418-26.
23. Clinical and Laboratory Standards Institute. *Performance standards for antimicrobial susceptibility testing*; 18th informational supplement. CLSI document M100 -S18. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.