# Penicillin resistant *Streptococcus pneumoniae* in India: Effects of new clinical laboratory standards institute breakpoint and implications

Dear Editor,

India has the lowest incidence of penicillin-resistant *Streptococcus pneumoniae* (PRSP) among the Asian countries.[1] A gradual increase in the intermediate resistance to penicillin (IRP) has been documented in India since 1995.[2-7] The minimum inhibitory concentration (MIC) penicillin breakpoints for *S. pneumoniae* [Table 1] that are recommended by Clinical Laboratory Standards Institute (CLSI) were used for interpretation and quality control in present studies. In 2008, new penicillin breakpoints for *S. pneumoniae* [Table 1] were published by CLSI.[8] Consequently, we revisited and applied new CLSI breakpoints to ours as well as to other published Indian studies on IRP/PRSP data.

The published studies on *S. pneumoniae* IRP included, 3.8% in 1996-1997;[1] 1.48% in 1993 -1997 and 7.8% in 2000-2001[1] among clinical isolates.[2] On re-evaluation, with the new CLSI breakpoints, considering, nonmeningitis, invasive isolates requiring intravenous penicillin therapy. These percentages changed to ≤1%. Likewise, the studies reported by other groups in India may also be overlooked because, as per the new breakpoints, most *S. pneumoniae* IRP isolates fall into susceptible range, i.e., 7.3% (*n*=11) (with exception of three CSF isolates) with penicillin MIC between 0.1 and 1 µg/mL;[4] 15.4% (*n = 2*) 0.75 and 0.125 µg/mL[5] and 25% (*n = 3*) with 0.19, 0.25, 0.38 µg/mL;[6] 20% (*n=30*) with 0.12-1 µg/mL and 2 µg/mL of 26 and 4 respiratory isolates, respectively.[7]

Conversely, in 1999,[3] a 4.6% (*n=25*) which included eight CSF isolates with intermediate resistant to penicillin (0.125-1.0 µg/mL) was reported and yet another study with three CSF isolates with penicillin MIC between 0.1 and 1 µg/mL[4] changes to complete resistant (≤ 0.06 µg/mL susceptible; ≥0.12 µg/mL resistant and with no intermediate breakpoint recommendation, because blood brain barrier reduces the infiltration of penicillin into cerebrospinal fluid) as per the new CLSI break point. This obviously confirms the pre-existence of PRSP causing invasive disease in India.

From this analysis, we conclude that the overall percentage determined as IRP is significantly reduced with the new CLSI breakpoint recommendation for non-meningitis isolates. Therefore penicillin is a preferred drug to treat non-meningitis *S. pneumoniae* infection. Further, microbiologists should encourage the prescription of narrow spectrum penicillin rather than broader spectrum antimicrobials, especially cephalosporins and fluoroquinolones. This may prevent the globally emergent multidrug resistant *S. pneumoniae* (especially serotype 19A, which are currently susceptible to penicillin; unpublished data) and greatly reduce the development and spread of hospital- and community-acquired infections due to antimicrobial resistance.

The additional emphasis includes

- Specimen, clinical and therapy details are mandatory for MIC interpretation of penicillin and third generation cephalosporins or in absence of these details, microbiologist need to report MIC interpretation for both meningitis and nonmeningitis for all isolates other than CSF.
- Physicians should be aware that the clinical syndrome and route of penicillin administration decides the MIC interpretation and effectiveness of therapy.
- The previously published literature based upon earlier CLSI criteria needs cautious re-evaluation.
- The ongoing antimicrobial resistance surveillance studies may observe decrease in the penicillin resistance IPD trends.
- This change in breakpoints reiterates the importance of surveillance studies to look for changes in percentage of penicillin/MDR resistance; serogroup/types and mutilocus sequence type, as we already established the presence of internationally disseminated multidrug-resistant clone Spain$^{23F}$ and Taiwan$^{19F}$-14 in India.

## References

1. Song JH, Jung SI, Ko KS, Kim NY, Son JS, Chang HH, *et al*. High prevalence of antimicrobial resistance among clinical *Streptococcus pneumoniae* isolates in Asia (an ANSORP

**Table 1: Change in the penicillin minimum inhibitory concentration criteria for *S. pneumoniae***

| Clinical syndrome and Penicillin administration route | Earlier CLSI | | | CLSI 2008 | | |
|---|---|---|---|---|---|---|
| | S | I | R | S | I | R |
| Meninigitis, IV penicillin | ≤ 0.06 | 0.12-1 | ≥2 | ≤ 0.06 | * | ≥0.12 |
| Nonmeningitis, IV penicillin | ≤ 0.06 | 0.12-1 | ≥2 | ≤2 | 4 | ≥8 |
| Nonmeningitis, oral penicillin V | ≤ 0.06 | 0.12-1 | ≥2 | ≤ 0.06 | 0.12-1 | ≥2 |

* No intermediate range for meningitis. S - Susceptible, I- Intermediate, R- Resistance.
IV - Intravenous

study). Antimicrob Agents Chemother 2004;48:2101-7.
2. Invasive Bacterial Infection Surveillance Group, International Clinical Epidemiology Network Prospective multicentre hospital surveillance of Streptococcus pneumoniae disease in India. Lancet 1999;353:1216-21.
3. Lalitha MK, Thomas K, Manoharan A, Song JH, Steinhoff MC. Changing trend in susceptibility pattern of Streptococcus pneumoniae to penicillin in India. Indian J Med Res 1999;110:164-8.
4. Kanungo R, Rajalakshmi B. Serotype distribution and antimicrobial resistance in *Streptococcus pneumoniae* causing invasive and other infections in south India. Indian J Med Res 2001;114:127-32.
5. Wattal C, Oberoi JK, Pruthi PK, Gupta S. Nasopharyngeal carriage of *Streptococcus pneumoniae*. Indian J Pediatr 2007;74:905-7.
6. Capoor MR, Nair D, Aggarwal P, Gupta B. Rapid diagnosis of community-acquired pneumonia using the BacT/Alert 3D system. Braz J Infect Dis 2006;10:352-6.
7. Goyal R, Singh NP, Kaur M, Talwar V. Antimicrobial resistance in invasive and colonising *Streptococcus pneumoniae* in North India. Indian J Med Microbiol 2007;25:256-9.
8. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; eighteenth informational supplement. CLSI document M100 –S 18. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.

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