**Review Article**

Indian J Med Res 149, February 2019, pp 87-96
DOI: 10.4103/ijmr.IJMR_214_18

Quick Response Code:

# Antimicrobial susceptibility profile & resistance mechanisms of Global Antimicrobial Resistance Surveillance System (GLASS) priority pathogens from India

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Received January 30, 2018

**Antimicrobial resistance is a major concern globally. Infections due to drug-resistant pathogens are becoming difficult and a challenge to treat. As treatment choices are limited due to the high-drug resistance rates, there is an increase in the health care cost, duration of hospital stay, morbidity and mortality rates. Understanding the true burden of antimicrobial resistance for a geographical location is important to guide effective empirical therapy. To have a national data, it is imperative to have a systemic data capturing across the country through surveillance studies. Very few surveillance studies have been conducted in India to generate national data on antimicrobial resistance. This review aims to report the cumulative antibiogram and the resistance mechanisms of Global Antimicrobial Resistance Surveillance System (GLASS) priority pathogens from India.**

**Key words** Antimicrobial - Global Antimicrobial Resistance Surveillance System priority pathogens - GLASS - India resistance - susceptibility

## Introduction

Infectious disease burden and antimicrobial resistance are major public health threat globally and particularly in India. While resistance is more significant in Gram-negative pathogens than Gram-positive organisms, the precise extent of this problem is not clear. In India, there is no systemic or national surveillance programme. Only a few multicentre studies and reports from individual units or hospitals have reported on antimicrobial resistance. In light of this, the Indian Council of Medical Research (ICMR), New Delhi, has established an antimicrobial resistance surveillance network (ICMR-AMRSN) in 2014 collaborating tertiary care hospitals across India (*http://iamrsn.icmr.org.in/index.php/amrsn/amrsn-network*). This enlightens the systemic data capturing system with reliable data generated with quality control in place. In this article, the cumulative antibiogram and the molecular mechanisms of antimicrobial resistance for Global Antimicrobial Resistance Surveillance System (GLASS) priority pathogens (Gram-positive and Gram-negative organisms) are discussed. GLASS priority pathogens include *Escherichia coli, Klebsiella pneumoniae, Acinetobacter baumannii,*

*Staphylococcus aureus, Streptococcus pneumoniae, Salmonella* spp. and *Shigella* spp. (*http://www.who.int/glass/en/*). Indian studies from the published literature (2011-2017) and data from the AMRSN network have been analyzed.

**Gram-positive organisms**

***Staphylococcus aureus***

In general, for *Staphylococcus aureus*, susceptibility profile of methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) is reported separately. Overall, the median MRSA proportion is 40 per cent, with an interquartile range 34-44 per cent [interquartile range (IQR): 37-41]. Currently, susceptibility profile among MSSA is as follows; gentamicin (68-96%; IQR: 83-92), erythromycin (43-74%; IQR: 56-60), clindamycin (71-90%; IQR: 80-85), co-trimoxazole (54-79%; IQR: 63-78) and ciprofloxacin (31-53%; IQR: 32.5-44.5). While for MRSA, poor susceptibility to gentamicin (28-44%; IQR: 30-43), erythromycin (9-69%; IQR: 13-51), clindamycin (35-71%; IQR: 44-63), co-trimoxazole (27-66%; IQR: 35-62) and ciprofloxacin (8-21%; IQR: 5-21) is seen[1-4]. Almost 100 per cent of methicillin resistance in *S. aureus* is recognized with *mec*A gene, but *mec*C-mediated methicillin resistance has not yet been reported from humans in India[3].

There are limited data on the distribution of aminoglycoside-modifying enzymes (AMEs) encoding for aminoglycoside resistance in *S. aureus*. Perumal *et al*[5] have reported the bi-functional enzyme *aac (6') Ieaph (2")* (55.4%) as the predominant AME followed by *aph (3') IIIa* (32.3%) and *ant (4') Ia gene* (9%). The incidence of inducible ($iMLS_B$) and constitutive ($cMLS_B$) clindamycin resistance was higher in MRSA ($iMLS_B$; 19-28%, $cMLS_B$; 17-41%) than MSSA ($iMLS_B$; 6-10 per cent, $cMLS_B$; 5-10%)[6-12]. Inducible clindamycin resistance is conferred through *erm*A (20%) and *erm* C (52%) genes[3].

Although 100 per cent susceptibility to vancomycin is seen for *S. aureus*, yet only limited information on vancomycin-intermediate *S. aureus* (VISA) and heteroresistant VISA (hVISA) are available. Studies reported 5.8-6.9 per cent hVISA prevalence and most of the isolates showed vancomycin minimum inhibitory concentration (MIC) of ≥1.5 µg/ml[13,14]. Our group has reported hVISA (n=17) harbouring multiple chromosomal mutations in teicoplanin-resistant operon (*tca*RAB), vancomycin resistance associated (*vra*SR), glycopeptide resistance-associated (*graSR*), cell wall regulating phosphorylase (*walKR*) two component systems (TCS) and *rpo*B gene[15,16]. In addition, 10 VISA isolates with the vancomycin MIC of 4 µg/ml by microbroth dilution method was reported[17]. A systemic review and meta-analysis on epidemiology of hVISA and VISA worldwide has reported the pooled prevalence of six and three per cent, respectively[18].

As of May 2015, there have been 14 vancomycin-resistant *S. aureus* (VRSA) cases reported in the USA since 2002[19]. Thus, the identification of a VRSA is rare and should be treated as a highly unusual event[20]. Glycopeptide non-susceptible coagulase-negative staphylococci (CoNS) have also been reported[21]. From India, two VRSA carrying *van*A gene was documented with the MIC of ≥32 µg/ml[22]. In addition, three isolates of linezolid-resistant *S. aureus* were reported (LRSA) with the MIC of >8 µg/ml; one isolate had the mutation of G2576U in 23S rRNA and the other two isolates were documented with plasmid linezolid resistant *cfr* gene[22,23]. Two reports of daptomycin non-susceptible *S. aureus* in MRSA with the vancomycin MIC of 2 µg/ml also appeared[24,25]. In the surveillance of *S. aureus*, hVISA, VISA, VRSA, LRSA and daptomycin non-susceptible *S. aureus* are of current interest.

***Streptococcus pneumoniae***

*S. pneumoniae* is the major cause of invasive bacterial diseases (meningitis and pneumonia) in children less than five years[26]. As a result, early diagnosis and antimicrobial susceptibility profile are essential for early and effective treatment. The most common antibiotics widely used for the treatment of invasive pneumococcal infections are penicillin and cefotaxime. The penicillin and cefotaxime susceptibility among isolates from meningitis in children was 83 and 97 per cent, respectively and in non-meningitis 100 per cent for both the antibiotics[27].

The overall susceptibility of *S. pneumoniae* to penicillin and cefotaxime among children was between 86-92 per cent and 92-100 per cent whereas in adults it was 91 and 94 per cent, respectively. In children, the percentage susceptibility to erythromycin and co-trimoxazole were 59-64 and 0-43 per cent, respectively[27] (CMC 2017, unpublished data). Susceptibility was 96 per cent to levofloxacin. The overall susceptibility in adults for penicillin was 90 per cent, cefotaxime 92 per cent, erythromycin 44 per cent and co-trimoxazole is 0 per cent; 100 per cent susceptibility was seen for vancomycin and linezolid across all age groups (CMC 2017, unpublished data).

High penetration of moxifloxacin, (4th-generation fluoroquinolone), in epithelial-lining fluid and alveolar macrophages makes it more effective against *S. pneumoniae* than gatifloxacin, levofloxacin, ofloxacin and ciprofloxacin in respiratory infections[28].

According to the 2018 European Committee for Antimicrobial Susceptibility Testing (EUCAST) guidelines[29], the susceptibility zone diameter of oxacillin has been changed to 20 mm and an algorithm has to be followed. In meningitis, the resistance to penicillin is reported if the oxacillin zone size is below 20 mm, and further penicillin MIC has to be done. In case of inhibition zone more than 20 mm, it is considered susceptible to all β-lactams except for cefaclor which is intermediate. Susceptibility to antibiotics such as ampicillin, amoxicillin and piperacillin with or without inhibitors and cefepime, cefotaxime, ceftaroline, ceftobiprole, ceftriaxone can be reported if the oxacillin zone is ≥8 mm and MIC needs to be determined if <8 mm. For meropenem, two new breakpoints have been introduced, the breakpoints for meningitis is susceptible ≤0.25 and resistant >1 mg/l, and for non-meningitis ≤2 and >2, respectively[29].

The genetic basis of penicillin resistance in *S. pneumoniae* is mainly due to mutations in penicillin-binding proteins (PBPs)[30]. The mutations in the conserved motifs of the major proteins, PBP2b, PBP2x and PBP1a, lead to alteration in PBPs and thereby resistance[30]. It has been reported that penicillin resistance in *S. pneumoniae* is due to the network of genes consisting of the three major PBPs and 10 other proteins. Within PBPs, there have been 161 sites associated with β-lactam resistance and coupling between sites in these genes constitutes changes in pneumococci and produces different susceptibility rates to β-lactams[31]. Mutations in PBPs are seen in all isolates with penicillin MIC ≥0.12 µg/ml (CMC, unpublished data). The other factors of non PBP mediated resistance is through *mur*M and N, *cia*H, *ftsl* and *gpB* genes[32,33]. The erythromycin resistance is due to *mef(*A/E) *erm*A/B and rarely due to ribosomal protein mutations in L4 and L22. *erm*(B) or the *erm*(A) genes give rise to high-level resistance- ($MLS_B$ type) and *mef*(A/E)-low-level resistance[34]. *mef*A/E is more prevalent (56%) than *erm*B (29%) in Indian isolates (CMC, unpublished data). Fluoroquinolone resistance is attributed due to mutations in g*yr*A*, gyr*B genes (DNA gyrase) and topoisomerase IV (*par*C, *par*E genes) and the presence of efflux protein PmrA. par*C* mutation leads to low-level resistance and *gyr*A mutation leads to high-level resistance[35].

***Enterococcus spp.***

*Enterococcus* species are common in nosocomial infections and their incidence is rising. Treatment of enterococcal infections is complicated due to the high-resistance rates, with inherent resistance to cephalosporins and an increasing prevalence of ampicillin and vancomycin resistance is reported. Among the *Enterococcus* spp., *E. faecium* is isolated at much higher rates than *E. faecalis*. It is highly important to identify the species, as resistance rates are more commonly seen in *E. faecium* than *E. faecalis* and treatment strategy must be species specific. Among the antimicrobials tested, ampicillin resistance is seen at higher rates[36-38].

Antimicrobial susceptibility profile for *Enterococcus* spp. was as follows: ampicillin (3-35%; IQR: 11-34), high-level gentamicin (16-89%; IQR: 26-71), vancomycin (77-100%; IQR: 80-93) and linezolid (98-100%; IQR: 99-100)[39]. Overall, vancomycin resistance was reported to be around 20 per cent. Molecular mechanism of vancomycin resistance is due to different genes namely *VanA, VanB, VanC, VanD, VanE* and *VanG*. In India, 91 per cent of the vancomycin resistance phenotypes are reported to be mediated by *VanA* gene, which confers high-level resistance. The second predominant is *VanC*1 gene, showing intrinsic low-level resistance to vancomycin[40].

**Gram-negative organisms**

***Escherichia coli***

*E. coli* represents a major cause of morbidity and mortality worldwide. The treatment of *E. coli* infections is complicated due to the emergence of antimicrobial resistance. *E. coli* species are being increasingly resistant to commonly prescribed antibiotics in many settings. The antimicrobial susceptibility pattern of *E. coli* observed was amoxicillin/clavulanic acid (11-38%), cefotaxime (14-76%; IQR: 19-60), ceftazidime (7-50%; IQR: 12-37), piperacillin+tazobactum (21-89%; IQR: 25-67), cefperazone+sulbactam (88-100%), imipenem (43-100%; IQR: 68-97), meropenem (67-89%; IQR: 71-86), amikacin (27-88%; IQR: 28-88), gentamicin (21-86%; IQR: 22-63), ciprofloxacin (15-67%; IQR: 22-49), levofloxacin (13-25%) and colistin (97-100%; IQR: 98-100)[41-48].

One of the most important mechanisms of resistance observed in *E. coli* is the production of extended-spectrum β-lactamase enzymes (ESBL). The ESBL-producing strains are of particular concern as

these are resistant to all penicillins and cephalosporins. Among these ESBLs, TEM (40-72%) and CTX-M (60-79%) types are more prevalent[49,50]. Of the different CTX-M–type ESBLs, CTX-M-15 has become the most widely disseminated enzyme worldwide. It was first identified in an isolate from India in 1999 and subsequently became prevalent around the world[51].

Resistance to carbapenems among *E. coli* is of particular importance as these agents are often the last line of effective therapy. New Delhi metallo-β-lactamase (NDM) and carbapenem-hydrolyzing oxacillinase-48 (OXA48-like) are the most common carbapenemases reported in *E. coli* with the prevalence rate of 38-92 and 15-26 per cent, respectively[49]. The less commonly seen were KPC, VIM and IMP genes.

Recently, emerging reports of plasmid-mediated colistin resistance, *mcr* genes in *E. coli* is alarming[52]. Polymyxins (colistin and polymyxin B) are the last-resort antibiotics for treating infections caused by carbapenemase producers[52]. Notably, *mcr*-1, *mcr*-2, *mcr*-3 and *mcr*-4 genes were first reported in *E. coli*[53]. Further, genes encoding resistance to tetracycline (*tet*A - 38%, *tet*B - 43%), trimethoprim (*dfr*A1 - 8%, *dfr*A17 - 45%), sulphonamides (*sul*1 - 70%, *sul*2 - 25%), chloramphenicol (*cat*A1 - 8%, *cat*B3 - 13%, *cat*B4 - 50%), streptomycin (*str*A/B - 5%) and plasmid mediated quinolone resistance determinants such as *aac(6')-lb-cr* (58%), *qnr*B1 (3%), and *qnr*S1 (5%) were reported in *E. coli* (CMC, unpublished data).

### *Klebsiella pneumoniae*

Monitoring trend of antimicrobial resistance among *K. pneumoniae* is essential for antimicrobial stewardship programmes. High rates of ESBL have been reported in India from various centers with susceptibility ranging from 10 to 60 per cent (IQR: 12-50)[41,54]. Susceptibility to carbapenems showed diverse range from 44 to 72 per cent (IQR: 55-72) in the last few years[54]. Susceptibility to amikacin has been 65 per cent over the past three years while gentamicin susceptibility was 55 per cent (CMC, unpublished data). At present, 37 per cent of the carbapenem-resistant *K. pneumoniae* is resistant to colistin is observed (CMC, unpublished data).

Molecular characterization of β-lactamases in India has shown that among ESBLs, coexpression of $bla_{SHV}$, $bla_{TEM}$ and $bla_{CTX-M}$ are common[54,55]. The prevalence of $bla_{SHV}$ ranged from 16 to 45 per cent; $bla_{TEM}$ 7 to 47 per cent and $bla_{CTX-M}$ from 37 to 43 per cent. $bla_{NDM}$ had a prevalence ranging from 7 to 70 per cent and $bla_{OXA48-like}$ 13 up to 55 per cent. These are the common carbapenem resistant genes[54-56]. $bla_{VIM}$ has been reported up to 18 per cent of the isolates[57]. $bla_{KPC}$ has been seldom reported from India[57].

Diverse mechanisms coding for aminoglycosides include AMEs and 16 S RMTases. *aadA2*, *aadA4* are the common AMEs and *rmtF* and *armA* are the frequently seen in India (CMC, unpublished data). However, tigecycline resistance encoded by efflux pumps with overexpression of *ramA* gene and *AcrAB* efflux pump has been reported[58]. Colistin resistance is mostly chromosomal among clinical specimens while a single report of plasmid-mediated *mcr* gene among environmental sample has been documented[59]. Chromosomal mutations reported have been in *mgrB*, *phoP, phoQ* and *pmrB*[60].

### *Shigella spp.*

*Shigella* species include four serogroups: *S. dysenteriae*, *S. flexneri*, *S. sonnei* and *S. boydii*. All four *Shigella* spp. may cause disease, *S. flexneri* with serotype 2a being the most commonly isolated serotype followed by *S. sonnei* in India. However, *S. dysenteriae* and *S. boydii* were less frequently isolated[61].

Multidrug-resistant Shigellae reported worldwide range from 36 to 98 per cent. In India, the antimicrobial susceptibility profile observed were, ampicillin (0-68%; IQR: 2-43), trimethoprim-sulphamethoxazole (0-33%; IQR: 5-27), chloramphenicol (30-90%; IQR: 44-75), tetracycline (2-70%; IQR: 6-34), nalidixic acid (0-66%; IQR: 4-41), ciprofloxacin (10-94%; IQR: 16-82), norfloxacin (14-94%; IQR: 22-95), ofloxacin (6-90%; IQR: 13-43) and cefixime (0-95%)[61-69]. Notably, changing trend was observed for ampicillin susceptibility between the species *S. flexneri* and *S. sonnei*. Ampicillin susceptibility was lesser in *S. flexneri* when compared to *S. sonnei*[61]. The susceptibility profile of other antibiotics remained unchanged. Besides, there was a rising trend in the ESBL rates among *Shigella* spp. (8-19%).

Among β-lactam resistance in *Shigella* spp., ampicillin resistance was encoded by OXA and TEM type β-lactamases. Resistance was predominantly due to $bla_{OXA-1}$ (30-100%) followed by $bla_{TEM-1}$ (20-100%)[70] (CMC, unpublished data). While for cephalosporin resistance, CTX-M-type β-lactamases $bla_{CTX-M-15}$, is the most common variant seen in India, to date, $bla_{CTX-M-15}$, $bla_{CTX-M-14}$, $bla_{CTX-M-3}$ and $bla_{CMY-2}$ genes have been reported[68].

Quinolone resistance in *Shigella* involves the accumulation of mutations in DNA gyrase and DNA topoisomerase IV and plasmid-mediated quinolone resistance (PMQR) determinants such as *qnrA, qnrB, qnrS* and *aac(6)-Ib-cr* genes which confer low-level resistance to quinolones. The varying prevalence rates of these genes were reported in several studies from India[61,63,68]. The trimethoprim-sulphamethoxazole resistances was due to *dhfr1A* gene (75-80%) followed by the *sulII* gene (70%) (CMC, unpublished data). Reports of *Shigella* resistant to azithromycin have been documented[71]. The genes that encode macrolide resistance were identified to be *mphA* and *ermB*. Resistance to chloramphenicol, tetracycline and streptomycin has mainly been attributed to the presence of *cat* (18-32%), *tet* (40-90%) and *str* (60%) genes[72] (CMC, unpublished data).

**Typhoidal and non-typhoidal *Salmonella***

Enteric fever is an endemic disease in India caused by *Salmonella* enterica serovar Typhi and Paratyphi with *S*. Typhi being the predominant. The major challenge in enteric fever at present is the increase in antimicrobial resistance in both *S*. Typhi and *S*. Paratyphi A. In *S.* Typhi, the antimicrobial susceptibility profile seen for different antimicrobials were, ampicillin (62-97%; IQR: 85-95), co-trimoxazole (73-98%; IQR: 82-97), chloramphenicol (78-98%; IQR: 90-97), nalidixic acid (0-24%; IQR: 0-19), ciprofloxacin (0-81%; IQR: 2-71), ceftriaxone (64-100%; IQR: 81-100), cefixime (98-100%) and azithromycin (52-97%; IQR: 72-94). For *S.* Paratyphi A, antimicrobial susceptibility profile reported ampicillin (71-100%; IQR: 84-100), co-trimoxazole (71-100%; IQR: 92-100), chloramphenicol (73-100%; IQR: 87-100), nalidixic acid (0-6%; IQR: 0-4), ciprofloxacin (0-80%; IQR: 2-54), ceftriaxone (46-100%; IQR: 71-100) and azithromycin (50-100%)[73-81] (CMC, unpublished data).

There is a downward trend in the MDR rates, declined from 26 per cent in 2004 to 1 per cent in 2017[82] (CMC, unpublished data). However, high-level resistance to fluoroquinolones was also observed. Among quinolone resistance in typhoidal *Salmonella*, the most common chromosomal mutations found in DNA gyrase and topoisomerase gene were at codon 83 and at codon 87[81,83]. Plasmid-mediated quinolone resistance (PMQR) genes documented were *qnr*B (57-100%) and *aac (6)-Ib-cr* (5-17%)[84].

Emergence of resistance to cephalosporin has also been documented. Resistance due to extended-spectrum β-lactamases (ESBLs) and AmpC is the major mechanism seen in *Salmonella*. Among ESBLs, TEM, SHV, PER, CTX-M families were reported with TEM and CTX-M being the most common. CMY-2 gene is the most predominant gene among AmpC β-lactamases. Other genes, such as *cat*, *sul* and *str* encode resistance for chloramphenicol, co-trimoxazole and streptomycin were also reported[68]. Non-typhoidal salmonellosis (NTS) refers to the infections caused by all the serotypes of *Salmonella* except *S*. Typhi, Paratyphi A, Paratyphi B, Paratyphi C and Sendai. Multidrug-resistant NTS has become a global concern now. Among NTS, susceptibility was observed for ampicillin (0-93%; IQR: 6-67), co-trimoxazole (42-93%; IQR: 54-83), chloramphenicol (45-100%; IQR: 64-100), nalidixic acid (23-76%), ciprofloxacin (9-100%; IQR: 31-88), ceftriaxone and azithromycin (>90%)[78,85,86] (CMC, unpublished data). The most common types of ESBLs encountered in NTS were CTX-M and TEM (54%). Common among TEM group of ESBLs are TEM-3, TEM-27 and TEM-52[87].

***Pseudomonas aeruginosa***

*Pseudomonas aeruginosa* causes severe nosocomial infections leading to high morbidity and mortality rates. Centers for Disease Control and Prevention (CDC) has prioritized *P. aeruginosa* in serious threats category due to its multidrug resistance phenomenon[88]. It is well known for its antimicrobial resistance due to its complex intrinsic resistance mechanisms.

Antimicrobial resistance in *P. aeruginosa* varies across different regions in India. Susceptibility to anti-pseudomonal are as follows: cephalosporins: ceftazidime/cefepime (31-76%; IQR: 32-66), piperacillin/tazobactam (36-76%; IQR: 37-75), carbapenems: imipenem/meropenem(33-73%; IQR: 43-66), fluoroquinolones: ciprofloxacin/ levofloxacin (29-75%; IQR:33-68), aminoglycosides: amikacin/ gentamicin (32-80%; IQR: 35-71) and colistin (99-100%; IQR: 99-100). Overall, multidrug-resistant (MDR) rates range from 20-25 per cent[36,89-91].

Molecular mechanism of antimicrobial resistance in *P. aeruginosa* is diverse. Screening of β-lactamases from MDR *P. aeruginosa* collected across India showed 30-40 per cent of positivity[92]. The most common being $bla_{VEB}$ (12-100%), $bla_{TEM}$ (3-10%) and less of $bla_{SHV}$ (1%) genes among ESBLs which confer resistance to anti-pseudomonal cephalosporins. $bla_{GES}$ (6-12%) in Class A carbapenemases, $bla_{VIM}$ (24-57%)

followed by $bla_{NDM}$ (8-19%) and $bla_{IMP}$ (4-5%) in Class B carbapenemases (metallo-β-lactamases) confer carbapenem resistance. Although carbapenemases are seen in *P. aeruginosa* isolates across India, a typical observation is of $bla_{NDM}$ being more in southern India, while $bla_{VIM}$ being more in northern part of India[92]. AmpC de-repression phenotype is seen among 80 per cent of carbapenem-resistant isolates with no carbapenemase production[92].

### *Acinetobacter baumannii*

*Acinetobacter* species have become a leading cause of nosocomial infections. *Acinetobacter calcoaceticus-baumannii* group (*Acb* complex) includes six species, *A. baumannii*, *A. pittii*, *A. nosocomialis*, *A. seifertii*, *A. dijkshoorniae* and *A. calcoaceticus*[93]. To differentiate *Acinetobacter* species, OXA-51 alone may not be sufficient. *gyrB* multiplex PCR and *rpoB* sequencing will help accurately identify species within the *Acb* complex. Bruker MALDI-TOF Biotyper system with updated database allows successful delineation of *Acinetobacter* species[93].

The susceptibility profile ranged against ceftazidime (0-79%; IQR: 14-31), piperacillin-tazobactam (10-66%; IQR: 13-44) imipenem (20-71%; IQR: 30-60), meropenem (10-73%; IQR: 24-49), amikacin (15-61%; IQR: 17-55), tobramycin (38-84%; IQR: 41-63), netilmicin (35-77%; IQR: 36-65) and colistin (78-100%; IQR: 86-99)[94-100] (ICMR-AMRSN, unpublished data).

Among β-lactam resistance, $bla_{PER\text{-}like}$ (41-76%)[101] gene is most predominantly reported followed by $bla_{TEM}$ like(8-87%)[101]. Carbapenem resistance in *A. baumannii* is predominantly mediated by class D carbapenemase $bla_{OXA\text{-}23\text{-}like}$ (42-99%) followed by Class B metallo-β-lactamase $bla_{NDM\text{-}like}$ (14-60%), $bla_{VIM\text{-}like}$ (1-59%) and $bla_{IMP\text{-}like}$ (36-55%)[94,96, 100-102].

Aminoglycoside resistance in *A. baumannii* is mainly due to AMEs and 16S rRNA methyltransferases (RMTase). AMEs such as *aac* (6), *ant* (2) and *aph* (3) were reported in 47.8, 17.4 and 8.7 per cent, respectively[99] in *A. baumannii*. The most common RMTase gene reported is *armA* (96.5%) followed by combination of *armA* with *rmtB* (3.5%) (CMC, unpublished data).

Colistin resistance in *A. baumannii* can be due to mutations in lipid A biosynthesis genes and point mutations in *Pmr*AB two-component regulatory system (TCS)[103]. Chromosomal mutations in *lpxA, lpxD, lpsB* and *pmrB* genes have also been observed (CMC, unpublished data).

## Conclusion

Antimicrobial resistance is a growing public health concern across the globe. Resistance is seen at higher rates in Gram-negative organisms than Gram-positives. Diverse molecular resistance mechanisms have been reported in Gram-negative organisms which include high ESBL rates in *E. coli*, *K. pneumoniae*; high carbapenem and colistin resistance in *K. pneumoniae* and increased carbapenem resistance rates in *A. baumannii* than in *P. aeruginosa*. Among Gram-positive organisms, *S. aureus* with high rates of inducible clindamycin resistance in MRSA compared to MSSA were observed. Increasing incidence of penicillin non-susceptible *S. pneumoniae* (PNSP) is alarming. Emergence of resistance to third generation cephalosporins and macrolides are also observed in enteric pathogens such as *Shigella* and non-typhoidal *Salmonella*. This indicates the need for continuous monitoring of AMR to document any changing trends in the near future. Although information has been retrieved from the available hospital based literature, there is still a lacuna with the current national surveillance systems due to the limited network sites. Improved surveillance networks including multiple sites across different geographical locations would enable improved data collection to derive the true burden of AMR at a national level.

***Financial support & sponsorship*:** The study was supported by the Indian Council of Medical Research, New Delhi.

***Conflicts of Interest*:** None.

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