

Short Communication

## Recent trend of aminoglycoside resistance among *Staphylococcus aureus* isolates in tertiary care hospital

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Aminoglycosides still play an important role in antistaphylococcal therapies, although emerging resistance amongst staphylococci is widespread. The objective of the present study was to know the percentage of aminoglycoside resistance among *Staphylococcus aureus* isolates. A total of 250 isolates of *S. aureus* were studied from different clinical specimens like blood, pus, wound swabs, sputum, ear swabs and body fluids. All the isolates were tested for their susceptibility to four aminoglycosides namely gentamicin, amikacin, tobramycin and netilmicin by Kirby Bauer disc diffusion method using criteria of standard zone of inhibition. Methicillin resistant *S. aureus* (MRSA) detection was done by cefoxitin disc diffusion method. Out of the 250 *S. aureus* isolates, 66 (26.4%) isolates demonstrated resistance to at least one of the four aminoglycosides tested. Four isolates were resistant to all the four aminoglycosides tested. All these four were MRSA. The most active antimicrobial agent against *S. aureus* was found to be netilmicin followed by amikacin. Continued surveillance at both the genotypic and phenotypic levels as well as adherence to well-designed antibiotic and infection control policies are necessary to understand and limit further rise of resistant isolates.

**Key words:** Aminoglycosides, *Staphylococcus aureus*.

### INTRODUCTION

*Staphylococcus aureus* is a major cause of hospital and community-acquired infections, and can result in serious consequences. The importance of *S. aureus* as a human pathogen, apart from its ability to cause a diverse range of life-threatening infections, is its extraordinary potential to develop antimicrobial resistance (Lowy, 2003).

One of the classes of antibiotics playing an important

role in the therapy of serious staphylococcal infections is aminoglycosides. Although aminoglycosides are predominantly used for the treatment of Gram-negative infections, they are also known to have antistaphylococcal activity (Jana and Deb, 2006). This becomes an important consideration when patients are treated empirically for suspected sepsis with an aminoglycoside and

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**Table 1.** Phenotypic resistance patterns of *S. aureus* (MRSA and MSSA) for four aminoglycosides.

Type	Resistance pattern				Number (%)		
	GEN	TOB	AMK	NET	MRSA	MSSA	Total
1	R	R	R	R	04 (3.7%)	-	04 (1.6%)
2	R	R	R	S	21 (19.6%)	01 (0.7%)	22 (8.8%)
3	R	R	S	S	35 (32.7%)	01 (0.7%)	36 (14.4%)
4	R	S	S	S	01 (0.9%)	03 (2.1%)	04 (1.6%)
5	S	R	R	S	-	-	-
6	S	S	S	S	46 (43.0%)	138 (96.5%)	184 (73.6%)
Total					107	143	250

GEN- Gentamicin; TOB- Tobramycin; AMK- Amikacin; NET- Netilmicin; S- sensitive; R- resistant; MRSA- methicillin resistant *S. aureus*; \* MSSA- methicillin sensitive *S. aureus*.

ureidopenicillin, other penicillins, or cephalosporins susceptible to staphylococcal beta-lactamases. In addition, the emergence of methicillin-resistant *S. aureus* is increasing the clinical importance of the antistaphylococcal activity of aminoglycosides (Hammerberg et al., 1986).

Increased resistance to these drugs have been reported from many countries (Hauschild et al., 2008) and little data is available on their resistance pattern in staphylococci from this part of India. So this study was undertaken to gain some insight into the susceptibility pattern of aminoglycosides among *S. aureus* in our tertiary care hospital.

## MATERIALS AND METHODS

This study was performed between November 2010 and April 2012 in the Department of Microbiology at our tertiary care hospital, India. A total of 250 isolates of *S. aureus* were isolated from different clinical specimens like blood, pus, wound swabs, sputum, ear swabs and body fluids. Only one isolate per patient was included in the study. All the isolates were tested for their susceptibility to gentamicin (10 µg), amikacin (30 µg), tobramycin (10 µg), netilmicin (30 µg) by Kirby Bauer disc diffusion method using criteria of standard zone of inhibition (CLSI, 2010). *S. aureus* ATCC 29213 was used as quality control strain for *in vitro* susceptibility testing. MRSA detection was done by ceftoxitin disc diffusion method.

## RESULTS

Of the 250 *S. aureus* isolates included in this study, 66 (26.4%) were resistant to at least one of the four aminoglycosides tested (Table 1). 04 (1.6%) *S. aureus* isolates were resistant to all the four aminoglycosides tested. All these four were MRSA. The most active antimicrobial agent against *S. aureus* was netilmicin. 21 (19.6%) MRSA isolates were resistant to gentamicin, tobramycin and amikacin and showed susceptibility only to netilmicin. 35 (32.7%) MRSA isolates showed resistance to gentamicin and tobramycin. Of the 107 MRSA

isolates, 61 (57.0%) were resistant to at least one of the four aminoglycosides tested.

## DISCUSSION

Aminoglycosides are potent bactericidal agents, inhibiting protein synthesis by binding to the 30S ribosomal subunit. Gentamicin and tobramycin are the most active against staphylococci and are often used in combination with either a  $\beta$ -lactam or a glycopeptide, especially in the treatment of staphylococcal endocarditis, as these drugs act synergically (Schmitz et al., 1999). Bacterial resistance to aminoglycosides is widely recognized as a serious health threat. The major mechanism of aminoglycoside resistance in staphylococci is drug inactivation by cellular aminoglycoside-modifying enzymes such as aminoglycoside acetyltransferases (AAC), aminoglycoside adenyltransferases (ANT) or aminoglycoside phosphotransferases (APH) activity (Jana and Deb, 2006).

Since the first report on gentamicin resistance among staphylococci, strains resistant to both methicillin and gentamicin have been the cause of serious infections and extensive outbreaks. Many of these organisms are often resistant to a number of other antibiotics (Anupurba et al., 2003). In 1969, the first clinical gentamicin-resistant MRSA (GR-MRSA) strain was isolated. By 1980s GR-MRSA had become epidemic in Australia, the United States and Europe (Cafferkey et al., 1983). In fact many strains of MRSA exhibit resistance to both  $\beta$ -lactams and aminoglycosides (Anupurba et al., 2003; Tiwari et al., 2008).

In the present study, 66 (26.4%) strains of *S. aureus* and 61 (57.0%) MRSA were resistant to gentamicin which correlates with the study from North India (Tiwari et al., 2008) which reported 55.8% gentamicin resistance among MRSA. Aminoglycoside resistance reported in *S. aureus* isolates from different countries, and especially gentamicin resistance, is of clinical importance because it can compromise the therapeutic effectiveness of these

antibacterial agents (Hauschild et al., 2008).

In this study, 62 (24.8%) *S. aureus* isolates were resistant to tobramycin which correlates well with the report from Europe (Schmitz et al., 1999) which reported 29.0 % resistance among *S. aureus* to tobramycin. A study from South Maharashtra region of India reported that more than 90% *S. aureus* isolates were resistant to gentamicin and tobramycin (Kandle et al., 2003).

In this study, 04 (1.6%) and 26(10.4%) *S. aureus* isolates were resistant to netilmicin and amikacin respectively. Another study from Poland reported 24.4% *S. aureus* strains were resistant to amikacin and that no strain of *S. aureus* was found resistant to netilmicin (Hauschild et al., 2008). Of the 250 *S. aureus* isolates, 66 (26.4%) were resistant to at least one of the four aminoglycosides tested which is somewhat lower than the finding of the authors (Hauschild et al., 2008) who reported that 38.1% of their isolates of *S. aureus* were resistant to one of the aminoglycosides tested.

In this study, 60 (56.1%) MRSA isolates were resistant to tobramycin, 25 (23.4%) to amikacin and 04 (3.7%) to netilmicin. Tiwari et al. (2008) reported 41.5% amikacin resistance among MRSA. In this study, netilmicin sensitivity is found to be higher than other aminoglycosides. A study from India and Korea reported 5.1% and less than 20% netilmicin resistance in their study, respectively (Rajadurai pandi et al., 2006; Kim et al., 2004).

In our study, members of aminoglycoside group were tested separately because *in vitro* testing of one member, however, may not predict *in vitro* result for other members in the group. Further genotypic studies are needed for the isolates demonstrating phenotypic resistance to any of the member of this class. It will help in the identification of the known or any new gene encoding aminoglycoside modifying enzyme in staphylococcal isolates which could account for the phenotype.

In summary, among the aminoglycosides tested, maximum susceptibility was found for netilmicin (98.4%) followed by amikacin (89.6%). Highest resistance was observed for gentamicin (26.4%). Continued surveillance at both the genotypic and phenotypic levels as well as adherence to well-designed antibiotic and infection control policies are necessary to understand and limit further rise of resistant isolates.

## Conflict of Interests

The author(s) have not declared any conflict of interests.

## REFERENCES

Anupurba S, Sen M, Nath G, Sharma B, Gulati A, Mohapatra T ( 2003).

- Prevalence of methicillin resistant *Staphylococcus aureus* in a tertiary referral hospital in eastern Uttar Pradesh. Indian J. Med. Microbiol. 21:49-51.
- Cafferkey M, Hone R, Falkinier F, Kean C, Pomeroy H (1983). Gentamicin and methicillin resistant *Staphylococcus aureus* in Dublin hospitals: clinical and laboratory studies. J. Med. Microbiol. 16:116-127.
- Clinical and Laboratory Standards Institute (CLSI) (2010). Performance Standards for Antimicrobial Susceptibility Testing; Twentieth informational supplement. M100-S20. Pennsylvania. CLSI document.
- Hammerberg O, Elder D, Richardson H, Landis S (1986). Staphylococcal resistance to aminoglycosides before and after Introduction of amikacin in two teaching hospitals. J. Clinical Microbiol. 24(4):629-632.
- Hauschild T, Sacha P, Wiczorek P, Zalewska M, Kaczynski K, Trzyniszewska E (2008). Aminoglycosides resistance in clinical isolates of *Staphylococcus aureus* from a University Hospital in Bialystok, Poland. Folia Histochemica et Cytobiologica. 46(2):225-228.
- Jana S, Deb J (2006). Molecular understanding of aminoglycoside action and resistance. Appl. Microbiol. Biotechnol. 70(2):140-50.
- Kandle S, Ghatole M, Takpere A, Hittinalli V, Yemul V (2003). Bacteriophage typing and antibiotic sensitivity pattern of *Staphylococcus aureus* from clinical specimen in and around Solapur (South Maharashtra). J. Commun. Dis. 35:17-23.
- Kim H, Jang H, Nam H, Choe K (2004). In vitro activities of 28 antimicrobial agents against *Staphylococcus aureus* from tertiary care hospitals in Korea: a nationwide survey. Antimicrob. Agents Chemother. 48(4):1124-1127.
- Lowy FD (2003). Antimicrobial resistance: the example of *Staphylococcus aureus*. J. Clin. Invest. 111:1265-1273.
- Rajadurai pandi K, Mani K, Panneerselvam K, Mani M, Bhaskar M, Manikandan P (2006). Prevalence and antimicrobial susceptibility pattern of methicillin resistant *Staphylococcus aureus*: a multicentre study. Indian J. Med. Microbiol. 24(1):34-38.
- Schmitz F, Fluit A, Gondolf M, Bayrau R (1999). The prevalence of aminoglycoside resistance and corresponding resistance genes in clinical isolates of staphylococci from 19 European hospitals. J. Antimicrob. Chemother. 43:253-259.
- Tiwari H, Sapkota D, Sen R (2008). High prevalence of multidrug-resistant MRSA in a tertiary care hospital of northern India. Infect. Drug Resist. 1:57-61.