

Correspondence

Trend of vancomycin susceptibility of staphylococci at a level 1 trauma centre of India

Sir,

Staphylococcus aureus causes a wide array of infections, both community acquired and nosocomial. It is the commonest cause of surgical site infections and a prominent hospital acquired pathogen from blood stream infections and pneumonia^{1,2}. Coagulase-negative staphylococci (CoNS) are an important cause of the device associated blood stream infections³. CoNS are more resistant to antibiotics than *S. aureus*³. The growing global prevalence of methicillin resistance among *Staphylococcus* is limiting the therapeutic options available to treat invasive staphylococcal infections. Till now both *S. aureus* and CoNS have remained by and large sensitive to glycopeptides except for a few case reports of vancomycin resistant and intermediate *S. aureus* (VRSA, VISA) and vancomycin resistant CoNS^{4,7}. However, there are reports of therapeutic failure to vancomycin treatment for serious infections when the organisms, although in susceptible range, have increased minimum inhibitory concentrations (MICs) (2 µg/ml)⁴. There have been reports from a few hospitals of increasing MICs of vancomycin (MIC creep) in *S. aureus*^{5,6}. Emergence of vancomycin resistance foretells a grave future for management of serious staphylococcal infections in view of the fact that no new antimicrobials are being developed and the recently introduced ones like tigecycline and daptomycin are very expensive.

The 165 bedded level-1 Trauma Centre of the All India Institute of Medical Sciences (AIIMS) hospital, New Delhi, India, became functional in November, 2006. The Microbiology Laboratory of the Trauma Centre receives around 12,000 samples annually from admitted trauma patients. Microorganisms are recovered from approximately 2500 of these samples. *Staphylococcus* spp. constitutes approximately 20 per cent of these isolates. In this study, we report the

changing pattern of vancomycin MIC for *S. aureus* since the centre began functioning and overall resistance for vancomycin among CoNS isolates during the four years (2007-2010).

All consecutive, non duplicate *Staphylococcus* isolates were identified to species level by the Vitek II (Biomérieux, France) (as per manufacturer's instructions) and conventional methods⁸. These clinical isolates were tested for vancomycin susceptibility by Vitek 2 and E-test⁹. The MICs were evaluated both by Vitek 2 version 4.01 system and E-test following Clinical and Laboratory Standards Institute (CLSI) recommendations⁹. Vancomycin MIC ≤ 2 µg/ml was considered susceptible, MIC in range 4-8 µg/ml as intermediate and ≥ 8 µg/ml as resistant for *S. aureus*. Vancomycin MIC ≤ 4 µg/ml was considered susceptible, MIC in range 8-16 µg/ml as intermediate and ≥ 32 µg/ml as resistant for CoNS. Methicillin susceptibility was determined using both oxacillin and cefoxitin disk under CLSI recommended conditions⁹. Methicillin susceptibility was also confirmed by cefoxitin screen in Vitek 2. All results were interpreted according to the CLSI document M-100 - S18¹⁰. The following strains were taken as controls: *S. aureus* ATCC 25923 (vancomycin susceptible, methicillin sensitive), *S. aureus* ATCC 43300 (vancomycin susceptible, methicillin resistant) and *S. aureus* ATCC 700699 (vancomycin intermediate *S. aureus*), *Enterococcus faecalis* ATCC 51299 (vancomycin susceptible *Enterococcus*) and *S. epidermidis* ATCC 12228 procured from ATCC (LGC Promochem, India).

A total of 449 isolates of *S. aureus* were recovered during the study period. These included 315 (70%) from pus/wound swabs of post-operative infections, 40 (9%) from blood, 29 (6%) from respiratory samples, 34 (7.5%) from central vascular lines tips, 15 (3%) from tissues and 8 (2%) each from urine and 8 (1.78%) from

Table. Vancomycin MICs of *S. aureus* isolates by E-test from 2007 to 2010 (N=449)

Year	MSSA	MRSA	Total	≤ 0.5 µg/ml			>0.5 - <2 µg/ml			2.0 µg/ml			GM (MIC)
				MSSA (%)	MRSA (%)	Total (%)	MSSA (%)	MRSA (%)	Total (%)	MSSA (%)	MRSA (%)	Total (%)	
2010	67	80	147	23 (34)	18 (22.5)	41 (28)	31 (46)	30 (37.5)	61 (41)	13 (19)	32 (40)	45 (31)	1.166
2009	49	88	137	0 (0)	2 (2)	2 (1)	45 (92)	67 (76)	112 (82)	4 (8.1)	19 (21.5)	23 (17)	1.16
2008	41	81	122	0 (0)	0 (0)	0 (0)	39 (95)	69 (85)	108 (88.5)	2 (5)	12 (15)	14 (11.5)	1.114
2007	18	25	43	1 (5.5)	0 (0)	1 (2)	17 (94.5)	21 (84)	38 (88)	0 (0)	4 (16)	4 (9)	1.081
Total	175	274	449	24 (14)	20 (7.3)	44 (10)	132 (75)	187 (68)	319 (71)	19 (11)	67 (24)	86 (19)	
<i>P</i> * value				0.25	0.17	0.2	0.48	0.87	0.73	0.07	0.01	0.025	0.033

**P* value for a linear trend by Pearson's correlation test
 MRSA, methicillin resistant *Staphylococcus aureus*; MSSA, methicillin sensitive *Staphylococcus aureus*; GM, geometric mean; MIC, minimum inhibitory concentration

body fluids. There were no discordant results regarding the interpretation of susceptibility testing as isolate being sensitive, intermediate or resistant between Vitek 2 and E-test. All isolates had vancomycin MIC in the susceptible range. However, a significant and progressive increase was observed in the percentage of isolates showing vancomycin MIC 2 µg/ml. In 2007 only 9 per cent isolates of *S. aureus* had an elevated vancomycin MIC, in contrast to 31 per cent in 2010 (Table).

Vancomycin MICs were determined for 127 CoNS using both Vitek 2 and E test. Of these, 116 (91%) were methicillin resistant and 19 (15%) had vancomycin MIC 4 µg/ml.

Thus, a trend of increasing vancomycin MICs among *S. aureus* isolates was observed. A lacuna of this study was that it could not be ascertained if the staphylococci with elevated MIC were associated with therapeutic failures since other antibiotics like linezolid or netilmicin were also administered for MRSA. In an earlier study from our Centre 58 per cent isolates were MRSA, and daptomycin was found to be an effective drug against MRSA¹¹. The rate of methicillin resistance was 100 per cent amongst 40 isolates of CoNS in another study from our centre¹². However, in the present study, the rates of methicillin resistance were 61 and 91 per cent, respectively in *S. aureus* and CoNS. Several studies from India have reported methicillin resistance varying from 50-80 per

cent and 30-60 per cent among *S. aureus* and coagulase negative staphylococci, respectively¹³⁻¹⁵.

As per the reports available from the world 3-11 per cent CoNS isolates have decreased susceptibility to vancomycin^{16,17}. In our study, 15 per cent CoNS isolates were observed with decreased susceptibility which is higher as compared to other studies. However, these CoNS isolates did not show any significant rising trend of vancomycin MICs.

In conclusion, the changing pattern of vancomycin MIC indicates the necessity of active surveillance for therapeutic failures and timely identification of VRSA and VISA isolates to prevent their transmission. Increasing vancomycin MICs at a centre which caters to trauma patients, who are otherwise usually immunocompetent indicate that strict infection control measures need to be instituted.

**Neetu Jain¹, Purva Mathur^{2,*}
& M.C. Misra¹**

Departments of ¹Microbiology &
²Laboratory Medicine
Jai Prakash Narayan Apex
Trauma Centre, All India Institute
of Medical Sciences
New Delhi 110 029, India

*For correspondence:
purvamathur@yahoo.co.in

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