International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2020): 7.803

*Methicillin Resistant S. aureus (*MRSA) Bacteremia: A Case Series and the Clinical Implications of Vancomycin MIC Creep

Gohel Swati Y, Praveen B, Thirunarayanan M A, Ramasubramanian V,

Senthur Nambi P, Gopalakrishnan R

Abstract: ***Purpose*: Methicillin resistant S. aureus (MRSA) bacteremia carries high morbidity and mortality.** *Very few studies from India have looked into the clinical features and outcome of MRSA bacteremia, at the same time some studies have noticed significant vancomycin MIC creep amongst MRSA isolates.* ***Materials and Methods*: It is a retrospective observational study conducted at a tertiary care centre over a period of five years, describing clinical characteristics and outcome of patients with MRSA bacteremia and attempted to analyse clinical implications of vancomycin MIC creep in MRSA bacteremia.** ***Results*: A total of 60 cases of MRSA bacteremia were studied.** *Prior antibiotic exposure (63.3%), recent hospitalisation (61.7%) and diabetes mellitus (40%) were the commonest potential risk factors.* **Fifteen percent of the study population had persistent bacteremia. There was no statistically significant difference in outcome between vancomycin and teicoplanin as empirical antibiotics. Our study demonstrated an increase in percentage of isolates with MIC ≥ 1 from 2011 to 2015. On an attempt to analyse clinical implication of this creep we found no statistically significant difference between high (MIC ≥ 1) and low (MIC<1) vancomycin MIC groups.** ***Conclusion*:** *We conclude that MRSA bacteremia is a serious infection with most patients requiring ICU admission, with almost one in seven patients having persistent bacteremia and an overall mortality rate of 16 percent. With a rise in vancomycin MIC further randomised studies are needed to see its clinical implication.*

Keywords: MRSA; bacteremia; Vancomycin; MIC creep; Staphylococcus aureus

1. Introduction

Staphylococcus aureus bacteremia carries a high morbidity and mortality and methicillin resistant *S. aureus (*MRSA) is now endemic in India. [(1)] A multicentre Indian study showed overall prevalence of MRSA was 41 percent [(1)] and single centre prevalence varies from 25 per cent in the western part of India [(2)] to 50 per cent in South India. [(3)] Community acquired MRSA (CA-MRSA) has been increasingly reported from India. [(4)] However, most of the published reports originate from developed nations, and data from Asian countries are grossly underrepresented.

Vancomycin has been the mainstay of therapy for serious infections caused by MRSA because of its relatively good safety profile, its low potential for inducing resistance, and for many years, the lack of other approved alternatives. [(5)] However, its efficacy has become uncertain because of its slow bactericidal activity, the emergence of isolates with reduced susceptibility and possible "MIC creep" among susceptible strains.6 The clinical significance of vancomycin MIC creep is unclear: some studies have shown a relationship between increasing MICs and reduced vancomycin efficacy and greater mortality. [(7-9)]

Few studies from India have looked at the clinical features and outcome of MRSA bacteremia [(10)] and some studies have noticed significant vancomycin MIC creep amongst MRSA isolates. [(11-13)] We hereby describe the clinical characteristics of patients with MRSA bacteremia and attempted to analyse the clinical implications of MIC creep in MRSA bacteremia.

2. Materials and Methods

We conducted a retrospective observational study at a 550 bedded tertiary referral centre in South India between January 2011 to December 2015. Inclusion criteria were patients with MRSA bacteremia that met the US Centres for Disease Control (CDC) criteria for bloodstream infection, received an appropriate antibiotic within 48 h of blood culture collection and survived 48 h after treatment initiation. If a patient had more than one episode during a study period, only the first episode was considered. For patients with multiple blood cultures growing MRSA, the vancomycin MIC of the index bloodstream isolate was considered in the analysis.

According to clinical and laboratory standards institute (CLSI) standards S. aureus isolates resistant to oxacillin on disc testing or with MIC of 4 microgram/mL or higher were classified as Methicillin Resistant *Staph Aureus* (MRSA). Vancomycin MIC of the 60 MRSA isolates was determined by E strip as described by CLSI. Quality control was performed using CLSI recommended reference strains.

Bloodstream infections were considered to be nosocomial when cultures of blood specimens obtained >48 h after hospital admission had positive results[25] and community acquired when culture samples were obtained prior to admission or during the first 48 h of hospitalization. Persistent bacteremia was defined as a persistently positive culture results obtained 4 days after the initiation of appropriate treatment. Treatment failure was defined as death related to the infection and/or persistent bacteremia in patients who had received appropriate antibiotics for at least 3 days. The following data was analysed by reviewing patients' case records: age, gender, medical history, source of bacteremia, antibiotic treatment data

(date, time, dosing regimen and duration) and outcome. Patients were followed up from the time of diagnosis of bacteraemia until in-hospital death or discharge from the hospital.

Clearance from the ethics committee of the hospital was obtained before commencement of the study.

Statistical analysis:

All continuous data were expressed either as a mean + standard deviation (SD) or median (interquartile range) based on the distribution. Categorical variables were analysed using Chi square test or Fisher's exact test (two-tailed). Continuous variables were compared by using Student's t test. A p value of <0.05 was considered as statistically significant.

3. Results

A total of 60 patients were studied, comprising 49 (81.7%) males and 11 (18.3%) females. The age of the patients ranged between 1 to 88 years, with a mean age of 50 years. Demographic details and co-morbidities of the study population are presented in Table 1.

Most patients (66.6%) were in the intensive care unit (ICU) at the time of MRSA bacteremia. Antibiotic exposure in previous 3 months (63.3%), recent hospitalisation in last 1 year (61.7%) and diabetes mellitus (40%) were the commonest potential risk factors. Thirty patients (50%) had MRSA bacteremia within 48 hrs of hospitalisation of whom 10 (33%) patients had a history of hospitalisation in the preceding one year.

The source of infection, clinical characteristics, treatment, and outcome of patients with MRSA bacteraemia are given in table 1. Skin and soft tissue infections (30%) were the most common source of MRSA bacteremia in our study population followed by central line and visceral abscess (16.7% patients each). Mean time for culture positivity after blood culture collection was 20.9hrs.

Vancomycin was the commonest antibiotic used for empiric therapy in 55 (33%) patients, followed by teicoplanin in 19 (33.3%). One patient did not receive coverage for MRSA due to discharge against medical advice before blood culture results. Antibiotics were changed after culture report based on vancomycin MIC, renal parameters, persistent bacteremia and clinical failure. Details of definitive anti MRSA therapy are mentioned in table 3. Mean duration of hospitalisation after culture positivity was 13.36 days. Nine (15%) patients had persistent bacteremia. Treatment failure was seen in 9 patients (15%).

We compared primary early outcomes between two empirical antibiotic group (vancomycin vs teicoplanin) as mentioned in table 2 (very few patients in our study received daptomycin as empirical treatment n=4). Baseline parameters between two groups were comparable except patients in vancomycin group had significantly more underlying CKD requiring hemodialysis compared to teicoplanin group. There was no statistically significant difference between bacteremia clearance time, persistent bacteremia and duration of hospitalisation between the two groups.

We compared two definitive treatment group (glycopeptide vs daptomycin). Baseline parameters were comparable for both the groups as shown in table 2. There was no difference in clinical outcome at discharge in terms of persistent bacteremia, clinical failure and death between this two treatment groups.

All isolates were sensitive to vancomycin according to CLSI criteria (MIC≤ 2). Figure 1 shows year wise distribution of vancomycin MIC. Twenty-two isolates (36.66%) had vancomycin MIC<1 while 38 (63.33%) isolates had vancomycin MIC ≥1. In the years 2011-2012 percentage of isolates with MIC≥1 were 59.4% which increased to 67.9% in years 2013-2015.

To investigate the association between vancomycin MIC and treatment outcome, the isolates were divided into two groups: low MIC group (MIC<1 mg/L) and high MIC group (MIC≥1) mg/L. Baseline characteristics of the two groups were as per table 3. In univariate analysis, there was no significant difference in age, gender, comorbid disease and risk factors between the two groups, though recent hospitalisation was commoner in the high MIC group (p= 0.05).

Only one out of 22 patients (4.5%) had persistent bacteraemia after 4 days of appropriate antibiotics in low MIC group while 8 out of 38 patients (21.1%) had persistent bacteraemia in high MIC group but the difference was not statistically significant (p=0.187). There was no significant difference in duration of stay, mortality or treatment failure between the two groups as shown in Table 4.

4. Discussion

We hereby document one of the largest clinical case series of MRSA bacteremia from India. [10] Though in vitro prevalence studies on MRSA from India are available, clinical data is lacking especially in the era of vancomycin MIC creep. [1, 4, 11-13]

Community acquired and hospital acquired MRSA bacteremia were equally common in our study which is different from those of developed nations where one third of Staph aureus bacteremia episodes have been found to be health care associated. [14-16] However, 33% of those with CA-SAB infections had health care-associated risk factor like previous hospitalization in past one year. Molecular typing to characterize the isolates into CA or HA was not done in our study. The majority of our study populations were admitted to the ICU (66.6%) at the time of bacteremia, comparable to another Indian study. [10]

Base line parameters and risk factors such as recent antibiotic exposure in last 3 months and hospitalisation in the past 1 year were similar to those identified in another study from India. [10] Skin and soft tissue infection was the

most common source of infection followed by central line infection, which is again comparable to that study. Clearance of blood cultures with bactericidal therapy is pivotal for a successful clinical outcome. [22]: 15% of our patients had persistent bacteremia which is higher than 6.5% noted in one study [7], but comparable to another study (15.7%) [17] and much lower than in a paediatric population (40.9%). [26]

At our centre most common empirical antibiotic used to cover MRSA was vancomycin (55%) followed by teicoplanin (33.33%). Empirical antibiotics were changed to definitive therapy after availability of sensitivity reports, vancomycin MIC, renal function and persistent bacteremia. Forty percent of the study population received vancomycin as definitive therapy followed by teicoplanin (30%) and daptomycin (25%). In our study 9 (15%) patients had persistent bacteremia, which is comparable to another study. [17] Mean duration of hospital stay after MRSA bacteremia was 13.36 days and mean treatment duration was 23.7 days which was longer than the duration reported in the study by Eshwara et al. [10]

We compared primary early outcomes between two empirical group (vancomycin vs teicoplanin) which were comparable with respect to baseline parameters. There was no statistically significant difference between bacteremia clearance time, persistent bacteremia and duration of hospitalisation between the two groups, which is comparable to other published studies and a meta-analysis. [18-20] We also compared two definitive treatment group (glycopeptide vs daptomycin) with comparable baseline characteristics and could find no difference in persistent bacteraemia, clinical failure and death between these two treatment groups.

Our study demonstrated an increase in percentage of isolates with MIC ≥ 1 from 2011 to 2015. Some studies from other parts of the world have shown this to be a risk factor for worse outcome and mortality. [7-9, 21] In our study, we compared outcomes amongst patients with a low and high vancomycin MIC. These two groups had comparable baseline parameters like age, risk factors and source of bacteremia. Recent hospitalisation was higher in the high MIC group (p=0.05), comparable to the study by Lodise et al. [7]

Our study showed that more patients had persistent bacteremia in the high MIC group, although this was not statistically significant. [7-9, 21] A recent meta-analysis also revealed that higher vancomycin MIC values (>1.5 µg/mL), irrespective of MIC testing methodology and infection source, were predictive of mortality. [23] We could not find significant differences in terms of overall mortality, duration of hospital stays and vancomycin treatment failure between the low and high MIC groups. This could have been because of our small study population; besides vancomycin susceptibility to *Staphylococcus aureus* is associated with reduction in bacterial virulence potential and phenotypic features that itself may reduce fatality rates. [17]

Our study has several limitations due to the retrospective study design and small numbers. We could not establish associations between several risk factors and outcome measures in various patient categories such as CA-and HA-MRSA. Molecular characterization of the isolates and epidemiological typing was not performed. We also could not demonstrate any association between vancomycin MIC creep and treatment with vancomycin or mortality, possibly due to small study numbers.

We conclude that MRSA bacteremia is a serious infection with most patients requiring ICU admission, with almost one in seven patients having persistent bacteremia and an overall mortality rate of 16 percent. Bacteremia can be both community and hospital acquired, though a third of patients with community acquisition had recent hospitalization. Vancomycin was the most commonly used antibiotic for both empiric and definitive therapy, and we could find no difference in outcomes between vancomycin and teicoplanin for empiric therapy or between glycopeptides and daptomycin for definitive therapy. We did demonstrate MIC creep over the study period but could not show differences in clinical outcome or vancomycin treatment failure between patients with low and high vancomycin MICs. Our study supports IDSA guidelines [6] recommending vancomycin therapy for patients with MRSA bacteremia irrespective of the vancomycin MIC, unless there is treatment failure.

Authors' Contributions Statement: All authors have contributed clinical cases. Gohel Swati Y has analyzed the data under guidance of Gopalakrishnan R. All authors read and approved the final version of the manuscript.

Conflicts of Interest: All authors-None to declare.

Funding: None to declare.

References

[1] Joshi S, Ray P, Manchanda V, Bajaj J, Chitnis DS, Gautam V et al. Methicillin resistant *Staphylococcus aureus* (MRSA) in India: Prevalence & susceptibility pattern. Indian J Med Res.2013; 137 (2): 363–69.
[2] Patel AK, Patel KK, Patel KR, Shah S, Dileep P. Time trends in the epidemiology of microbial infections at a tertiary care centre in west India over last 5 years. J Assoc Physicians India 2010; 58 (Suppl): 37-40.
[3] Gopalakrishnan R, Sureshkumar D. Changing trends in antimicrobial susceptibility and hospital acquired infections over an 8-year period in a tertiary care hospital in relation to introduction of an infection control programme. J Assoc Physicians India 2010; 58 (Suppl): 25-31.
[4] D'Souza N, Rodrigues C, Mehta A. Molecular characterization of Methicillin-resistant Staphylococcus aureus with emergence of epidemic clones of sequence type (ST) 22 and ST 772 in Mumbai, India. J Clin Microbiol 2010; 48 (5): 1806-11.
[5] T. M. Scott. Alternatives to vancomycin for the treatment of methicillin-resistant *Staphylococcus*

aureus infections. Clin Infect Dis. 2007 Sep 15; 45 Suppl 3: S184-90.

[6] Liu c, Bayer A., Cosgrove S. E., *et al.* Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children: executive summary. Clin Infect Dis, 52 (2011), pp.285–292.

[7] Lodise TP, Graves J, Evans A. et al. Relationship between Vancomycin MIC and Failure among Patients with Methicillin-Resistant Staphylococcus Aureus Bacteremia Treated with Vancomycin. Antimicrobial Agents and Chemotherapy, September 2008 vol.52 no.9. P.3315-3320.

[8] Abhay Dhand and George Sakoulas et al. Reduced vancomycin susceptibility among clinical Staphylococcus aureus isolates ('the MIC Creep'): implications for therapy. F1000 Medicine Reports 2012, 4: 4 (doi: 10.3410/M4-4).

[9] Chang W et al. Vancomycin MIC creep in methicillin-resistant *Staphylococcus aureus* (MRSA) isolates from 2006 to 2010 in a hospital in China. Indian J Med Microbiol, 2015; 33: 262-266.

[10] Eshwara VK, Munim F et al. *Staphylococcus aureus* bacteremia in an Indian tertiary care hospital: observational study on clinical epidemiology, resistance characteristics, and carriage of the Panton–Valentine leukocidin gene. Int J Infect Dis. 2013 Nov; 17 (11): e1051-5.

[11] Dorairajan S, Gopalakrishnan R, Ghafur A and Ramsubramanian V. Vancomycin MIC Creep Among Methicillin Resistant Staphylococcus Aureus: A Report. American Medical Journal 2013, 4 (2): 197-200.

[12] Nagasundaram N, Sistla S et al. Worrisome trends in rising minimum inhibitory concentration values of antibiotics against methicillin resistant *Staphylococcus aureus* – Insights from a tertiary care centre, South India. Braz j infect dis.2 0 15; 19 (6): 585–589.

[13] Jain N, Mathur P & Misra MC. Trend of vancomycin susceptibility of staphylococci at a level 1 trauma centre of India. Indian J Med Res.2013 Dec; 138 (6): 1022–1024.

[14] Collignon P, Nimmo GR, Gottlieb T, Gosbell IB, on behalf of the Australian Group on Antimicrobial Resistance. *Staphylococcus aureus* Bacteremia, Australia. *Emerging Infectious Diseases*.2005; 11 (4): 554-561.

[15] Laupland KB, Ross T, Gregson DB. *Staphylococcus aureus* bloodstream infections: risk factors, outcomes, and the influence of methicillin resistance in Calgary, Canada, 2000–2006. J Infect Dis, 198 (2008), pp.336–343.

[16] Sader HS, Jones RN, Andrade-Baiocchi S, Biedenbach DJ; SENTRY Participants Group (Latin America) . Four-year evaluation of frequency of occurrence and antimicrobial susceptibility patterns of bacteria from bloodstream infections in Latin American medical centers. Diagn Microbiol Infect Dis, 44 (2002), pp.273–280.

[17] Chong YP, Park SJ, Kim HS et al. Persistent Staphylococcus aureus bacteremia: a prospective analysis of risk factors, outcomes, and microbiologic and genotypic characteristics of isolates. Medicine (Baltimore). 2013; 92 (2): 98-108.

[18] Svetitsky S, Leibovici L, Paul M. Comparative Efficacy and Safety of Vancomycin versus Teicoplanin: Systematic Review and Meta-Analysis *Antimicrobial Agents and Chemotherapy*.2009; 53 (10): 4069-4079.

[19] Peng Y, Ye X, Li Y, Bu T, Chen X, et al. Teicoplanin as an Effective Alternative to Vancomycin for Treatment of MRSA Infection in Chinese Population: A Meta-analysis of Randomized Controlled Trials. PLoS ONE 2013 8 (11): e79782. doi: 10.1371/journal. pone.0079782.

[20] Yoon YK, Park DW, Sohn JW, et al. Multicenter prospective observational study of the comparative efficacy and safety of vancomycin versus teicoplanin in patients with health care-associated methicillin-resistant Staphylococcus aureus bacteremia. Antimicrob Agents Chemother.2014; 58 (1): 317-324.

[21] Sakoulas G, Moise-Broder PA, Schentag J, Forrest A, Moellering RC, Eliopoulos GM. Relationship of MIC and Bactericidal Activity to Efficacy of Vancomycin for Treatment of Methicillin-Resistant *Staphylococcus Aureus* Bacteremia. *Journal of Clinical Microbiology*.2004; 42 (6): 2398-2402.

[22] Soriano A, Marco F, Martinez J, Pisos E, Almela M, Dimova V, *et al*. Influence of vancomycin minimum inhibitory concentration on the treatment of methicillin-resistant *Staphylococcus aureus* bacteremia. Clin Infect Dis 2008; 46: 193-200.

[23] Van Hal SJ, Lodise TP, Paterson DL. The clinical significance of vancomycin minimum inhibitory concentration in *Staphylococcus aureus* infections: A systematic review and meta-analysis. Clin Infect Dis 2012; 54: 755-71.

[24] Howden BP, Davies JK, Johnson PD, Stinear TP, Grayson ML. Reduced vancomycin susceptibility in *Staphylococcus aureus*, including vancomycin-intermediate and heterogeneous vancomycin-intermediate strains: Resistance mechanisms, laboratory detection, and clinical implications. Clin Microbiol Rev 2010; 23: 99-139.

[25] Garner JS, Jarvis WR, Emori TG, Horan TC, and Hughes JM. CDC definitions for nosocomial infections. Am. J. Infect. Control.1988 Jun; 16 (3): 128–140.

[26] Welsh K J et al. Clinical Characteristics, Outcomes and Microbiological features Associated with Methicillin-Resistant Staphylococcus Aureus Bacteremia in Pediatric Patients Treated with Vancomycin. Journal of clinical Microbiology, Mar.2010, p.894-899.

Table 1: Demographic and baseline characteristics of patients with MRSA bacteremia

Study variables	*MRSA bacteremia (N=60) (%)*
Gender	
Male	49 (81.7%)
Female	11 (18.3%)
Age	
1-18yrs	6 (10%)
19-59yrs	31 (51.66%)
≥60yrs	23 (38.33%)
Acquisition of infection	
Hospital acquired	30 (50%)
Community acquired	30 (50%)
Site of admission	
ICU	40 (66.6%)
Non-ICU	20 (33.3%)
Co-morbidities	
Previous antibiotics (past 3 months)	38 (63.3%)
Recent hospitalisation (past 1 year)	37 (61.7%)
Diabetes mellitus	24 (40%)
Chronic kidney disease	17 (28.3%)
Burns	11 (18.3%)
Central line present	10 (16.7%)
Chronic liver disease	5 (8.3%)
Source of infection	
Skin and soft tissue	18 (30%)
Central line	10 (16.7%)
Visceral abscess (including osteomyelitis)	10 (16.7%)
Septic thrombophlebitis	5 (8.3%)
Infective endocarditis	7 (11.67%)
Osteomyelitis	6 (10%)
Mean time for culture positivity (hours)	20.9hrs
Empirical antibiotics	
Vancomycin	33 (55%)
Teicoplanin	19 (33.33%)
Daptomycin	4 (6.7%)
Clindamycin	1 (1.7%)
Linezolid	2 (3.3%)
None	1 (1.7%)
Definitive treatment	
Vancomycin	24 (40%)
Teicoplanin	18 (30%)
Daptomycin	15 (25%)
Clindamycin	1 (1.7%)
Persistent bacteraemia	9 (15%)
Mean duration of antibiotics (days)	23.7 days
Mean duration of hospital stay after culture positivity (days)	13.36days
Outcome	
Discharge	42 (70%)
Death	10 (16.66%)
Treatment failure	9 (15%)

Table 2: Outcomes in empiric and definitive treatment groups

Baseline characteristics and primary treatment outcomes of two empirical treatment group			
Characteristics	***Vancomycin (n=33) (%)***	***Teicoplanin (n=19) (%)***	***P value***
Risk factors			
Diabetes mellitus	15 (45.5%)	5 (26.3%)	0.172
CKD	13 (39.4%)	2 (10.5%)	0.031
CLD	3 (9.1%)	1 (5.3%)	1
Central line	8 (24.2%)	1 (5.3%)	0.130
Burns	4 (12.1%)	5 (26.3%)	0.260
Site of admission			
Ward	11 (33.3%)	5 (26.3%)	0.598
ICU	22 (66.7%)	14 (73.7%)	
Requirement of HD	20 (60.6%)	4 (21.1%)	0.009
Persistent bacteraemia	4 (18.2%)	3 (20%)	1
Median duration of hospitalisation (interquartile range)	8 (6-14)	7 (4.5-10.5)	0.391
Median blood culture clearance time in hours (interquartile range)	72 (72-120)	72 (48-96)	0.281

Comparison of outcome in two definitive treatment group (Glycopeptides vs Daptomycin)			
Study variables	***Glycopeptides (vancomycin/ teicoplanin) N=32 (%)***	***Daptomycin N=15 (%)***	***P value***
Risk factors			
Diabetes mellitus	17 (40.5%)	4 (26.7%)	0.534
CKD	11 (26.2%)	4 (26.7%)	1
CLD	3 (7.1%)	2 (13.3%)	0.467
Central line	6 (14.3%)	4 (26.7%)	0.429
Burns	7 (16.7%)	4 (26.7%)	0.455
Persistent bacteremia	5 (16.7%)	4 (33.3%)	0.406
Treatment failure	5 (11.9%)	4 (26.7%)	0.305
Death	6 (14.3%)	4 (26.7%)	0.507

Table 3: Baseline characteristics of patients in high and low MIC groups

Baseline characteristics	***Vancomycin MIC<1 (N=22)***	***Vancomycin MIC≥1 (N=38)***	***P value***
Age in year (mean)	55.68	47.86	
Male gender	19 (86.4%)	30 (78.9%)	0.731
ICU admission at the time of index culture	14 (63.6%)	26 (68.4%)	0.706
Risk factors			
Diabetes	11 (50%)	13 (34.2%)	0.229
Chronic kidney disease	8 (36.4%)	9 (23.7%)	0.294
Hemodialysis requirement	10 (45.5%)	17 (44.7%)	0.957
Chronic liver disease	2 (9.1%)	3 (7.9%)	1.0
Burns	3 (13.6%)	8 (21.1%)	0.731
Recent hospitalization (last 3 months)	10 (45.5%)	27 (71.1%)	0.05
Recent surgery (last 3 months)	2 (9.1%)	6 (15.8%)	0.698
Source of bacteraemia			
Skin and soft tissue infection	7 (31.8%)	11 (28.9%)	0.815
Infective endocarditis	3 (13.6%)	1 (2.6%)	0.135
Osteomyelitis	3 (13.6%)	3 (7.9%)	0.659
Visceral abscesses	4 (18.2%)	6 (15.8%)	1.0
Central line	3 (13.6%)	7 (18.4%)	0.732
Septic thrombophlebitis	1 (4.5%)	4 (10.5%)	0.643

Table 4: Clinical outcome between high and low MIC groups

Outcome	***Vancomycin MIC<1 (N=22)***	***Vancomycin MIC≥1 (N=38)***	***P value***
Persistent bacteremia	1 (4.5%)	8 (21.1%)	0.187
Hospital stay after index blood culture (median days)	9 (5-15)	8 (5-14)	0.896
Hospital stay Before bacteremia	11.5 (10.5-41)	10 (6-15.5)	0.307
Mortality	5 (22.72%)	5 (13.16%)	0.726
Treatment failure	4 (18.18%)	5 (13.16%)	0.696

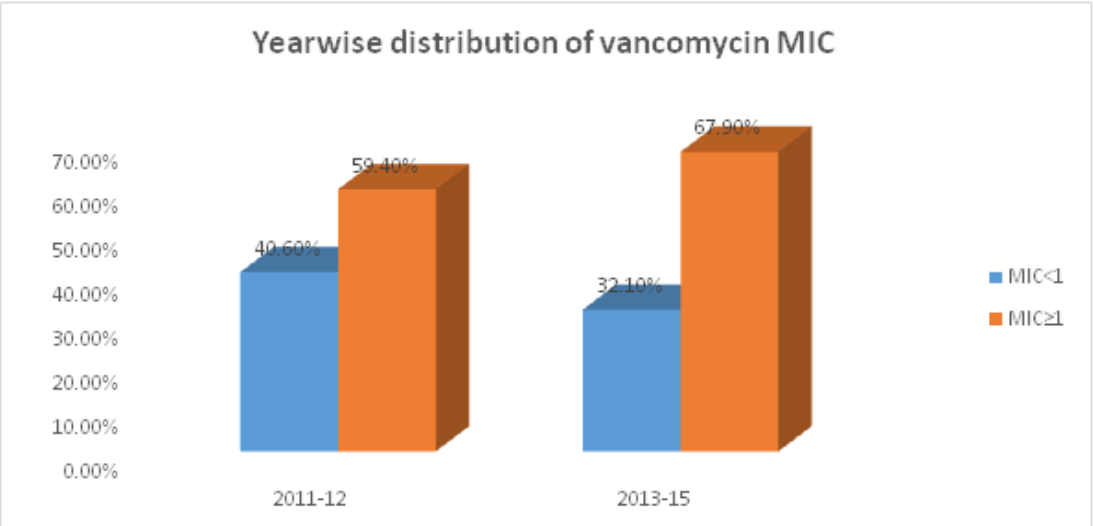

Figure 1: Year wise distribution of vancomycin MIC