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Original Article

Microbiology Section

Minimum Inhibitory Concentration of Vancomycin against Methicillin Resistant *Staphylococcus aureus* Strains Isolated from a Tertiary Care Hospital

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ABSTRACT

Introduction: Methicillin Resistant *Staphylococcus aureus* (MRSA) is one major healthcare associated infection. Prevalence of MRSA and its antibiotic susceptibility changes from time to time. Disc diffusion method remains the most widely used antibiotic susceptibility method in routine clinical laboratories but MIC detection is essential for checking susceptibility to Vancomycin.

Aim: To detect MRSA isolates both by disc diffusion method and Minimum Inhibitory Concentration (MIC) method using E-test, their susceptibility to common antibiotics.

Materials and Methods: A cross-sectional study was conducted on different samples for culture and sensitivity in the microbiology laboratory of a tertiary care centre for six months. Antibiotic susceptibility testing was done in *Staphylococcus aureus* isolates by disc diffusion method in Mueller Hinton agar. Cefoxitin and Vancomycin MIC of different isolates were detected. Frequencies of MRSA isolates from different clinical samples and their susceptibility to various common antimicrobial agents such as Penicillin (10 units), Cefoxitin (30 µg), Erythromycin (15 µg), Clindamycin (2 µg), Cotrimoxazole (1.25/23.75 µg) and Linezolid (30 µg) were determined. Data were analysed using the IBM SPSS version 23. Descriptive statistics were used.

Results: Total 353 *S.aureus* isolated over six months period, 100 were Methicillin Resistant (28.3%). A 66% were from males and 34% were from females. MIC50 of Cefoxitin was found to be 16 while the Vancomycin MIC50 was 0.38 and Vancomycin MIC90 was 0.25.

Conclusion: Percentage of MRSA out of *S. aureus* isolates was 28.3%. Pus swabs were the major sample. All the MRSA isolates had a Vancomycin MIC ≤1.5 µg/mL. E-test has the advantage of detecting even minor changes in MIC.

Keywords: Antimicrobial susceptibility, Cefoxitin, Infections, Penicillins

INTRODUCTION

The MRSA is one major bug causing healthcare associated infections. Many factors contribute to MRSA infection and colonisation in patients with history of recent hospital admission especially in ICUs, chronic skin condition, diabetes, presence of open wound and placement of central line [1,2]. Prevalence of MRSA and its antibiotic susceptibility changes from time to time. It varies regionally also.

From worldwide data, the Community Acquired-MRSA (CA-MRSA) carriage prevalence ranges from 0% to 23.5% and India with the highest prevalence (16.5%-23.5%), followed by Vietnam (7.9%) and Taiwan (3.5%-3.8%) and in hospital settings, it is 0.7% to 10.4% [3].

In hospital settings of India, it is around 29-46% [4,5]. MRSA are considered to be resistant to all Penicillinases-stable Penicillins including Oxacillin, Methicillin, Nafcillin, Cloxacillin, and Dicloxacillin. In addition, they are resistant to all other beta lactam agents and have become resistant to Aminoglycosides and Fluoroquinolones. Multidrug resistant MRSA poses serious infections which are difficult to treat. Therapeutic options for MRSA include Glycopeptides (Vancomycin, Teicoplanin) Lipopeptides (Daptomycin), fifth generation Cephalosporins and Oxazolidinones (Linezolid). The first isolate with reduced susceptibility to Vancomycin was reported from Japan in 1997 [6]. Emergence of *Staphylococcus* strains with full resistance to Vancomycin (VRSA) has given rise to serious problem worldwide.

Disc diffusion method remain the most widely used antibiotic susceptibility method in routine clinical laboratories. Mueller Hinton Agar (MHA) medium is commonly used for disc diffusion assay. For detection of methicillin resistance, some commercial automated methods are increasingly used [7]. MIC detection using E-test can also be used to detect MRSA isolates [8,9]. Disc diffusion method is not much reliable for Vancomycin testing [10]. Based on the MIC of the isolate for Vancomycin, either Vancomycin or any other anti MRSA drugs should be used [11]. There are many methods for Vancomycin MIC detection. Vancomycin MIC for MRSA isolates differ with different susceptibility methods [12]. E-test is a convenient method of antimicrobial susceptibility testing. It directly detects MIC values of an antibiotic. E-test comprises a predefined gradient of Vancomycin which is used to determine the MIC (µg/mL) of the antibiotic against microorganisms on agar media after an overnight incubation [13]. Because of its high cost, it is not used routinely in laboratories and not many studies [14-16] are conducted based on it especially in Southern part of our country [17,18].

So, this study was aimed to detect MRSA isolates both by disc diffusion and E-test, their susceptibility to common antibiotics, also their Vancomycin MIC with E-test from samples received in Microbiology lab in a tertiary care centre in Southern India.

MATERIALS AND METHODS

Study Design

The cross-sectional study was conducted in Government Medical College, Thrissur, Kerala, India from January, 2015 to June, 2015 for a period of six months, after obtaining ethical clearance. (B6-15426/2014/MCTCR dt.23.2.15 Date of ethical board review: 29.05.2015).

According to previous study of Chaterjee A et al., [19], prevalence of MRSA reported was 52%. Therefore, minimum sample size calculated for 95% significant level with relative precision of 20% of 'p' was 92 (rounded to 100).

All samples (pus aspirates, pus swabs, urine etc.,) received in the Microbiology lab over the six month period were included in this study. After antibiotic sensitivity testing, isolates which were sensitive to Cloxacillin (MSSA) were excluded from further study. Patients included paediatric population to old aged and severely ill like patients in ICU, chronic renal disease, chronic liver diseases and trauma cases. Only one isolate per patient was included in the study. Informed consent was taken from the patients before proceeding with the isolates.

Study Procedure

Clinical samples were sent from patients with discharge from fracture wound, surgical site infection or infected implant. The samples were inoculated to blood agar and MacConkey agar. Manual identification methods were used as per lab Standard Operating procedures [20]. The isolates were identified as *Staphylococcus aureus* by Gram staining of the colony smear (Gram positive cocci in clusters), and biochemical reactions (slide coagulase and tube coagulase test both positive). Antibiotic susceptibility testing was done in these isolates by disc diffusion method in Mueller Hinton agar as per CLSI guidelines [21]. The discs used were Penicillin (10 units), Cefoxitin (30 µg), Erythromycin (15 µg), Clindamycin (2 µg), Cotrimoxazole (1.25/23.75 µg) and Linezolid (30 µg). Induced Clindamycin resistance was also checked by Erythromycin and Clindamycin discs spaced 15 mm apart as mentioned in CLSI guidelines [21,22]. All the isolates resistant to Cefoxitin were considered as MRSA. These isolates were again subjected to antimicrobial susceptibility testing by E-test method to determine the MIC against micro organisms as tested on agar media for Cefoxitin and Vancomycin together [14]. Here, a dual E-test (Vancomycin-CefoxitinEzy MIC™ Strip from Himedia) was used which comprised of a predefined gradient of both Cefoxitin (0.5-64 mcg/mL) and Vancomycin (0.19-16.0 mcg/mL) both in one strip, so the MIC s of both antibiotics could be detected simultaneously. Cefoxitin and Vancomycin MIC of different isolates were detected. Quality control of the strip was also done with standard ATCC cultures (*S.aureus* ATCC 25923) recommended by CLSI on suitable medium incubated appropriately [21].

STATISTICAL ANALYSIS

Data were analysed using the IBM SPSS version 23. Descriptive statistics were used to determine the frequencies of MRSA isolates from different clinical samples, their susceptibility to various antimicrobial agents, MIC's of Cefoxitin and Vancomycin.

RESULTS

In a six month period, 100 (28.3%) MRSA strains were isolated from 353 different samples received in Microbiology laboratory Sixty six (66%) were from males and 34 (34%) were from females. Maximum number of patients was in the age group 41-50 (29/100). Mean age was 40.89±.22. New borns were five and children less than 10 years were nine in number [Table/Fig-1]. Hundred samples received were from various specialities like surgery, orthopaedics, paediatrics and super specialities like neurosurgery and paediatric surgery [Table/Fig-2]. High vaginal swabs were sent from women who had rupture of membranes at 35-37 weeks of pregnancy (2/100). Pus swabs were maximum, 72% of total samples (72/100). Maximum strains were isolated from Orthopaedic department (35/100). MRSA was isolated from umbilical swabs taken from two new borns (2/100). Though pus aspirates are better specimens than swabs, we received more swabs as specimens as it is easier to collect.

Age group	Male	Female	Percentage
New born	3	2	5.0
Less than 1 year	1	0	1.0
1-10 years	4	4	8.0
11-20 years	2	2	4.0
21-30 years	10	5	15.0
31-40 years	7	6	13.0
41-50 years	22	7	29.0
51-60 years	6	4	10.0
61-70 years	10	3	13.0
71-80 years	1	1	2.0
Total	66	34	100.0

[Table/Fig-1]: Distribution of age and gender.

Over a period of six months, 353 strains of *S. aureus* were isolated. Among these isolates, 100 (28.3%) were Methicillin Resistant and 253 (71.6%) were Methicillin sensitive (MSSA) by cefoxitin disc diffusion method.

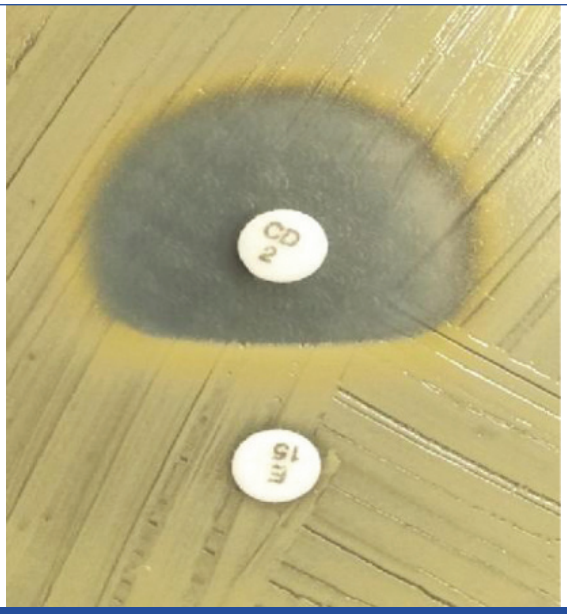
The results of antibiotic susceptibility tests were studied in detail [Table/Fig-3]. Out of these 100 isolates, all of them were susceptible to high end antibiotics like Vancomycin and Linezolid. Oxacillin resistant *S.aureus* are considered resistant to other beta lactam agents, Beta Lactam combination agents, Cephems and Carbapenems. Erythromycin and Clindamycin are poorly concentrated in urine. So, they were not checked routinely in urine isolates. Linezolid is a reserve antibiotic for urinary tract infections caused by Vancomycin Resistant Enterococci (VRE). Hence, it was not checked for the MRSA strain isolated from urine here. Sensitivity to Clindamycin and Cotrimoxazole were around 50% for pus swabs and aspirates. Out of the 100 MRSA isolates, 47 were susceptible and 52 were resistant (one urine isolate not checked) to Clindamycin. Among the resistant population, 32/52 had resistance induced by Erythromycin which was detected by D zone testing [22] [Table/Fig-4].

Department	Samples								
	Pus swab	Pus aspirate	High vaginal swab	Urine	Ear and nasal swab	Umbilical swab	Conjunctival swab	Throat swab	Total
Surgery	12	10	0	1	1	0	0	0	24
Orthopaedics	31	4	0	0	0	0	0	0	35
Paediatrics	6	1	0	0	2	2	2	0	13
Dermatology	11	0	0	0	0	0	0	0	11
Obstetrics and gynaecology	8	0	2	0	0	0	0	0	10
ENT	0	0	0	0	1	0	0	0	1
Neurosurgery	2	0	0	0	0	0	0	0	2
Paediatric surgery	1	1	0	0	0	0	0	0	2
Radiation oncology	1	0	0	0	0	0	0	1	2
Total	72	16	2	1	4	2	2	1	100

[Table/Fig-2]: Type of samples received from different departments.

	No. of isolates	Penicillin	Erythromycin	Clindamycin*	Cotrimoxazole	Linezolid	Vancomycin
Pus swab	72	0	5 (6.9%)	35 (48.6%)	37 (51.4%)	72 (100%)	72 (100%)
Pus aspirate	16	0	1 (6.3%)	9 (56.3%)	9 (56.3%)	16 (100%)	16 (100%)
Urine	1	0	Not checked	Not checked	1 (100%)	Not checked	1 (100%)
Otherswabs†	11	0	0	3 (27.3%)	8 (72.7%)	11 (100%)	11 (100%)

[Table/Fig-3]: Antibiogram of MRSA isolates (Susceptible population).
*Out of the 52 isolates which were resistant to Clindamycin, 32 had resistance induced by Erythromycin which was detected by D zone testing
†Includes high vaginal swab, ear and nasal swab, umbilical swab, conjunctival swab and throat swab



[Table/Fig-4]: D-test showing induced clindamycin resistance.

Cefoxitin and Vancomycin MIC values were obtained with E-test [Table/Fig-5-7]. All had Cefoxitin MIC of 8 and above, 49% had an MIC value of >64. MIC50 was 16. Vancomycin MIC was 1.5 and below for all isolates. MIC ranged from 0.19 to 1.5. Vancomycin MIC50 is 0.38 and Vancomycin MIC90 is 0.25. Maximum MIC was 1.5 found in one isolate, which is again in the susceptible range.

Cefoxitin MIC (µg/mL)	Percentage
8	29.0
12	15.0
16	6.0
24	1.0
>64	49.0
Total	100.0

[Table/Fig-5]: Cefoxitin MIC checked in MRSA isolates.

Vancomycin MIC (µg/mL)	Percentage
0.19	9.0
0.25	10.0
0.38	37.0
0.50	29.0
0.75	13.0
1.00	1.0
1.50	1.0
Total	100.0

[Table/Fig-6]: Vancomycin MIC of MRSA isolates.

DISCUSSION

In a six month period, out of 353 *S. aureus* isolated, 100 were Methicillin Resistant (28.3%). Overall prevalence of MRSA in India was found to be 30 to 80% [13-15]. A study by Anupurba S et al., shows a prevalence of 54.8% of MRSA in Eastern Uttar Pradesh [23]. In another study by Joshi S and Ray P which was conducted in 15 Indian tertiary care centres during a two year period, the

[Table/Fig-7]: Cefoxitin and Vancomycin combined E-test for MIC detection.

overall MRSA prevalence was 41% [24]. A study from South Western India by Chatterjee A et al., shows an MRSA prevalence of 52% [19]. Different International and National studies show that around 20 to 30% of *S.aureus* is MRSA [25-27]. Study by Stürenburg E, Rajaduraipandi K et al., and Dar JA et al., shows an MRSA prevalence of 15-20%, 31.1% and 35.1%, respectively [25-27]. This study correlates with the world statistics. MRSA was more common in males (66%) than females (34%). Majority of the samples were pus swabs (72/100). Maximum number of MRSA isolates was from Orthopaedic department (35/100). Samples were taken from discharge from fracture wound, surgical site infection or infected implant.

Regarding the antibiogram of MRSA isolates using disc diffusion method, all were susceptible to Linezolid. 55% of isolates were susceptible to Cotrimoxazole. Erythromycin susceptibility was much lower, only 6 out of 99 isolates (not tested in one sample of urine) were susceptible. Clindamycin also was not checked in urine isolate but 47 isolates from other samples were susceptible. Out of 52 Clindamycin resistant isolates, 32 had induced Clindamycin resistance. So out of 100 MRSA isolates, 32 had induced Clindamycin resistance (32%). This is in accordance with the study of Gadepalli R et al., which showed it as 30% in MRSA [28]. Other studies like Yilmaz G et al., and Rahabar M and Hajia M showed 24.4% and 22.6% in MRSA, respectively [29,30]. On the contrary, Levin TP et al., showed an inducible Clindamycin resistance of only 12.5% in MRSA [31].

Regarding the MIC detection with E-test, all had Cefoxitin MIC of 8 and above. So the MRSA isolates detected by disc diffusion method were confirmed as the same with MIC method also. Vancomycin MIC was 1.5 and below for all isolates which were in the susceptible range. Vancomycin MIC50 is 0.38 and Vancomycin MIC90 is 0.25. In a study conducted by Chaudhari CN et al., 92% of MRSA strains had a Vancomycin MIC of ≤2 µg/mL [10]. A 5.6% and 1.7% isolates had MIC in the range of 2.5-3.5 and 4 µg/mL, respectively. MIC50 and MIC90 of these isolates by E-test were 0.75 and 2 µg/mL, respectively.

According to the study of Song KH et al., in which they compared Vancomycin MIC's by E-test and broth microdilution method, the numbers of isolates with high MIC (≥1.5 mg/litre) were 19.5% by E-test and 8.5% by broth microdilution [32]. In a study by Kumari J et al., Vancomycin MIC as detected by E-test ranged from 0.75-4 µg/mL [33]. A 4.1% of the studied MRSA strains were Vancomycin intermediate (VISA, Vancomycin MIC 4 µg/mL). MIC90 and MIC50 by E-test were 3 µg/mL and 2 µg/mL respectively. They concluded that E-test can be used to determine Vancomycin MIC in the intermediate zone even minor changes in MIC and study "MIC creep". MIC90 and MIC50 were higher compared to the present study.

Overall, the prevalence of MRSA according to this study correlates with national and international statistics [Table/Fig-8] [10,14,16-18,32,33]. Induced Clindamycin resistance, also is routinely tested in the laboratory by the D zone test, as missing of this type of resistance may lead to therapeutic failure by Clindamycin. There were no Vancomycin intermediate or Vancomycin resistant strains obtained in this study which could easily be found out with the E-test method used here.

Author, Place	No. of samples	Vancomycin MIC of MRSA isolates minimum value µg/mL	Vancomycin MIC of MRSA isolates maximum value µg/mL
Chaudhari CN et al., Pune, India [10]	232	≤2	4
Katiyar R et al., Lucknow, India [14]	62	0.75	3
Niveditha N and Sujatha S Pondicherry, India [16]	200	0.125	3
Moses V et al., Telangana, India [17]	115	0.5	32
Amberpet R et al., Pondicherry, India [18]	500	0.25	2
Song KH et al., South Korea [32]	673	≤1	2
Kumari J et al., Karnataka, India [33]	98	0.75	4

[Table/Fig-8]: Comparative study of Vancomycin MIC [10,14,16-18,32,33].

Limitation(s)

Only one method was used to detect the MIC values due to high cost of tests and could not be compared with other methods.

CONCLUSION(S)

From the present study, it was concluded that the percentage of MRSA out of *S. aureus* isolates was 28.3%. Pus swabs were the major sample. All the MRSA isolates had a Vancomycin MIC ≤1.5 µg/mL which was determined by using Vancomycin E-test. All the isolates were in susceptible range. Using an E-test has the advantage of detecting even minor changes in MIC. It is recommended that there should be a continued surveillance to detect the changing patterns of reduced Vancomycin MIC among MRSA isolates from clinical samples to evaluate the clinical outcomes of serious MRSA infections.

REFERENCES

[1] Fukuta Y, Cunningham CA, Harris PL, Wagener MM, Muder RR. Identifying the risk factors for hospital-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) infection among patients colonised with MRSA on admission. Infect Control Hosp Epidemiol. 2012;33(12):1219-25.

[2] Torres K, Sampathkumar P. Predictors of methicillin-resistant *Staphylococcus aureus* colonisation at hospital admission. Am J Infect Control. 2013;41(11):1043-47.

[3] Wong JW, Ip M, Tang A. Prevalence and risk factors of community-associated methicillin resistant *Staphylococcus aureus* carriage in Asia-Pacific region from 2000 to 2016: A systematic review and meta-analysis. Clin Epidemiol. 2018;10:1489-501.

[4] Pai V, Rao VI, Rao SP. Prevalence and antimicrobial susceptibility pattern of methicillin resistant *Staphylococcus aureus* (MRSA) isolates at a tertiary care hospital in Mangalore, South India. J Lab Physicians. 2010;2(2):82-84.

[5] Arora S, Devi P, Arora U, Devi B. Prevalence of methicillin resistant *Staphylococcus aureus* in a tertiary care hospital in Northern India. J Lab Physicians. 2010;2:78-81.

[6] Hiramatsu K, Hanaki H, Ino T, Yabuta K, Oguri T, Tenover FC. Methicillin-resistant *Staphylococcus aureus* clinical strain with reduced vancomycin susceptibility. J Antimicrob Chemother. 1997;40(1):135-36.

[7] Harbarth S. Control of endemic methicillin-resistant *Staphylococcus aureus*-recent advances and future challenges. Clin Microbiol Infect. 2006;12(12):1154-62.

[8] Gupta M, Kaore N, Gupta A. Comparative evaluation of MIC by E-test and Cefoxitin disc diffusion for detection of Methicillin Resistant *Staphylococcus aureus* (MRSA). Indian J Microbiol Res. 2016;3(4):408-11.

[9] Sharma S, Srivastava P, Kulshrestha A, Abbas A. Evaluation of different phenotypic methods for the detection of methicillin resistant *Staphylococcus aureus* and antimicrobial susceptibility pattern of MRSA. Int J Community Med Public Health. 2017;4(9):3297-301.

[10] Chaudhari CN, Tandel K, Grover N, Bhatt P, Sahni AK, Sen S, et al. In vitro vancomycin susceptibility amongst methicillin resistant *Staphylococcus aureus*. Medical Journal, Armed Forces India. 2014;70(3):215-19.

[11] Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, 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. 2011;52(3):285-92.

[12] Kruzel MC, Lewis CT, Welsh KJ, Lewis EM, Dundas NE, Mohr JF, et al. Determination of vancomycin and daptomycin MICs by different testing methods for methicillin-resistant *Staphylococcus aureus*. J Clin Microbiol. 2011;49(6):2272-73.

[13] Jorgensen JH, Ferraro MJ. Antimicrobial susceptibility testing: A review of general principles and contemporary practices. Clin Infect Dis. 2009;49(11):1749-55.

[14] Katiyar R, Chowdhry S, Kaistha S, Dhole TN. Analysis of vancomycin resistance among Methicillin Resistant *Staphylococcus aureus* in HIV patients suffering from respiratory illness. World Journal of Pharmaceutical Research. 2017;6(5):976-83.

[15] Diaz R, Afreixo V, Ramalheira E, Rodrigues C, Gago B. Evaluation of vancomycin MIC creep in methicillin-resistant *Staphylococcus aureus* infections- A systematic review and meta-analysis. Clinical Microbiology and Infection. 2018;24(2):97-104.

[16] Niveditha N, Sujatha S. Worrisome trends in rising minimum inhibitory concentration values of antibiotics against methicillin resistant *Staphylococcus aureus*- Insights from a tertiary care center, South India. Braz J Infect Dis. 2015;19(6):585-89.

[17] Moses V, Kandi V, Rao SD. Minimum Inhibitory concentrations of Vancomycin and Daptomycin against Methicillin resistant *Staphylococcus aureus* isolated from various clinical specimens: A study from South India. Cureus. 2020;12(1):6749.

[18] Amberpet R, Sistla S, Sugumar M, Nagasundaram N, Manoharan M, Parija SC. Detection of heterogeneous vancomycin-intermediate *Staphylococcus aureus*: A preliminary report from south India. Indian J Med Res. 2019;150(2):194-98.

[19] Chatterjee A, Rai S, Guddattu V, Mukhopadhyay C, Saravu K. Is methicillin-resistant *Staphylococcus aureus* infection associated with higher mortality and morbidity in hospitalized patients? A cohort study of 551 patients from South Western India. Risk Manag Healthc Policy. 2018;11:243-50.

[20] Winn WC, Koneman EW. Koneman's color atlas and textbook of diagnostic microbiology. Philadelphia: Lippincott Williams & Wilkins; 2006.

[21] Clinical and Laboratory Standards Institute (CLSI) (2015): Performance standards for antimicrobial susceptibility testing; Twenty-fifth informational supplement. CLSI document M100-S26. Wayne, PA: Clinical and Laboratory Standards Institute.

[22] Deotale V, Mendiratta DK, Raut U, Narang P. Inducible clindamycin resistance in Staphylococcus aureus isolated from clinical samples. Indian J Med Microbiol. 2010;28(2):124-26.

[23] Anupurba S, Sen MR, Nath G, Sharma BM, Gulati AK, Mohapatra TM. Prevalence of methicillin resistant *Staphylococcus aureus* in a tertiary referral hospital in eastern Uttar Pradesh. Indian J Med Microbiol. 2003;21(1):49-51.

[24] Joshi S, Ray P. Indian Network for Surveillance of Antimicrobial Resistance (INSAR) group, India. Methicillin resistant *Staphylococcus aureus* (MRSA) in India: Prevalence and susceptibility pattern. Indian J Med Res. 2013;137(2):363-69.

[25] Stürenburg E. Rapid detection of methicillin-resistant *Staphylococcus aureus* directly from clinical samples: Methods, effectiveness and cost considerations. GMS Ger Med Sci. 2009;7:Doc06.

[26] Rajaduraipandi K, Mani KR, Panneerselvam K, Mani M, Bhaskar M, Manikandan P. Prevalence and antimicrobial susceptibility pattern of methicillin resistant *Staphylococcus aureus*: A multicentre study. Indian J Med Microbiol. 2006;24(1):34-38.

[27] Dar JA, Thoker MA, Khan JA, Ali A, Khan MA, Riswan M, et al. Molecular epidemiology of clinical and carrier strains of methicillin resistant *Staphylococcus aureus* (MRSA) in the hospital settings of north India. Ann Clin Microbiol Antimicrob. 2006;5:22.

[28] Gadepalli R, Dhawan B, Mohanty S, Kapil A, Das BK, Chaudhry R. Inducible clindamycin resistance in clinical isolates of *Staphylococcus aureus*. Indian J Med Res. 2006;123(4):571-73.
[29] Yilmaz G, Aydin K, Iskender S, Caylan R, Koksal I. Detection and prevalence of inducible clindamycin resistance in *Staphylococci*. J Med Microbiol. 2007;56(Pt 3):342-45.
[30] Rahabar M, Hajia M. Inducible clindamycin resistance in Staphylococcus aureus: A cross sectional report. Pak J Biol Sci. 2007;10(1):189-92.
[31] Levin TP, Suh B, Axelrod P, Truant AL, Fekete T. Potential clindamycin Resistance in clindamycin-susceptible, erythromycin-resistant *Staphylococcus aureus*: Report of a clinical failure. Antimicrob Agents Chemother. 2005;49(3):1222-24.
[32] Song KH, Kim M, Kim CJ, Cho JE, Choi YJ, Park JS, et al. Impact of vancomycin MIC on treatment outcomes in invasive *Staphylococcus aureus* infections. Antimicrob Agents Chemother. 2017;61(3):1845-16.
[33] Kumari J, Shenoy SM, Chakrapani M, Vidyalakshmi K, Gopalkrishna Bhat K. Comparison of etest and agar dilution for determining minimum inhibitory concentration of vancomycin to healthcare-associated methicillin-resistant *Staphylococcus aureus*. Asian Journal of Pharmaceutical and Clinical Research. 2016;9(4):189-91.

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