Original Article

DOI: 10.7860/NJLM/2023/59758.2699

Microbiology Section

In-vitro Susceptibility of Linezolid and Teicoplanin in Methicillin-resistant *Staphylococcus aureus* by E-test

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ABSTRACT

Introduction: *Staphylococcus aureus* (*S. aureus*) is a ubiquitous pathogen causing various infections in humans. The emergence of drug resistance in *S. aureus*, especially methicillin resistance, has made treating these infections increasingly tricky, with only a few antibiotics being effective. Vancomycin, teicoplanin, and linezolid are the antibiotics of choice for treating Methicillin-resistant *Staphylococcus aureus* (MRSA) infections, though occasional resistance to these antibiotics has also been reported.

Aim: To know the prevalence of MRSA and subject the MRSA isolates to linezolid and teicoplanin susceptibility testing by Epsilometer test (E-test).

Materials and Methods: This was a cross-sectional study done between April 2021 to March 2022. A total of 210 consecutive *S. aureus* isolates from various clinical samples were isolated and processed in the Department of Microbiology, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India. Screening for methicillin resistance was done by cefoxitin disc diffusion testing and Chromogenic agar (CHROMagar) MRSA, with American Type Culture Collection (ATCC) *S. aureus* 25923 strain as a negative control and a known inhouse strain was used as a positive control. All the MRSA isolates were tested for linezolid and teicoplanin susceptibility for the E-test to determine the Minimum Inhibitory Concentration (MIC). Data were entered into Microsoft excel 2019, and International Business Machines (IBM) Statistical Package for the Social Sciences (SPSS) version 20.0 was used for analysis.

Results: Out of 210 *S. aureus*, 100 (47.6%) were MRSA isolates. MRSA was predominantly isolated from pus (58%), sputum (19%) and urine (9%) samples. Higher resistance was observed against cotrimoxazole (72%), ciprofloxacin (54%) and amikacin (37%). Teicoplanin and linezolid were both susceptible in all of the isolates. MIC_{50} and MIC_{90} against linezolid and teicoplanin was 0.5 and 1 mcg/mL and 0.5 and 0.75 µg/mL respectively.

Conclusion: The MRSA isolates are increasingly becoming resistant to multiple antibiotics. Linezolid and glycopeptides are still the mainstays for treating MRSA infections, as most isolates are susceptible to these drugs.

Keywords: Antibiotic resistance, Chromogenic agar, Epsilometer test, Glycopeptide, Minimum inhibitory concentration, Oxazolidinone

INTRODUCTION

S. aureus is a potentially pathogenic gram-positive organism causing a wide spectrum of diseases ranging from local infections to systemic infections that may threaten life. The MRSA has increased dramatically during the previous 20 years and has been a cause of concern in many hospitals due to its capability of developing new clones resistant to almost any available antibiotics like cephalosporins, aminoglycosides, macrolides, and quinolones [1]. MRSA was first reported in 1961, within a year of methicillin's introduction [2]. Since, then, MRSA strains have spread rapidly among hospitals and have been the predominant nosocomial infections next to *Pseudomonas* and *Mycobacterium tuberculosis*. Intrinsic virulence capacity is the primary reason for their pathogenicity, which takes any form. They can adapt rapidly to the selective pressure of antibiotics, which has spread these infections. Only a few antibiotics are available for the treatment of these drug-resistant infections. This ubiquitous pathogen has been associated with treatment difficulties because only a few antibiotics are available for treating these infections [3]. Teicoplanin which is a glycopeptide antibiotic is one of the first or second-line agents for treating MRSA infections, whereas linezolid is also commonly used in the treatment of these infections [4,5]. Many studies in the past few years have been comparing the safety and efficacy of teicoplanin and linezolid, but the results are diverse and they show no distinct clinical superiority over each other [6]. Some recent reports even indicate cryptic resistance for linezolid among the susceptible isolates due to irrational use [7]. In light of these studies, attempts were made by the authors to identify similar resistant patterns in our region and found sparse data regarding it. In view of it, the present study was intended to isolate *S. aureus* to know the prevalence and susceptibility testing of MRSA isolates to linezolid and teicoplanin by E-test.

MATERIALS AND METHODS

This was a cross-sectional descriptive study done in the Department of Microbiology, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India, between April 2021 to March 2022. Ethical clearance certificate was taken from the Institutional Ethics Committee (IEC), Andhra Medical College, Andhra Pradesh, India. (Serial No.: 127/IEC AMC/FEB/2021).

Inclusion criteria: All new MRSA isolates from various clinical samples like pus, blood, urine, sputum and body fluids, were included from all age groups and genders from both Outpatient Department (OPD) and Inpatient Departments (IPD). Patients who have provided consent or for whom a legal guardian has consented to participate were included in the study.

Exclusion criteria: Methicillin-sensitive *Staphylococcus aureus* (MSSA) isolates and patients who were already on antibiotic treatment for known MRSA infections were excluded. Patients who did not provide consent to participate were excluded from the study.

Sample size calculation: The sample size was calculated as 210 samples using the online sample size calculator (OpenEpi: Sample Size for a Proportion or Descriptive Study, taking anticipated frequency of 16.3% as per our prospective review, confidence interval of 95% and the margin of error of 5%) [8]. Convenient (non probability) sampling technique was exercised.

Brief clinical data regarding age, sex, history of presenting illness, treatment history for the ailment and past history, if any, was collected from patients and hospital medical records. If the isolate is from an inpatient, data regarding the admission date, duration of admission and date of sending the sample were recorded. All the samples were collected using sterile aseptic precautions.

Study Procedure

Culture and identification: All the samples were inoculated on nutrient agar, blood agar and mannitol salt agar and were incubated at 37°C for 18-24 hours. Isolates of *S. aureus* were identified by colony morphology, Gram stain and coagulase test [9]. As per the Clinical and Laboratory Standards Institute (CLSI) 2019 guidelines, Kirby-Bauer disk diffusion method was performed to assess the susceptibility pattern of all isolates [10,11]. Antibiotic discs used were penicillin G, amoxiclav, amikacin, cotrimoxazole, ciprofloxacin, clindamycin, vancomycin, linezolid and teicoplanin were purchased from HiMedia Laboratories Pvt. Limited.

Screening for methicillin resistance in *S. aureus*: All *S. aureus* isolates were screened for methicillin resistance by using Standard disc diffusion testing using a 30 µg cefoxitin disc, in accordance with CLSI 2019 guidelines [10] .

Quality control: On every day of testing the isolates, a reference ATCC *S. aureus* 25923 strain (KWIK-STIK Plus) procured from HiMedia Laboratories Pvt. Limited, which was stored on nutrient agar slants, was subjected to a similar screening with other isolates, as a negative control [10]. An *S. aureus* isolate which was resistant to cefoxitin, was isolated in our lab during the month of January 2021, was stored on a nutrient agar slope and was categorised as an inhouse MRSA strain and was used as a positive control.

Other screening tests: Additionally, all *S. aureus* isolates were also inoculated on CHROMAgar MRSA procured from Chromogenic Life Sciences India Pvt. Ltd. As per the manufacturer's instructions, media was prepared and the isolates were inoculated by streak culture method. MRSA isolates show a characteristic pink colour colony, whereas MSSA isolates were inhibited [12].

E-test (Epsilometer test): Commerical E-test strips for linezolid and teicoplanin were purchased from HiMedia Laboratories Pvt. Limited (Ezy MIC strips), to determine the MIC for all the MRSA isolates were tested. MRSA isolates were inoculated in peptone water by direct colony suspension method to achieve turbidity of 0.5 McFarland standard. Using a sterile cotton swab, Mueller Hinton agar was inoculated by lawn culture method and an E-strip was placed on the lawn culture within 15 minutes of inoculation and the plates were incubated at 37°C for 18-24 hours. An elliptical zone of inhibition was produced on incubation. The antibiotic concentration at which the edge of the eclipse intersects with the strip was taken as the value for MIC [13].

STATISTICAL ANALYSIS

Data were tabulated and entered in Microsoft excel 2019 and all analysis was performed by IBM SPSS 20.0. Data were expressed in terms of frequency and percentage and were presented in the form of tables.

RESULTS

A total of 210 isolates of *S. aureus* were screened during the study period to identify MRSA. Out of 210 *S. aureus*, 100 (47.6%) were MRSA isolates which were further tested by E-test for linezolid and teicoplanin to determine the MIC. Among the 100 MRSA isolates, the incidence was higher in males (55%) than in females (45%). They are predominantly isolated in the age group of 21-30 years (42%) and less frequently isolated in the age group of 41-50 years (11%). The isolates majorly obtained from patients presented with skin and soft tissue infections (46%), treatment history and past history were inconsistent, particularly in patients attending the OPD and the data was not utilised for analysis.

MRSA was detected 100% by using cefoxitin disc diffusion and only 96% by CHROMagar MRSA [Table/Fig-1]. Isolates of MRSA were predominantly identified from pus (58%), sputum (19%), urine (9%), blood (7%), vaginal swab (5%), pleural/ascitic fluid (2%) respectively [Table/Fig-2]. Most MRSA isolates were resistant to cotrimoxazole (72%) and ciprofloxacin (54%). Vancomycin resistance was observed in 2% of isolates. All the isolates were uniformly susceptible to teicoplanin and linezolid [Table/Fig-3].

Method	Resistance	Susceptible
Cefoxitin disc diffusion (30 mcg)	100%	0
CHROMagar MRSA	96%	4%

[Table/Fig-1]: Detection of MRSA by cefoxitin disc diffusion and CHROMagar MRSA.

Type of samples	No. of MRSA (n=100)
Pus	58
Sputum	19
Urine	9
Blood	7
Vaginal swab	5
Pleural/Ascitic fluid	2
Total	100

[Table/Fig-2]: Isolation of MRSA from various samples.

Antibiotic disc	Resistant (%)	Susceptible (%)
Penicillin G	100	-
Amoxiclav	100	-
Cefoxitin	100	-
Amikacin	37	63
Cotrimoxazole	72	28
Ciprofloxacin	54	46
Clindamycin	4	96
Vancomycin	2	98
Linezolid	-	100
Teicoplanin	-	100

[Table/Fig-3]: Antibiotic susceptibility of MRSA (n=100).

The MIC for linezolid by E-test observed in the present study was between 0.25-2.0 µg/mL. MIC_{50} and MIC_{90} against linezolid were 0.5 and 1 µg/mL [Table/Fig-4]. MIC for teicoplanin by E-test observed in the present study was between 0.25-1.5 µg/mL. The MIC_{50} and MIC_{90} against teicoplanin were 0.5 and 0.75 µg/mL [Table/Fig-5].

MIC value (µg/L)	No. of isolates
0.25	2
0.38	16
0.50	28
0.75	36
1.0	14
1.5	3
2.0	1

[Table/Fig-4]: The MIC values of linezolid against MRSA isolates by E-test (n=100).

MIC value (µg/L)	No. of isolates
0.25	6
0.38	12
0.50	14
0.75	42
1.0	16
1.5	10

[Table/Fig-5]: The MIC values of teicoplanin against MRSA isolates by E-test (n=100).

DISCUSSION

Staphylococcus aureus is associated with various infections, both community-associated and hospital-acquired. In recent years the prevalence of MRSA has been continuously increasing, and the widespread outbreaks of infections by MRSA have warranted the study of susceptibility patterns in MRSA to help the clinician to use appropriate antibiotics for treating patients. Only a few antibiotics are available for the treatment of MRSA infections. Vancomycin, linezolid and teicoplanin have a spectrum of activity limited to gram-positive bacteria [14]. These drugs are new options for MRSA with an excellent in-vitro effect on MRSA. The prevalence of MRSA in the present study was 47.6%. The percentage of MRSA resistance detected by cefoxitin disc diffusion was 100% compared to CHROMagar MRSA. The use of CHROMagar for the detection of MRSA compared with cefoxitin disc diffusion, with a specificity of 99.4% in the present study, was correlated with Datta P et al., with a specificity of 99.2% [15]. *S. aureus* isolates were predominantly isolated from male patients (55%), which correlated with Kumar A et al., (males 55%) and Vijaymohan N and Nair SP, (males 59%) [16,17]. The majority of MRSA isolates in the present study were from pus samples (58%) which were consistent with Khan MF et al., (pus 55%), Mir BA and Srikanth, (pus 52%), Husain A et al., (pus 94.5%) [18-20]. The highest percentage of *S. aureus* from pus samples was observed in the study of Huang and Platt R, at 61.4% [21]. The above studies show that *S. aureus* remains the most predominant aetiology of pyogenic infections. In the present study, higher resistance was observed among cotrimoxazole (72%), ciprofloxacin (54%) and amikacin (37%), respectively. All isolates were 100% resistant to penicillin G, amoxiclav and cefoxitin [Table/Fig-6] [19,22-27].

The 72% of MRSA isolates in the present study were resistant to cotrimoxazole which was consistent with Saikia L et al., (73.12%) study [28]. The resistance pattern to cotrimoxazole was comparatively higher in other studies like Vijaymohan N and Nair SP (82%) [17].

The MRSA isolates in the present study were 37% resistant to amikacin and 54% resistant to ciprofloxacin which correlated with Tripathi A and Chaudhury U et al., studies [24,29]. The highest resistance to amikacin was seen with Tripathi A (71.42%) [24].

Only 2% of MRSA isolates in the present study were resistant to vancomycin, with similar results by Mir BA and Srikanth and Husain A et al., (2%) [19,20]. Whereas all the MRSA isolates were uniformly susceptible with no resistance towards linezolid or teicoplanin.

A MIC zone of less than or equal to 4 µg/mL was the susceptibility range of the linezolid E-test for *S. aureus*, considered as breakpoint MIC. The present study had a MIC range for linezolid ranging from 0.25-2.0 µg/mL, which correlates with other studies [Table/Fig-7] [20,30-34], and Niveditha N and Sujatha S, (0.016-2.0 µg/mL) and Tahira Y et al., (0.064-2.0 µg/mL) [32,33]. The study by Thool VU et al., (0.5-4.0 µg/mL) in 2012 and Husain A et al., (0.75-4.0 µg/mL) in 2018 has higher MIC ranges compared to the present study [20,30]. MIC_{50} and MIC_{90} against linezolid were 0.5 and 1 µg/mL, respectively.

A MIC zone of less than 8 µg/mL was the susceptibility range of the teicoplanin E-test for *S. aureus*, which was breakpoint MIC. The present study had a MIC range of 0.25-1.5 µg/mL, the MIC_{50} and MIC_{90} against teicoplanin were 0.5 and 0.75 µg/mL which showed similarity with Aoyagi T et al., [Table/Fig-8] [31,35-38].

Multidrug resistant strains resistant to more than three antibiotics are frequently observed among MRSA isolates. Only a few alternative drugs like vancomycin are commonly used because of their effectiveness against MRSA isolates. Until now, resistance to these antibiotics is rarely seen, with few isolates showing decreased susceptibility to vancomycin in-vitro [39].

Teicoplanin and Linezolid are the other alternatives for treating patients with MRSA infections. In the present study, all the isolates were susceptible to teicoplanin (100%) and linezolid (100%).

The present study identifies the in-vitro activity of antibiotics like vancomycin, teicoplanin, and linezolid which aid in treating MRSA infections. The study helps to understand the baseline antibiogram in and around Visakhapatnam, which helps in formulating an effective strategy to prevent the spread of these infections by adopting control strategies.

Year	Author	Place of study	Pn	AMC	AK	COT	CIP	CD	VA	LZ	TEI
2013	Mir BA and Srikanth [19]	Gulbarga, India	-	-	6.9	69	-	70.7	3.5	-	-
2014	Hajera M et al., [22]	Hyderabad, India	100	86.3	18.1	-	56.8	29.5	0	6.8	2.2
2014	Fomda BA et al., [23]	Srinagar, Kashmir, India	100	-	-	60	20	33.3	0	-	-
2015	Tripathi A, [24]	Bhopal, India	100	-	71.42	21.4	14.2	4.2	0	0	0
2015	Abbas A et al., [25]	Jaipur, India	-	-	13.9	32.1	54.5	46.1	0	0	16
2019	Abimana JB et al., [26]	Ishaka, Uganda	100	100	9	-	75	6	0	-	-
2020	Kot B et al., [27]	Siedlce, Poland	100	-	14.2	8	83	72.3	-	0	0
2023	Present study	Visakhapatnam, India	100	100	37	72	54	4	2	0	0

[Table/Fig-6]: Comparative table showing antibiotic resistance patterns of MRSA isolates in % [19,22-27].
Pn: Penicillin-G; AMC: Amoxiclav; AK: Amikacin; COT: Cotrimoxazole; CIP: Ciprofloxacin; CD: Clindamycin; VA: Vancomycin; LZ: Linezolid and TEI: Teicoplanin

Year	Author	Place of study	MIC range in µg/mL	MIC_{50}	MIC_{90}
2012	Thool VU et al., [30]	Nagpur, India	0.5-4.0	1.5	3
2013	Chitnis S et al., [31]	Indore, India	0.25-1.0	-	-
2015	Niveditha N and Sujatha S, [32]	Puducherry, India	0.016-2.0	0.38	1.5
2015	Tahira Y et al., [33]	Srinagar, Kashmir, India	0.064-2.0	-	-
2018	Husain A et al., [20]	Haldwani, Uttarakhand, India	0.75-4.0	2	3
2021	Aktas G, [34]	Capa-Istanbul, Turkey	0.38-1.5	1	1.5
2023	Present study	Visakhapatnam, India	0.25-2.0	0.5	1.0

[Table/Fig-7]: Comparative analysis of susceptibility of linezolid by E-test [20,30-34].

Year	Author	Place of study	MIC range in µg/mL	MIC_{50}	MIC_{90}
2013	Chitnis S et al., [31]	Indore, India	1.5-4.0	-	-
2014	Aoyagi T et al., [35]	Tohoku, Japan	-	0.75	1
2015	Singh A et al., [36]	Lucknow, India	0.50-2.0	-	-
2017	Jiang B et al., [37]	Chongqing, China	1.47-2.44	0.5	1.5
2021	Pantel A et al., [38]	Nîmes, France	0.25-0.5	0.25	0.50
2023	Present study	Visakhapatnam, India	0.25-1.5	0.5	0.75

[Table/Fig-8]: Comparative analysis of susceptibility of teicoplanin E-test [31,35-38].

Limitation(s)

Molecular methods were not used in the confirmation of these findings due to cost constraints. The follow-up to treatment response was not documented.

CONCLUSION(S)

Drug resistance in Staphylococcal isolates continues to be high, especially the emergence of MRSA isolates with resistance to multiple antibiotics is a significant cause of concern. Only a few alternatives like vancomycin, teicoplanin and linezolid are left over in the antibiotic pipeline to treat these infections. The study demonstrates that linezolid and glycopeptides antibiotics are the most effective for treating MRSA infections, with most isolates being susceptible to these groups of drugs, as shown in the study.

Acknowledgement

Author would like to appreciate the Department of Microbiology for supporting the project from which this paper grew and acknowledge the infrastructure and support of Andhra Medical College and Hospital. Author would like to thank Dr. B. Sreekanth Reddy, Assistant Professor, ACSR Govt. Medical College, for supporting their work in manuscript editing.

REFERENCES

[1] Tomasz A. Multiple-antibiotic-resistant pathogenic bacteria- A report on the Rockefeller University workshop. N Engl J Med. 1994;330(17):1247-51. Available from: https://www.nejm.org/doi/full/10.1056/nejm199404283301725.

[2] Harkins CP, Pichon B, Doumith M, Parkhill J, Westh H, Tomasz A, et al. Methicillin-resistant *Staphylococcus aureus* emerged long before the introduction of methicillin into clinical practice. Genome Biol. 2017;18(1):130. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5517843/.

[3] Swartz MN. Use of antimicrobial agents and drug resistance. N Engl J Med [Internet]. 1997;337(7):491-92. Available from: https://www.nejm.org/doi/10.1056/NEJM199708143370709.

[4] Zhao W, Zhang D, Storme T, Baruchel A, Declèves X, Jacqz-Aigrain E, et al. Population pharmacokinetics and dosing optimization of teicoplanin in children with malignant haematological disease. Br J Clin Pharmacol. 2015;80(5):1197. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4631192/.

[5] Álvarez-Lerma F, Muñoz-Bermúdez R, Samper-Sánchez MA, Gracia Arnilla MP, Grau S, Luque S, et al. Successful treatment of Panton-Valentine leukocidin-positive methicillin-resistant Staphylococcus aureus pneumonia with high doses of linezolid administered in continuous infusion. Med Intensiva [Internet]. 2017;41(1):56-59. Available from: https://pubmed.ncbi.nlm.nih.gov/27269810/.

[6] Kalil AC, Murthy MH, Hermsen ED, Neto FK, Sun J, Rupp ME, et al. Linezolid versus vancomycin or teicoplanin for nosocomial pneumonia: A systematic review and meta-analysis. Crit Care Med [Internet]. 2010;38(9):1802-08. Available from: https://pubmed.ncbi.nlm.nih.gov/20639754/.

[7] Tayal A, Singh NP, Rai S, Gupta K, Gupta A, Agarwal AN, et al. First study on detection of cryptic resistance to linezolid among clinical isolates of methicillin resistant Staphylococcus aureus from India. Indian J Med Microbiol [Internet]. 2022;40(3):384-88. Available from: https://pubmed.ncbi.nlm.nih.gov/35667921/.

[8] Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for Public Health, Sample Size for a Proportion or Descriptive Study. https://www.openepi.com/SampleSize/SSPropor.htm. 2003.

[9] Collee JG, Fraser AG, Marmion BP, Simmons A, editors. Mackie & McCartney Practical Medical Microbiology. 14th ed. RELX India Pvt. Ltd.; 2016. 978 p.

[10] Clinical and Laboratory Standards Institute (CLSI), Performance Standards for Antimicrobial Susceptibility Testing. 29th ed. Wayne, Pennyslvania. USA; 2019. 320 p.

[11] Bauer AW, Kirby WM, Sherris JC, Turck M. Antibiotic susceptibility testing by a standardized single disk method. Am J Clin Pathol. 1966;45(4):493-96.

[12] CHROMagar MRSA. Chromogenic Life Sciences India Pvt. Ltd. 2021. Available from: https://www.chromagar.com/wp-content/uploads/2021/11/NT-EXT-012-V10.0.pdf.

[13] Ezy MIC Strip. HiMedia Laboratories Pvt. Limited. 2021. Available from: https://himedialabs.com/TD/EM029.pdf.

[14] Murphy S, Pinney RJ. Teicoplanin or vancomycin in the treatment of gram-positive infections? J Clin Pharm Ther. 1995;20(1):05-11. Available from: https://pubmed.ncbi.nlm.nih.gov/7775615/.

[15] Datta P, Gulati N, Singla N, Vasdeva HR, Bala K, Chander J, et al. Evaluation of various methods for the detection of meticillin-resistant *Staphylococcus aureus* strains and susceptibility patterns. J Med Microbiol. 2011;60(11):1613-16. Available from: https://www.microbiologyresearch.org/content/journal/jmm/10.1099/jmm.0.032219-0.

[16] Kumar A, Kumar S, Farooq U, Begum R, Kansal S, Venkatesan A, et al. Prevalence of methicillin resistant *Staphylococcus aureus* in patients admitted in a tertiary care hospital of North India. International Journal of Advance Research and Innovation. 2015;3(1):113-17. Available from: https://ijari.org/assets/papers/3/1/IJARI-MS-15-03-102.pdf.

[17] Vijayamohan N, Nair SP. A study of the prevalence of methicillin-resistant *Staphylococcus aureus* in dermatology inpatients. Indian Dermatol Online J. 2014;5(4):441. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4228637/.

[18] Khan MF, Neral A, Yadav VC, Khan FA, Ahmed S. Incidence and antibiotic susceptibility of methicillin resistant Staphylococcus aureus in pus samples of patients of Bastar region, Central India. South Asian Journal of Experimental Biology. 2012;2(5):204-08. Available from: https://sajeb.org/index.php/sajeb/article/view/91.

[19] Mir BA, Srikanth. Prevalence and antimicrobial susceptibility of Methicillin resistant *Staphylococcus aureus* and Coagulase-negative Staphylococci in a tertiary care hospital. Asian Journal of Pharmaceutical and Clinical Research [Internet]. 2013;6(7):231-34. Available from: https://innovareacademics.in/journals/index.php/ajpcr/article/view/237.

[20] Husain A, Rawat V, Umesh, Kumar M, Verma PK. Vancomycin, linezolid and daptomycin susceptibility pattern among clinical isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) from Sub-Himalyan Center. J Lab Physicians [Internet]. 2018;10(2):145. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5896179/.

[21] Huang SS, Platt R. Risk of methicillin-resistant *Staphylococcus aureus* infection after previous infection or colonization. Clin Infect Dis [Internet]. 2003;36(3):281-85. Available from: https://academic.oup.com/cid/article/36/3/281/352004.

[22] Hajera M, Mustafa M, Reddy SC, Kumar KV, Rayalu JD. Prevalence and antibiotic susceptibility pattern of Methicillin resistant Staphylococci from a tertiary care hospital in Hyderabad. International Journal of Plant, Animal and Environmental sciences. 2014;4(2):65-69. Available from: https://www.fortunejournals.com/ijpaes/admin/php/uploads/482_pdf.pdf.

[23] Fomda BA, Thokar MA, Khan A, Bhat JA, Zahoor D, Bashir G, et al. Nasal carriage of Methicillin-resistant *Staphylococcus aureus* among healthy population of Kashmir, India. Indian J Med Microbiol. 2014;32(1):39-43.

[24] Tripathi A. Prevalence and antimicrobial susceptibility pattern of methicillin resistant *Staphylococcus aureus* in central India. MedPulse-International Medical Journal [Internet]. 2015;2(1):45-48. Available from: https://www.medpulse.in/Article/Volume2Issue1/MedPulse_2_1_15.pdf.

[25] Abbas A, Nirwan P, Srivastava P. Prevalence and antibiogram of hospital acquired-methicillin resistant *Staphylococcus aureus* and community acquired-methicillin resistant Staphylococcus aureus at a tertiary care hospital National Institute of Medical Sciences. Community Acquired Infection. 2015;2(1):13. Available from: http://www.caijournal.com/article.asp?issn=2225-6482;year=2015;volume=2;issue=1;spage=13;epage=15;aulast=Abbas.

[26] Abimana JB, Kato CD, Bazira J. Methicillin-resistant *Staphylococcus aureus* nasal colonization among healthcare workers at Kampala International University Teaching Hospital, Southwestern Uganda. Can J Infect Dis Med Microbiol. 2019. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6431477/.

[27] Kot B, Wierzchowska K, Piechota M, Gruzewska A. Antimicrobial resistance patterns in methicillin-resistant *Staphylococcus aureus* from patients hospitalized during 2015-2017 in hospitals in Poland. Medical Principles and Practice [Internet]. 2020;29(1):61. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7024858/.

[28] Saikia L, Nath R, Choudhury B, Sarkar M. Prevalence and antimicrobial susceptibility pattern of methicillin-resistant *Staphylococcus aureus* in Assam. Indian J Crit Care Med. 2009;13(3):156. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2823098/.

[29] Chaudhury U, Behara S, Sharma A. A comparative study of community and health care associated methicillin resistant *Staphylococcus aureus* infections. Int J Pharma Bio Sci. 2012;3(3):717-22.

[30] Thool VU, Bhoosreddy GL, Wadher BJ. Detection of resistance to linezolid in *Staphylococcus aureus* infecting orthopedic patients. Indian J Pathol Microbiol. 2012;55(3):361-64. Available from: https://pubmed.ncbi.nlm.nih.gov/23032832/.

[31] Chitnis S, Katara G, Hemvani N, Pareek S, Chitnis DS. In vitro activity of daptomycin & linezolid against methicillin resistant *Staphylococcus aureus* & vancomycin resistant enterococci isolated from hospitalized cases in Central India. Indian J Med Res [Internet]. 2013;137(1):191. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3657887/.

[32] 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. Brazilian Journal of Infectious Diseases. 2015;19(6):585-89. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9425378/.

[33] Tahira Y, Sajad Y, Kakru DK, Mohammad S. Screening of MRSA and VRE antibiotic sensitivity or susceptibility towards daptomycin, linezolid and vancomycin. World J Pharm Pharm Sci [Internet]. 2015;4(11):2007-22. Available from: https://storage.googleapis.com/journal-uploads/wjpps/article_issue/1446637650.pdf.

[34] Aktas G. Efficacy of vancomycin in combination with various antimicrobial agents against clinical methicillin resistant *Staphylococcus aureus* strains. Pak J Med Sci [Internet]. 2021;37(1):151. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7794130/.

[35] Aoyagi T, Kaito C, Sekimizu K, Omae Y, Saito Y, Mao H, et al. Impact of psm-mec in the mobile genetic element on the clinical characteristics and outcome of SCCmec-II methicillin-resistant *Staphylococcus aureus* bacteraemia in Japan. Clin Microbiol Infect. 2014;20(9):912-19. Available from: http://www.clinicalmicrobiologyandinfection.com/article/S1198743X14650990/fulltext.

[36] Singh A, Prasad KN, Rai RP, Singh SK, Rahman M, Tripathi A, et al. Glycopeptide and daptomycin susceptibility trends among clinical isolates of methicillin-resistant *Staphylococcus aureus* in a tertiary care center in North India. J Infect Public Health. 2015;8(4):341-45.

[37] Jiang B, Yin S, You B, Huang G, Yang Z, Zhang Y, et al. A 5-year survey reveals increased susceptibility to glycopeptides for methicillin-resistant *Staphylococcus aureus* isolates from *Staphylococcus aureus* bacteremia patients in a Chinese Burn Center. Front Microbiol [Internet]. 2017;8:2531. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5735371/.

[38] Pantel A, Nachar O, Boudet A, Loubet P, Schuldiner S, Cellier N, et al. In vitro activity of dalbavancin against Gram-positive bacteria isolated from diabetic foot osteomyelitis. J Antimicrob Chemother [Internet]. 2021;76(8):2057-60. Available from: https://pubmed.ncbi.nlm.nih.gov/33842980/.

[39] Howden BP, Davies JK, Johnson PDR, 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 [Internet]. 2010;23(1):99. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2806658/.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Aug 27, 2022
- Manual Googling: Oct 15, 2022
- iThenticate Software: Oct 25, 2022 (5%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Aug 20, 2022**
Date of Peer Review: **Sep 22, 2022**
Date of Acceptance: **Oct 26, 2022**
Date of Publishing: **Jan 01, 2023**