RESEARCH PAPER

Emerging Resistance Patterns in Methicillin-Resistant Staphylococcus aureus Isolated from Soft Tissue Infections: Clinical and Microbiological Study

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ABSTRACT

Staphylococcus aureus is a highly pathogenic bacterium responsible for a wide range of infections occurring in both healthcare settings and the community. It possesses a remarkable ability to adapt and evolve rapidly, enabling it to survive environmental pressures, including exposure to antimicrobial agents. The development of drug-resistant variants, particularly methicillin-resistant Staphylococcus aureus (MRSA) and other multidrug-resistant strains, has become a significant challenge in clinical management. MRSA is now recognized as one of the most prevalent and problematic pathogens globally. Infections caused by MRSA often require extended and carefully monitored treatment regimens to achieve complete eradication. The emergence of methicillin-resistant S. aureus (MRSA) poses serious challenges in clinical management and contributes substantially to global antimicrobial resistance, which accounted for more than 100,000 deaths worldwide in 2019. The present is done to study the prevalence and emerging resistance patterns of MRSA isolated from soft tissue infections. This research was carried out between January and August 2024 in the Delhi NCR area. A total of 110 soft tissue samples were collected from both the indoor and outpatient departments. Isolation and identification of S. aureus were done by following the routine microbiological techniques. Cefoxitin (30 µg) disc diffusion was used to identify MRSA and the E-test (Epsilometer test) was used to determine minimum inhibitory concentrations (MICs). Out of 110 samples, 24 (21.8%) were reported as prevalence for MRSA. Highest resistance is reported from Ciprofloxacin (77%) followed by ceftazidime (73%). Linezolid and vancomycin were also very effective and showed 96% and 88% sensitivity, respectively. These results are in line with the trends of MRSA resistance in the world, with the isolates displaying a wide range of β-lactam resistance but being susceptible to last-line antimicrobial agents.

Keywords: Ceftazidime, Cefoxitin disc diffusion, Ciprofloxacin, E-test, Linezolid, Methicillin-resistant Staphylococcus aureus, Vancomycin

How to cite this article: Shelja, Brar B. Emerging Resistance Patterns in Methicillin-Resistant Staphylococcus aureus Isolated from Soft Tissue Infections: Clinical and Microbiological Study. Int J Drug Deliv Technol. 2026;16(21s): 48-55. DOI: 10.25258/ijddt.16.21s.5

Source of support: Nil.

Conflict of interest: None

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a severe community health issue due to the fact that it caused diverse ailments and also had resistance to all the existing beta-lactam antibiotics that were in treatment during the period (Jevons. et .al 1961). The soft body tissue infections which include skin, muscles and connective tissues are more susceptible to the colonization and invasion of the MRSA in the hospitals and within the community as well as in mild abscesses and cellulitis and necrotizing fasciitis which is severe and needs immediate medical attention (Dayan et al., 2016). A Cefoxitin and E strips antibiotics disc used to screen MRSA isolates of in clinical setting(Assadullah et al., 2003, Ikuta and Sharara, 2022).

A few of the most popular clinical manifestations of MRSA include soft tissue infections which include skin, muscle, subcutaneous tissue, and connective structure infections (Ikuta and Sharara, 2022). The infections may start as mild local abscesses, furuncles or cellulitis, however, may develop into more serious illnesses like deep-seated abscesses, pyomyositis or even a fatal necrotizing fasciitis (Patel et al., 2010). The community-acquired (CA-MRSA) and HA-MRSA have been associated with soft tissue infections and the community-acquired one has been on the rise in the recent years. The soft tissue habitat is especially vulnerable to MRSA infection due to their capability to colonize the injured tissue and to invade it as well (Dayan et al., 2016).

The MRSA resistance to standard antibiotics, such as -lactams, macrolides, the fluoroquinolones (and even the last-resort medicine, the vancomycin or the linezolid) is a severe challenge in the scope of doctors. Diagnosis and appropriate characterization of MRSA isolates early are essential in making the appropriate choice in treatment, as well as restricting further spread. Antimicrobial susceptibility testing is a widely used form of laboratory identification by phenotypic screening. The disc diffusion with cefoxitin is often considered to be a valid surrogate endpoint of mecA-mediated resistance due to the high mecA gene activation. In addition, quantitative measures of antibiotic susceptibility are offered by MIC-based methods, including the E-test (Epsilometer test), which are increasingly finding use in most general microbiology laboratories (An et al., 2024; Assadullah et al., 2003).

The comparison of cefoxitin disc diffusion and the cefoxitin E -test is particularly crucial in regions where the limitation of resources and not afford the cost of the molecular detection such as PCR. Phenotypic methods of MRSA identification that are both cost-efficient and accessible are of paramount importance in empirical treatment prescription, monitoring trends in resistance development, and instituting infection control programs. Consequently, the present research was designed to determine the prevalence of MRSA in the soft tissue infections and evaluate the effectiveness of cefoxitin disc diffusion and cefoxitin E-test systems in the identification of MRSA isolates in clinical practice.

Material and Methods

Total of 309 samples for *S. aureus* were collected by the trained staffs the from soft body tissue as shown in (figure1) between January 2024 and February 2025 in the department of microbiology Delhi - NCR tertiary Hospital and screened by applying the standard microbiological technique of MRSA. Soft body tissue sample streaked on media such as MacConkey agar and identified using standard tests such as colony morphology, catalase testing and coagulase testing (tube coagulase, which followed the normal microbiology protocols during culture and sensitivity determination to antibiotics as part of a universal precaution. The antimicrobial susceptibility was determined by performing the Epsilometer test (E-test) and cefoxitin disc diffusion test in line with the (CLSI) recommendations (Gopalakrishnan et.al 2010). A bacterial suspension in sterile saline was prepared that confirm the 0.5 McFarland turbidity criterion. To obtain a consistent culture of lawn, the Mueller-Hinton agar (MHA) plates were inoculated with sterilized cotton swab. The disc diffusion technique entailed the inoculated agar with a 30 µg cefoxitin disc (Oxoid or HiMedia) on its surface and incubated the plates with 18 to 24 hours at 35ºC. Incubation was followed by a measurement of the diameter of the zone of inhibition. Whereas the inhibitory zone diameter of 21 mm or less was considered the methicillin-resistant S. aureus (MRSA), the 22 mm or more was considered methicillin-sensitive *S. aureus* (MSSA). The lowest possible concentration of cefoxitin to inhibit specific isolates was also determined using the E-test.

The E -test strips (Himedia) were placed on the agar surface following the application of uniformly spread standard inoculation on the MHA plates. The plates were then incubated at 35ºC after that. The interpretation of results was based on CLSI or EUCAST breakpoint, and the MIC values were obtained at the point of intersection of the strip elliptical zone of inhibition. It was detected with E test of MIC of cefoxitin of MRSA isolates and also done using HI comb strips Hi-Media, Mumbai. Also, the pattern of sensitivity or resistance to different antimicrobials was determined on Muller-Hinton agar using the standard zone widths of inhibition criterion on the day of isolation using modified Kirby Bauer disc diffusion method of determining susceptibility of Methicillin-resistant S. aureus strains (D'Souza et. al 2010). Penicillin-G (10mcg); ceftazidime (30mcg) , cefepime (30mcg) , cefoxitin (30mcg). A reference strain that was used to assist in the standardization of antibiotic susceptibility testing was *S. aureus* ATCC 29223 and finally the data were recorded and analyzed towards the end of the study as recommended by the CLSI.

Fig 1: Sample collection- soft body tissue

Results

Out of the total of 309 soft body tissue samples, 39 isolates were identified as MRSA using either the cef oxitin disk method or the E-strip method indicating a prevalence rate of 13 %. Soft body tissue sample streaked on media such as MacConkey agar and showing the colony morphology. All isolates were identified using standard tests such as colony morphology, catalase testing (figure 3) and coagulase testing (Figure 4). All the 24 isolates were identified as MRSA using either cefoxitin disc method or the E strips method. The MRSA isolates are confirmed by the E test of MIC of cefoxitin of MRSA isolates (Figure.5) and also confirmed using HI comb strips Hi-Media, Mumbai (Figure 7).

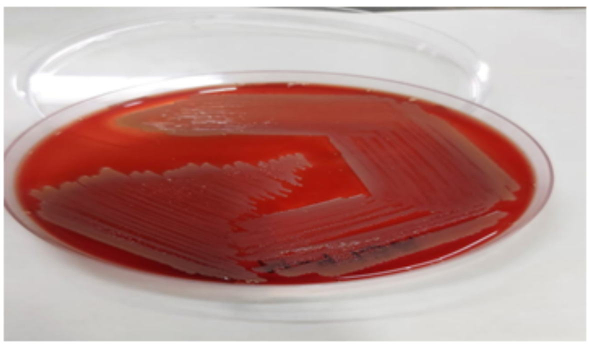

Figure 2: *Staphylococcus aureus* in blood agar media

A(Negative) B(Positive)

Figure 3: *Staphylococcus aureus* Catalase test

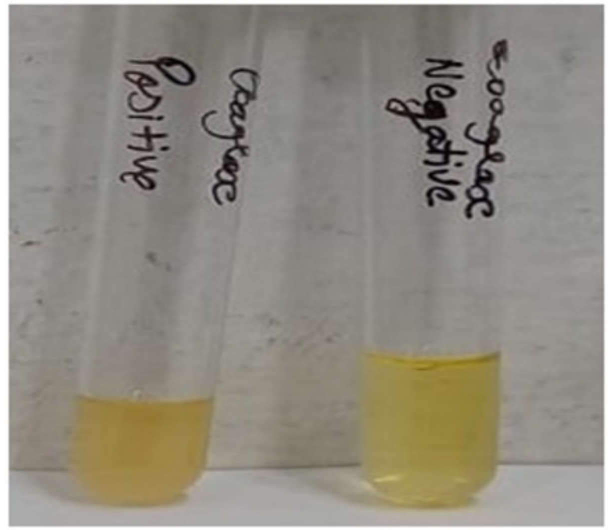

Figure: 4 Tube coagulase test *Staphylococcus aureus*

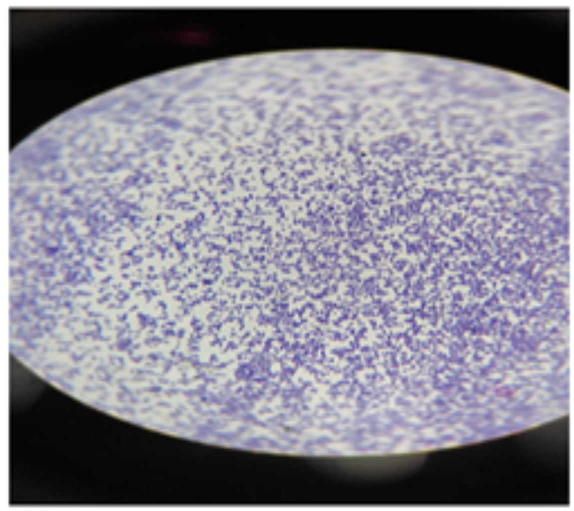

Figure 5: Microscopic view of Gram staining ¬*Staphylococcus aureus*

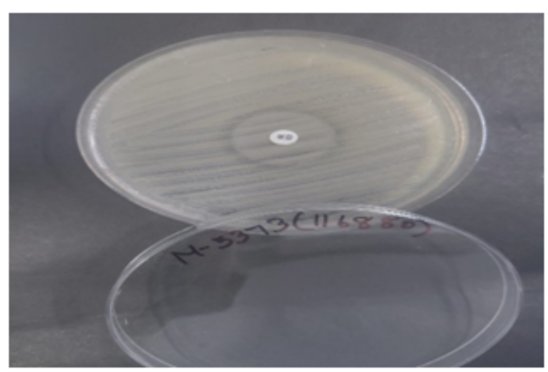

Figure 5: Detection of MRSA by cefoxitin (30 ug) disc

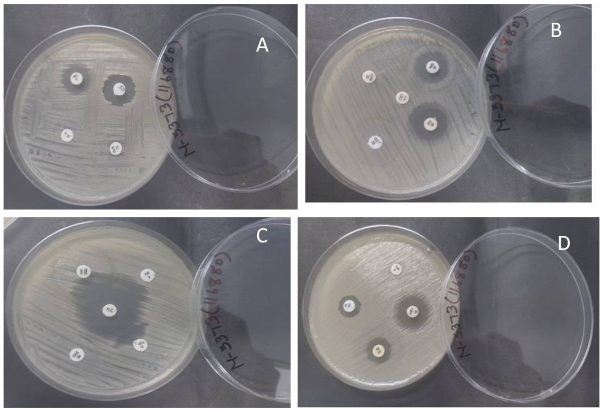

Figure 6: Antibiotic susceptibility test of MRSA in MHA medium against various antibiotics

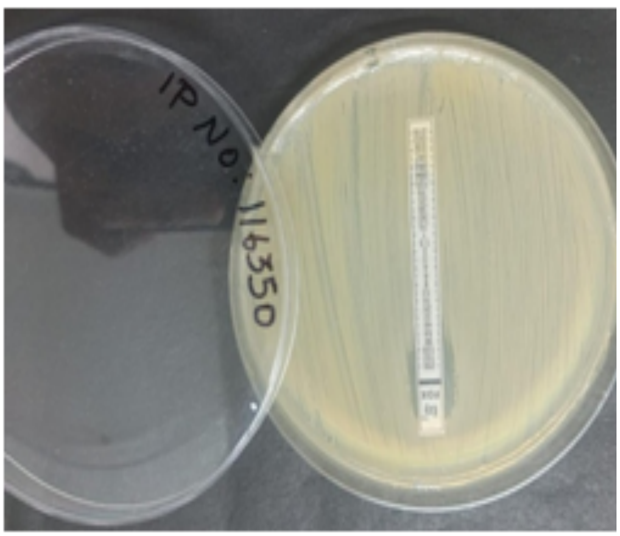

Figure 7: Hi comb Cefoxitine MIC test MRSA strains

All the 39 isolates were tested for each antibiotic; the percentages of resistant and susceptible isolates were calculated by dividing the respective number by the total number of isolates (resistant + susceptible) for that antibiotic, then multiplying by 100. Sensitive isolates were calculated by dividing the respective count by the total number of isolates (Resistant + Sensitive) for that antibiotic, then multiplying by 100.

- **% Resistant** = (Resistant / (Resistant + Sensitive)) × 100
- **% Sensitive** = (Sensitive / (Resistant + Sensitive)) × 100

The resulting percentages, rounded to one decimal place, are summarized in table 1 and figure 8. Linezolid and vancomycin had the highest sensitivity rates (95.8% and 87.5% sensitive, respectively, showed the 4.2% and 12.5% resistance), while cefoxitin had 100.0% resistance (0.0% sensitivity) among the isolates examined. Several antibiotics showed differing levels of sensitivity and resistance (table 1 and figure 8). These values are usually produced via established testing procedures, such as disk diffusion and Estrip method, following criteria from organizations like (CLSI) or the (EUCAST). These patterns help clinicians choose the most appropriate antibiotic therapy and inform infection control practices.

Table 2-Antiobiotic susceptibility pattern of MRSA isolates

Antibiotics	Resistant	Sensitive
Ceftazidime (30 Mcg)	17(70.8%)	7 (29.2%)
Cefepime (30 Mcg)	17 (70.8%)	7(29.2%)
Cefoxitin (30 Mcg)	24 (100.0%)	0 (0.0%)
Ciprofloxacin (5 Mcg)	19(79.2%)	5 (20.8%)
Co-Trimoxazole (25 Mcg)	10 (41.7%)	14 (58.3%)
Gentamycin (10 Mcg)	11 (45.8%)	13 (54.2%)
Pencillin (10 Units)	15 (62.5%)	9(37.5%)
Minocycline (30mcg Units)	16(66.7%)	8 (33.3%)
Tigecycline (15 Mcg)	10(41.7%)	14 (58.3%)
Doxycycline (30 Mcg)	6 (25.0%)	18 (75.0%)
Teicoplanin (30 Mcg)	7 (29.2%)	17 (70.8%)
Linezolid (30 Mcg)	1(4.2%)	23 (95.8%)
Vancomycin (10mcg)	3(12.5%)	21(87.5%)
Ceftriaxone Sulbactam C/ S (30/ 15 Mcg)	13 (54.2%)	11 (45.8%)
Ticarcillin+ Clavulanic Acid 75/ 10 Mcg	12 (50.0%)	12 (50.0%)
Cefaparazone Tazobactam (75/ 10mcg)	17 (70.8%)	7 (29.2%)
Clarithromycin (Clr) 15 Mcg	14(58.3%)	10 (41.7%)

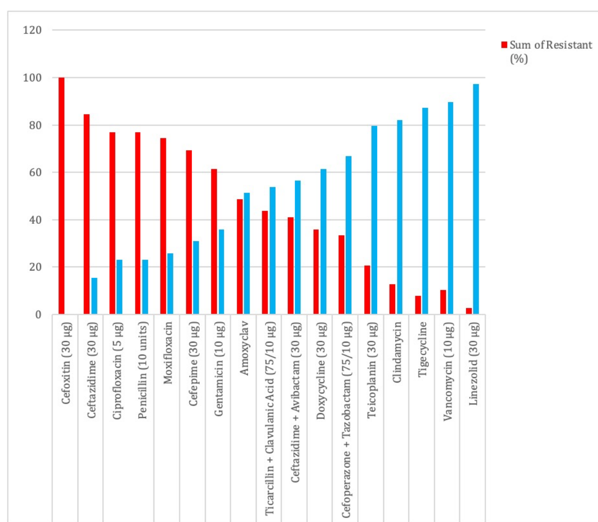

Figure: 8 Antibiotic sensitivity and resistance percentage of MRSA

Cefoxitin has a minimum inhibitory concentration (MIC) range of 8 µg/mL to 256 µg/mL for 24 *Staphylococcus aureus* isolates. The average MIC value for & isolates were 16 µg/mL. *Staphylococcus aureus* isolates with cefoxitin MICs ≤4 µg/mL are sensitive, while those with MICs ≥8 µg/mL are resistant . According to the *Clinical and Laboratory Standards Institute (CLSI)* criteria, 4 isolates (10.3%) exhibited high-level resistance (MIC ≥128 µg/mL). Intermediate resistance (MIC 64–96 µg/mL) was observed in 16 isolates (41.0%), while lower resistance (MIC 8–32 µg/mL) was identified in 19 isolates (48.7%). Notably, even isolates with the lowest MIC values (8 µg/mL) fall within the resistant category based on current CLSI breakpoints., underscoring the prevalence of cefoxitin resistance among the tested *Staphylococcus aureus* isolates.

Table 2: E strips of Cefoxitin MIC Distribution with Percentage

MIC (µg/mL)	Number of Isolates	Percentage (%)
8	5	12.8%
16	6	15.4%
32	8	20.5%
64	8	20.5%
96	8	20.5%
128	2	5.1%
192	1	2.6%
256	1	2.6%

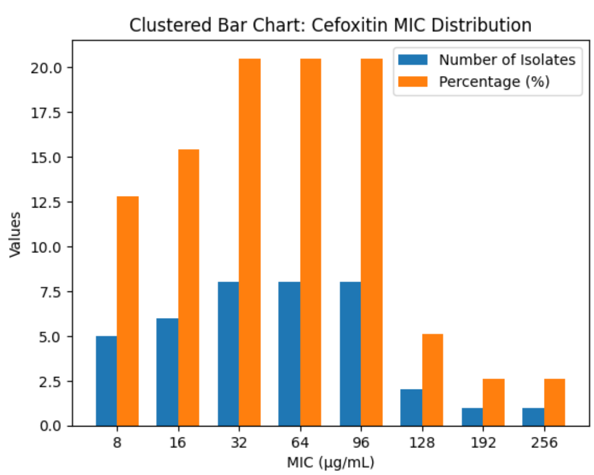

Figure 9: Percentage distribution of isolates on the basis of cefoxitin MIC (E-test)

The occurrence of antibiotic resistance especially with 3-lactams and fluoroquinolones. A 100 percent resistance to cefoxitin showed that prevalence of MRSA is very high. Our data indicates that empirical treatment with either Linezolid or Vancomycin anti-microbial agents has been shown to be effective against the MRSA (Methicillin-resistant *Staphylococcus aureus*). The present research is aimed at the emerging trends in antimicrobial resistance of MRSA isolates in soft tissue infections. In this study, the prevalence of β-lactam antibiotic resistance was high, and this is congruent with the biology of MRSA. The mecA gene, that curbs the affinity of these bacteria to 2-lactam medicines, is present in MRSA. The observation of 100% cefoxitin resistance has been a significant indication of the existence of methicillin resistance, which acts as an indicator that cefoxitin would be useful as a phenotypic marker in identifying MRSA. A number of studies have validated such results whereby, cefoxitin disc diffusion corroborates as a reliable and cost-efficient method of screening MRSA, especially in those laboratories that have limited molecular diagnostic capabilities

The great percentages of resistance to ciprofloxacin and third-generation cephalosporins such as ceftazidime are becoming a problem in regards to the application of these antibiotics as empirical treatment in soft tissue infection (Shariati et al., 2022). Selective pressure and wide usage have led to the rise in resistance to fluoroquinolone in MRSA, worldwide. These results are in agreement with previous Indian and international studies which have established high resistance to fluoroquinolones and cephalosporins. The decreased sensitivity of MRSA to a number of commonly used antibiotics limits their treatment action and must be approached with careful antibiotic stewardship.

Although there is huge resistance to many antibiotic types, the research discovered that linezolid has potential susceptibility of 96% and *vancomycin* has a potential susceptibility of 88%. These two drugs continue to form the basis of treatment of MRSA. First line treatment of serious infections caused by MRSA is *Vancomycin* and the high rate of susceptibility indicated that the clinical efficacy of *Vancomycin* has not declined. Nevertheless, even the fact of the occurrence of even a small proportion of isolates with decreased susceptibility is to be considered with some caution, since already in many areas vancomycin-intermediate *S. aureus* (VISA) strains have emerged. The fact that linezolid has a good sensitivity profile is an added value to its use as an alternate therapy option, particularly in cases where vancomycin is not available.

The trends of resistance mentioned in this work highlight the importance of continuous monitoring since the trends of antimicrobial resistance can vary according to the geographical area and the clinical context. The increasing opposition to the regular use of antibiotics emphasizes the significance of using antibiotics wisely and following the rules on protecting against infections as a means of preventing the occurrence of resistant bacteria. Moreover, the cefoxitin disc diffusion versus the E-test illustrates the need to include the right and cost-effective diagnostic measures in the routine clinical practice.

The results of the present study align with earlier investigations conducted in Odisha and by, which documented *Staphylococcus aureus* isolation rates of 55%, 65%, and 76%, respectively (Sharma et al., 2013; Pai et al., 2010). 8–10 A notable observation in our research was the substantial proportion of methicillin-resistant *S. aureus* (MRSA) among the total *S. aureus* isolates, accounting for 49%, reflecting a considerable burden of antimicrobial resistance. Comparable MRSA prevalence rates, ranging between 46% and 54%, have been reported from studies carried out in Karnataka, Maharashtra, North-East India, and Delhi across various clinical specimens. The significant presence of MRSA identified in our study underscores the urgent need to strengthen infection prevention and control strategies to limit dissemination of resistant strains within the community. Additional investigations are warranted to explore the determinants responsible for the elevated MRSA prevalence observed in our population.

Our findings also demonstrated that MRSA isolates exhibited greater resistance to multiple antibiotic classes, including *Rifampicin, Erythromycin*, and *Amikacin*, when compared with methicillin-sensitive *S. aureus* (MSSA) isolates. Similar trends have been described in various studies, which reported higher resistance profiles among MRSA strains relative to MSSA strains. These observations emphasize the critical importance of rational antibiotic prescribing practices to curb the development and spread of resistant organisms (Mallick et al. (2011, Gupta et al., 2014, and Bhowmik et al., 2019). Continuous monitoring of both MRSA and MSSA susceptibility patterns remains essential to guide appropriate therapeutic decisions. Further research should focus on elucidating the molecular and genetic mechanisms driving antibiotic resistance in MRSA strains.

In the current study, all MRSA isolates remained susceptible to *vancomycin* and *linezolid*-agents commonly recommended for the management of MRSA infections. This finding is consistent with most reports from India, which have similarly documented high susceptibility rates to these drugs (Mallick et al. 2011; Gupta et al., 2014 and Bhowmik et al., 2019). Nevertheless, emerging resistance to glycopeptides has been reported in certain regions. Tiwari et al. (2008) described the occurrence of vancomycin-resistant *Staphylococcus aureus* (VRSA) in Varanasi, Uttar Pradesh, with prevalence rates of 1% in 2006 and 0.3% in 2008.16–17 Furthermore, studies by Mallick et al. and Mandal et al. identified vancomycin-resistant *S. aureus* rates of 15% in Rajasthan and West Bengal, respectively (Mandal et al., 2015; Mallick et al. 2011). These findings indicate that vancomycin resistance is emerging as a significant concern in India and globally, and its frequency may increase if antibiotic stewardship is not rigorously implemented. Beyond complete resistance, intermediate resistance phenotypes such as vancomycin-intermediate *S. aureus* (VISA) and heteroresistant vancomycin-intermediate *S. aureus* (hVISA) have also been reported worldwide (Singh et al., 2015; Bhowmik et al., 2019)

Conclusion

Methicillin-resistant Staphylococcus aureus (MRSA) is also a significant and emerging issue of global health concern. The capacity to obtain and disseminate resistance determinants especially the mecA and mecC genes that encode the altered penicillin-binding proteins has made a number of 2-lactam naturally effective antibiotics insignificant, and therapy choices are limited. The MRSA load is made worse by the fact that it is also related to serious clinical manifestations, including skin and soft tissue infections, bloodstream infections, pneumonia, surgical site infections, and indwelling medical device infections. These infections have been associated with increased morbidity and mortality, increased hospitalization, and increased healthcare costs especially in countries with limited resources. Out of the total 110 samples 21.8% showed the MRSA samples. The results of this research paper underscore the role of phenotypic antimicrobial susceptibility testing, including cefoxitin screening and minimum inhibitory concentration (MIC) determination with E-test (E-strip) in the accurate identification and treatment of MRSA in the normal clinical microbiology laboratory. Where molecular methods are not extensively accessible, conventional culture-based and susceptibility testing tools have been reliable, cost-effective and clinically relevant tools to support specific antibiotic therapy. Infection prevention and control measures are still central to ensuring that the spread of MRSA is reduced in healthcare facilities and community. High-risk patient screening, isolation or cohorting, strict hand hygiene, and use of personal protective equipment have been proved to reduce the rate of colonization and infection of MRSA drastically. Healthcare personnel and patient training as well as training of caregivers are also essential in maintaining these preventive measures. In the clinics, patients with severe and unexplained infections are often in need of the prompt initiation of broad-spectrum empirical antibiotic treatment to avoid the development of the illness and adverse outcomes.

Nonetheless, the results of the current study and other studies point to the relevance of timely de-escalation of drug use according to the cultural and susceptibility information. It is not only an effective method of improving patient outcomes, but also a significant factor in antimicrobial stewardship since it reduces unjustified exposure to broad-spectrum medications and resistance selection pressure. Within clinical practice, when patients have an acute infection with an unknown pathogen, the urgent prescription of a broad-spectrum empirical antibiotic therapy is often needed because the disease may develop and there are adverse outcomes. Nevertheless, the results of this and other researches reiterate the importance of de-escalating medicine in a timely fashion, according to culture and sensitivity. The practice is not only better to patient outcomes, but also facilitates antimicrobial stewardship of exposing patients to unnecessary exposure to the broad-spectrum medications and the selection pressure of resistance development.

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