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Assessment of Mupirocin Resistance among Methicillin-Resistant Staphylococcus aureus (MRSA) Isolates in a Tertiary Care Hospital

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Abstract

Background: Mupirocin is a topical antibiotic used extensively for decolonization of MRSA carriers in both hospital and community settings. Its easy application and effectiveness in nasal and skin colonization sites make it a frontline agent in MRSA infection control. However, increasing resistance to mupirocin, particularly high-level resistance, is a growing concern that compromises decolonization strategies and increases the risk of persistent colonization and transmission. **Objective:** To determine the prevalence of low-level mupirocin resistance among Methicillin-Resistant *Staphylococcus aureus* (MRSA) isolates from various clinical specimens and to analyze the association of mupirocin resistance with different clinical sources and patient demographics in a tertiary care hospital setting. **Methods:** This prospective study was conducted in the Department of Microbiology at a tertiary care hospital over 12 months. A total of 114 MRSA isolates, confirmed by cefoxitin disc diffusion, were subjected to mupirocin susceptibility testing using 5 µg discs on Mueller-Hinton agar. Resistance was categorized based on inhibition zones: ≤13 mm indicated resistance, ≥14 mm indicated sensitivity. Due to resource limitations, high-level resistance testing using 200 µg discs or molecular methods was not performed. **Results:** Among 114 MRSA isolates, 6 (5.26%) exhibited low-level resistance to mupirocin, while 108 (94.73%) remained sensitive. No high-level resistance was detected. The majority of resistant isolates were derived from pus (4/6), followed by blood (1) and sputum (1). Urine, vaginal, and pleural fluid isolates were fully sensitive to mupirocin. The rate of resistance observed aligns with Indian studies and is lower than rates reported internationally. **Conclusion:** Low-level mupirocin resistance was detected in a small proportion of MRSA isolates. Although high-level resistance was not observed, the continued use of mupirocin, especially in unregulated topical applications, risks resistance escalation. Routine mupirocin sensitivity screening is recommended, alongside antimicrobial stewardship to preserve the efficacy of this vital topical agent.

Keywords: MRSA, mupirocin resistance, decolonization, low-level resistance, topical antibiotics, disc diffusion.

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most significant pathogens in healthcare settings. It is responsible for a broad spectrum of infections ranging from skin and soft tissue infections to severe invasive diseases such as bloodstream infections, pneumonia, and osteomyelitis [1]. MRSA is particularly concerning due to its resistance to all β-lactam antibiotics and frequent multidrug resistance.

Efforts to reduce MRSA transmission often focus on decolonization, especially in patients with persistent nasal colonization, a known risk factor for infection [2]. Mupirocin is a topical antibiotic derived from *Pseudomonas fluorescens* that inhibits isoleucyl-tRNA synthetase, preventing bacterial protein synthesis [1,3]. Its ability to eradicate *S. aureus* from nasal mucosa has made it a key agent in MRSA control programs.

However, resistance to mupirocin is an emerging threat. Resistance occurs due to:

- Low-level mupirocin resistance (MuL): MIC 8–256 µg/ml, caused by point mutations in the chromosomal ileS gene [4].

- High-level mupirocin resistance (MuH): MIC ≥512 µg/ml, usually plasmid-mediated via mupA or mupB genes [5,6].

High-level resistance is especially problematic as it is associated with decolonization failure, prolonged carrier states, and increased risk of transmission in hospitals [7,8]. Mupirocin resistance is linked to inappropriate use of over-the-counter mupirocin ointments, widespread topical applications on wounds, and use beyond nasal carriage treatment [8–10].

Globally, mupirocin resistance rates vary widely—from 1% to 50%—depending on regional usage patterns [7]. In India, studies report a prevalence ranging from 4% to 15% [11–13].

Given the critical role mupirocin plays in infection control, especially in surgical and ICU settings, this study aims to evaluate the prevalence of mupirocin resistance in MRSA isolates from a tertiary care hospital and characterize the resistance phenotype.

OBJECTIVE

To determine the prevalence of low-level mupirocin resistance among Methicillin-Resistant *Staphylococcus aureus* (MRSA) isolates from various clinical specimens and to analyze the association of mupirocin resistance with different clinical sources and patient demographics in a tertiary care hospital setting.

MATERIALS AND METHODS

Study Design

This was a prospective cross-sectional study conducted over a 12-month period in the Department of Microbiology at a tertiary care teaching hospital, after obtaining institutional ethics committee approval.

Sample Collection and Identification

Clinical samples were collected from inpatients and outpatients across various departments. A total of 114 MRSA isolates were obtained from pus, blood, urine, sputum, vaginal swabs, and pleural fluids. All samples were processed by standard microbiological protocols. *S. aureus* identification was based on colony morphology, Gram stain, catalase test, coagulase test (slide and tube), DNase test, and mannitol fermentation [138].

MRSA Confirmation

Cefoxitin disc diffusion (30 µg) was used for MRSA detection. Isolates with a zone diameter ≤21 mm were interpreted as MRSA based on CLSI guidelines [12].

Mupirocin Susceptibility Testing

Mupirocin resistance was tested using the Kirby-Bauer disc diffusion method with 5 µg mupirocin discs (HiMedia). Mueller-Hinton agar plates were inoculated with 0.5 McFarland standard suspensions and incubated at 35°C for 24 hours.

Interpretation was as follows:

- **Sensitive:** Zone ≥14 mm
- **Resistant:** Zone ≤13 mm
- High-level testing (200 µg disc or MIC) was not performed due to financial constraints.

Inclusion and Exclusion Criteria

Inclusion Criteria

- All non-duplicate clinical isolates of *Staphylococcus aureus* from patients during the study period.
- Isolates confirmed as methicillin-resistant Staphylococcus aureus (MRSA) by the cefoxitin disc diffusion method.
- Isolates obtained from clinical specimens such as pus, blood, body fluids, and catheter tips.
- Patients of all ages and both sexes, from both inpatient and outpatient departments.

Exclusion Criteria

- Duplicate isolates from the same patient.
- Isolates identified as methicillin-sensitive Staphylococcus aureus (MSSA).
- Contaminated cultures or non-viable growth.
- Environmental samples or screening swabs not related to clinical infection.

Data Interpretation

Mupirocin resistance data were analyzed by clinical specimen type and compared with previously published literature.

RESULTS

Out of 304 *S. aureus* isolates, 114 (37.5%) were confirmed to be MRSA using the cefoxitin disc diffusion method.

Figure 1: Cefoxitin disc diffusion test for phenotypic detection of MRSA

- **Demographic Profile of Patients:**

Age Group (Years)	No. of Patients	Percentage (%)
0–14	4	3.5%
15–29	18	15.7%
30–44	30	26.3%
45–59	35	30.7%
≥60	27	23.7%

Majority of MRSA cases (57%) occurred in adults aged 30–60 years, a group with higher ambulatory activity and hospital interaction.

- **Gender Distribution:**

Gender	No. of Patients	Percentage (%)
Male	82	71.9%
Female	32	28.1%

MRSA infections were more common among males, similar to findings in other Indian and international studies.

- **Sample-wise Distribution of MRSA Isolates**

Clinical Sample	Number (n)	Percentage (%)
Wound/Exudate	90	78.94%
Blood	14	12.28%
Urine	4	3.5%
Sputum	3	2.63%
Vaginal Swab	1	0.87%
Pleural Fluid	1	0.87%
Ascitic Fluid	1	0.87%

The majority of MRSA isolates (78.94%) were obtained from wound or pus samples, indicating skin and soft tissue as the most common sites of MRSA infection. Blood was the second most common source (12.28%), followed by a few isolates from urine, sputum, and body fluids.

- **MRSA Susceptibility to Alternative Antibiotics**

Antibiotics	Sensitive n (%)	Resistant n (%)
Linezolid	114 (100%)	0 (0%)
Tigecycline	114 (100%)	0 (0%)
Quinupristin-dalfopristin	107 (93.85%)	7 (6.14%)
Mupirocin*	108 (94.73%)	6 (5.26%)

Linezolid and tigecycline demonstrated 100% efficacy against all MRSA isolates, supporting their role as key alternative agents. Quinupristin-dalfopristin showed good sensitivity (93.85%). Although mupirocin was not part of the primary objective, it showed 94.73% sensitivity.

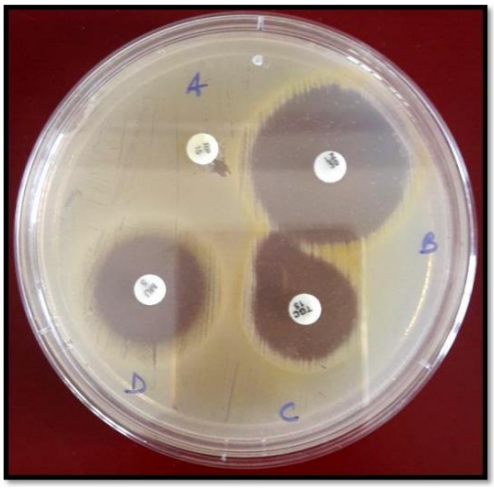

Figure 1: Antibiotic sensitivity testing of alternate antibiotics for MRSA
A.Quinpristin-Dalfopristin B.Linezolid C.Tigecycline D.Mupirocin

- **Mupirocin Sensitivity among MRSA Isolates**

Resistance Type	Number of Isolates	Percentage (%)
Sensitive	108	94.73%
Low-level resistance	6	5.26%
High-level resistance	0	0%

This table presents the overall sensitivity pattern of 114 MRSA isolates to mupirocin, tested using a 5 µg disc for low-level resistance. Out of the total isolates, 108 (94.73%) were found to be sensitive to mupirocin, while 6 isolates (5.26%) demonstrated low-level resistance. Importantly, no isolates exhibited high-level mupirocin resistance in this study. These results suggest that mupirocin remains largely effective against MRSA isolates in the current setting. However, the emergence of low-level resistance, though limited, highlights the need for prudent mupirocin use and continued surveillance to prevent the development of high-level resistance and therapeutic failure.

- **Distribution of Mupirocin Resistance by Clinical Sample**

Sample Type	Total MRSA	Sensitive	Resistant	% Resistance
Pus	90	86	4	4.4%
Blood	14	13	1	7.14%
Urine	4	4	0	0%
Sputum	3	2	1	33.3%
Vaginal Swab	1	1	0	0%
Pleural Fluid	1	1	0	0%

This table provides a breakdown of mupirocin sensitivity among MRSA isolates according to the type of clinical sample from which they were obtained. Among the 90 isolates from pus, 86 (95.6%) were sensitive while 4 (4.4%) were resistant. Blood samples showed 1 resistant isolate out of 14 (7.14%), and sputum samples had 1 resistant strain out of 3 (33.3%). All isolates from urine, vaginal swab, pleural fluid, and ascitic fluid were fully sensitive to mupirocin (100%). The highest resistance was observed in sputum samples proportionally, though the absolute number was small. These findings suggest that mupirocin resistance is more common in isolates from wound-related specimens, likely due to frequent topical application in these sites, reinforcing the need for rational antibiotic use in clinical practice.

- **Mupirocin Sensitivity of MRSA Isolates Based on Vancomycin MIC**

Vancomycin MIC (µg/mL)	Mupirocin Sensitive n (%)	Mupirocin Resistant n (%)
0.5	2 (100%)	0 (0%)
1.0	84 (98.83%)	1 (1.17%)
2.0	22 (100%)	0 (0%)
16.0 (VRSA)	0 (0%)	5 (100%)

Among the MRSA isolates tested, mupirocin sensitivity showed a decreasing trend with increasing vancomycin MIC, suggestive of potential cross-resistance or co-selection of resistance traits.

- **At MIC 0.5 µg/mL (n = 2)**: All isolates (100%) were mupirocin-sensitive.

- **At MIC 1 µg/mL (n = 85)**: 84 isolates (98.83%) were mupirocin-sensitive, and 1 isolate (1.17%) showed resistance.
- **At MIC 2 µg/mL (n = 22)**: All 22 isolates (100%) retained mupirocin sensitivity.
- **At MIC 16 µg/mL (VRSA, n = 5)**: All 5 isolates (100%) were resistant to mupirocin, indicating complete loss of susceptibility in vancomycin-resistant strains.

DISCUSSION

This study identified low-level mupirocin resistance in 5.26% of MRSA isolates. All resistant isolates showed low-level resistance; no high-level resistance was detected. This aligns with the findings of Parul et al. (2014), who reported 8.23% low-level resistance [11]. The absence of high-level resistance corresponds with Oommen et al. (2010), who found 2% high-level resistance only [13].

The highest number of resistant isolates were found in pus samples (4/6; 66.6%), followed by one each from blood and sputum. Urine, vaginal swab, and pleural fluid isolates were fully sensitive to mupirocin. These findings echo Dardi et al. (2014), who reported 15.35% resistance, with higher rates seen in wound samples [12].

Resistance is likely driven by irrational use of mupirocin, particularly in skin and wound care, beyond its primary role in nasal decolonization. Hogue et al. (2010) emphasized that mupirocin overuse, especially in topical settings, increases the risk of resistance [14].

Our findings support routine mupirocin sensitivity screening, especially in surgical and ICU settings, where mupirocin is often used empirically. While resistance is still low, continuous monitoring is necessary to prevent emergence of high-level resistance, which is associated with treatment failure, prolonged colonization, and outbreak potential [15].

Natural agents like tea tree oil, honey, bacteriophages, and novel compounds (e.g., Octenidine, Lysostaphin) are being explored as alternative decolonization agents. Further studies are needed to evaluate their efficacy [13].

Implications:

- **Clinical:** Continued mupirocin effectiveness depends on limiting its usage to decolonization in carriers.
- **Policy:** High-risk units (ICUs, surgical wards) should have resistance surveillance built into infection control programs.
- **Research:** There is a need for molecular screening of mupirocin resistance genes (mupA, mupB) in future studies

CONCLUSION

Low-level mupirocin resistance was seen in a small but significant proportion (5.26%) of MRSA isolates. Most resistant strains originated from pus, suggesting inappropriate topical use. There is a need for **antimicrobial stewardship**, restricted mupirocin use, and regular screening to preserve its role in **MRSA decolonization protocols**.

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