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# High and Low Level Mupirocin Resistance among Clinical Isolates of Methicillin Resistant *Staphylococcus aureus* (MRSA)

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## ABSTRACT

**Objective:** *Staphylococcus aureus* is a significant source of nosocomial infections, causing illnesses ranging from minor to life-threatening septic shock. Routine culturing and specific testing can confirm the presence of the bacteria. Antibiotic resistance is a major concern, and methicillin-resistant *Staphylococcus aureus* (MRSA) is particularly dangerous as it has mutations in the mecA gene, making it resistant to beta-lactam antibiotics. Mupirocin is an effective antibiotic against MRSA, binding to isoleucyl transfer-RNA synthetase to inhibit protein and RNA synthesis. In this study, two different doses (5 µg and 200 µg) of mupirocin were tested against MRSA.

**Methodology:** This study aimed to determine the antimicrobial susceptibility of methicillin-resistant *Staphylococcus aureus* (MRSA) against two different doses of mupirocin. Clinical samples were collected in the duration of one year from different wards of Jinnah Hospital Lahore and processed in microbiology laboratory of Allama Iqbal Medical College and after confirmation of *Staphylococcus aureus*, the modified Kirby Bauer method was used to test antimicrobial susceptibility. MRSA was confirmed by resistance to cefoxitin. High and low-level doses of mupirocin were applied, and zone sizes were measured.

**Results:** Total 172 isolated methicillin resistant *Staphylococcus aureus* (MRSA) from all age groups and genders were tested against two doses of mupirocin. 97.10% MRSA were sensitive against both doses (5 µg and 200 µg) of mupirocin.

**Conclusion:** After the resistance of all beta lactam drugs, mupirocin can be very helpful topically in the treatment of MRSA infections.

**Key Words:** MRSA, Mupirocin

Authors' Contribution:
*[1,2]Conception; Literature research; manuscript design and drafting; [2,3] Critical analysis and manuscript review; [3]Data analysis; Manuscript Editing.*

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## Introduction

*Staphylococcus aureus is a significant threat to humans, as they are a major source of nosocomial infections.* Nasal carriers are a significant source of infection spread in hospitals, particularly among immunocompromised patients. These Gram-positive cocci also cause many illnesses like folliculitis to life-threatening septic shock. One great thing is that laboratories can detect it quickly and minimize the complications due to these bugs.[1, 2] Another essential addition to its threatening ability is its resistance for many common antibiotics.[4]

Antibiotic resistance is a threat causing alarm for humankind, but *S. aureus* becomes more dangerous than others when it gains drug resistance. *S. aureus,* becomes more dangerous when it gets mutation in specific gene mecA and survives in the presence of all beta-lactam drugs. Due to this new adaptation, the treatment of *S.aureus* infections is complicated. This mutated bug is known as Methicillin-Resistant *Staphylococcus aureus* is known as "MRSA". Many methods for its confirmation, like, detection of PBPa2 proteins, the Use of selective chrome agar and genes amplification through PCR, are available but, the most economical method is the cefoxitin disc diffusion method .[3, 5]

Few drugs act as the last hope to kill this highly resistant infectious agent. Among these, mupirocin is available with two different dose levels to cure infections. Mupirocin is an effective agent against MRSA. This antibiotic acts by binding with the isoleucyl transfer-RNA (tRNA) synthetase. Then inhibition of the action of these enzymes causes failure in the conversion and isoleucine and tRNA, hence no protein and RNA synthesis.[4, 6]

Mupirocin is a naturally synthesized antibiotic and is active against many gram-positive and a few gram-negative bacteria.[7] It has a unique structure and is obtained with fermentation by *Pseudomonas fluorescence.* It is already available in the market for tropical use and provides a potential role in eradicating the nasal carriage when administered intranasal. The high metabolism of this drug is a significant hurdle in its use against systemic infections .[8]

## Methodology

The ethical review board of Allama Iqbal Medical College and Jinnah Hospital Lahore given the approval of this study in 39th meeting. MRSA from all clinical samples, age groups, and genders were included in the study, and methicillin-sensitive *Staphylococcus aureus* (MSSA) were excluded. Samples were collected from different wards and cultured on blood and MacConkey agar. After 48 hours of incubation, colonial morphology was noted, and gram staining was performed. Catalase test was done to differentiate between *Staphylococcus* and *Streptococcus.* Coagulase, DNAse, and mannitol salt agar tests were performed to confirm *Staphylococcus aureus.*

After confirming *Staphylococcus aureus*, antimicrobial susceptibility testing was performed with the modified Kirby Bauer method. Isolates resistant to cefoxitin were labelled as methicillin-resistant *Staphylococcus aureus* (MRSA). After the confirmation of MRSA, high (MUP-200 µg) and low-level (MUP-5 µg) doses of mupirocin were applied to analyse the antimicrobial susceptibility against MRSA using the modified Kirby Bauer method. Plates were incubated for 24 hours at 37°C, and zone sizes were measured. Zone size for the sensitive isolates of MRSA for 5µg mupirocin disc was 14 mm, and for the 200µg disc was 30 mm. 5µg is considered low-level dose and 200µg were considered high dose mupirocin. All data were recorded and analysed by SPSS.

## Results

Among 172 samples 39.5% and 60.5% were from female and male respectively as shown in table 1:

All patients were divided into four age groups, minimum age was 1-year-old and maximum was 80 years old. Table 2 is the representation of population in all age groups and among them it was highest in between 21-40 years.

**Table 1: Frequency of both genders in study**

| Gender | | Frequency | Percent |
|---|---|---|---|
| | Female | 68 | 39.5 |
| | Male | 104 | 60.5 |
| | Total | 172 | 100.0 |

| Table 2: Frequency of patients in different age groups | | | |
|---|---|---|---|
| Age Groups | | Frequency | Percent |
| | 1-20 years | 28 | 16.3 |
| | 21-40 years | 82 | 47.7 |
| | 41-60 years | 48 | 27.9 |
| | 61-80 years | 14 | 8.1 |
| | **Total** | 172 | 100.0 |

| Table 3: Frequency of MRSA isolated form different clinical specimens | | |
|---|---|---|
| Specimens | Frequency | Percent |
| Blood | 3 | 1.7% |
| CVP Tip | 3 | 1.7% |
| Fluid | 6 | 3.5% |
| HVS | 2 | 1.2% |
| Nasal Swab | 2 | 1.2% |
| Pus | 96 | 55.8% |
| Sputum | 7 | 4.1% |
| Tissue | 1 | .6% |
| Tracheal Secretions | 5 | 2.9% |
| Urine | 2 | 1.2% |
| Wound Swab | 45 | 26.2% |
| Total | 172 | 100.0% |

Antimicrobial susceptibility testing was performed on all isolates and results were noted for all antibiotics low and high dose of mupirocin. Table 4 is the representation of all antibiotics except both doses of mupirocin. MRSA were isolated from different clinical specimens and table 3 is the representation of it. MRSA were highest in pus and wound swabs, 55.8% and 26.2% respectively. As two doses of mupirocin were applied, low dose (MUP-5) and high dose (MUP-200) on all the isolated MRSA.

| Table 4: Antimicrobial susceptibility pattern of MRSA | | |
|---|---|---|
| Drug | Sensitive | Resistant |
| Amoxicillin/Clavulanic Acid | 0% | 100% |
| Methicillin | 0% | 100% |
| Ciprofloxacin | 6.4% | 93.6% |
| Gentamicin | 37.8% | 62.2% |
| Amikacin | 45.3% | 54.7% |
| Erythromycin | 24.4% | 75.6% |
| Clindamycin | 45.9% | 54.1% |
| Erythromycin | 24.4% | 75.6% |
| Fusidic Acid | 59.3% | 40.7% |
| Co-trimoxazole | 12.8% | 87.2% |
| Doxycycline | 48.8% | 51.2% |
| Chloramphenicol | 54.1% | 45.9% |
| Vancomycin | 99.4% | 0.6% |
| Linezolid | 100% | 0% |

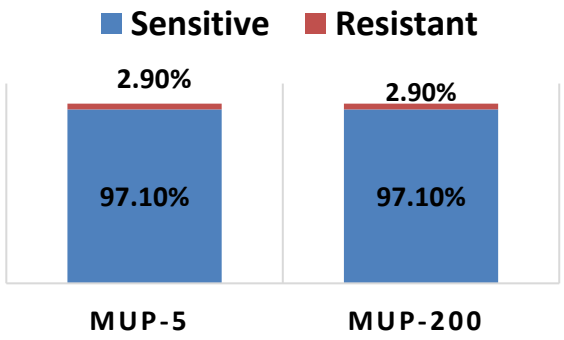


Fig. 1: Susceptibility of mupirocin (low and high dose)

## Discussion

In our study, both the 5 µg and 200 µg doses of mupirocin exhibited high efficacy, demonstrating sensitivity in approximately 97.10% of MRSA isolates. It's a positive finding, suggesting the effectiveness of mupirocin in our specific context.

However, when we consider the broader spectrum illuminated by other studies, nuances emerge. The global overview [9] indicates a variable prevalence of mupirocin resistance worldwide, ranging from 7.6% to 13.8%. This suggests that while mupirocin may work well in some regions, resistance is a

noteworthy concern on a global scale. The longitudinal study[10]spanning four years raises concerns about the persistent rise in mupirocin resistance despite ongoing infection control efforts. It prompts us to reflect on the challenges of maintaining the efficacy of this antimicrobial agent over time.

The genetic insights provided in a study [11] underscore the complexity of mupirocin resistance mechanisms. The study reveals a global emergence of resistance genes, emphasizing the adaptive nature of bacteria in response to antimicrobial agents. On a more localized scale, the study involving medical students [12] indicates a low risk of MRSA and mupirocin resistance within this demographic. However, the study in Malaysia [13] highlights higher resistance rates in specific MRSA types, signalling the importance of tailoring interventions based on regional dynamics.

In the hospital setting [14], the observed 13% overall mupirocin resistance rate necessitates regional vigilance. Meanwhile, the evolving molecular epidemiology in Singapore [15] underscores the need for continuous surveillance to adapt to changing MRSA trends over time. In summary, while our study reflects positive outcomes for mupirocin in our specific setting, the global and temporal perspectives provided by other studies emphasize the need for a nuanced and adaptive approach. Mupirocin resistance is not only a regional concern but also a dynamic global challenge that warrants ongoing attention and strategic antimicrobial stewardship.

## Conclusion

High susceptibility pattern of mupirocin in MRSA showed that, it can be used to cure infections due to methicillin resistant *Staphylococcus aureus* (MRSA) especially in soft tissues and skin wounds. This study was limited to susceptibility testing through the disc diffusion method.

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