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# Incidence of Mupirocin Resistance in Staphylococcus Aureus Isolated from Rural Population: A New Emerging Challenge

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## ABSTRACT

**Introduction:** *Staphylococcus aureus* is the most common bacteria linked to disease and death, causing serious community-acquired and nosocomial infections. Therefore mupirocin has been frequently used for treatment *Staphylococcus aureus* infections.

**Aim:** This research was conducted to evaluate the prevalence of mupirocin (Mup) resistance in our tertiary care hospital.

**Methods:** All strains of *S. aureus* were isolated from various clinical samples from patients either attending the outdoor services or getting treatment in the hospital. Detection of Mup-resistant *Staphylococcus aureus* was done by disc diffusion and E-test methods.

**Results:** Overall 265 *S. aureus* was obtained from numerous clinical samples. Among these, 111 isolates (42%) were MRSA. The overall occurrence of mupirocin resistance was 13% among all *S. aureus* isolates. Mupirocin resistance was found 19% in MRSA and 09% in MSSA.

**Conclusion:** Mupirocin resistance can be reduced by proper use of mupirocin and conducting regular tests to manage *S. aureus* colonization among health care workers.

**Key Words:** Mupirocin resistance, High-level, Low-level, *Staphylococcus aureus*, Methicillin-Resistant *S. aureus* (MRSA), methicillin-susceptible *S. aureus* (MSSA).

## INTRODUCTION

Infections caused by *Staphylococcus aureus* are most common and threatening, including osteomyelitis, bacteremia, skin-soft tissue infections, pneumonia seen in developing as well as developed countries.[1] Carriage of *Staphylococcus aureus* in nose, perineum, axilla, hands of health care workers and patients are the leading cause for *Staphylococcus aureus* acquisition along with its expansion. Decolonization from the site of carriage of *S. aureus* is one of the important modalities for prevention.[2,3] Various topical antibiotics have been applied to eliminate the *Staphylococcus aureus* infection and carriage. Currently the most effective topical antibiotic for removal of *Staphylococcus Aureus*is Mup. Mupirocin or pseudomonic acid A is one of the structurally associated antibiotics of pseudomonic acids (A, B, C and D). It is a correspondent of amino acid isoleucine and derivative of *Pseudomonas Fluorescens*. Mupirocin inhibits the bacterial isoleucyl transfer-RNA (t-RNA) sythetase, blocking the formation of t-RNA isoleucyl enzyme, which inhibits bacterial protein synthesis. Irrational usage along with the excessive accessibility has lead to the resistance of this drug which causes inappropriate decolonization of *S. aureus* and facilitates the spread of infection. Mupirocin susceptibility can be classified into Mupirocin-sensitive with minimum inhibitory concentration (MIC) of < 4 µg/ml [MupS], Low-level Mupirocin-resistance (MupRL) with MIC of > 8–256 µg/ml and High-level Mupirocin-resistance (MupRH) with MIC of > 512 µg/ml.[4-6] Therefore this study was planned to primarily assess the rates of high-level and low-level Mup resistance in *S. aureus* by disc diffusion

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and MIC methods and secondarily to compare its association with methicillin-resistant isolates.

## MATERIAL AND METHODS

The present study was conducted in the Microbiology Department of Santosh Medical College and Hospital, Ghaziabad with Approval from the Institutional Ethical Committee was obtained F. No. SU/2017/683 (15) on 26/05/2017. All clinical samples from in and outpatient departments of our tertiary care hospital were included for the present study. All clinical samples received in the laboratory were processed as per the standard microbiological procedure for the isolation of *Staphylococcus aureus*. 5%-Blood agar along with MacConkey agar (MA) was used for all clinical samples except urine. CLED (Cysteine-lactose-electrolyte-deficient) agar media was used for urine samples. The growth was recognized as *Staphylococcus aureus* with the help of standard biochemical methods.[1,7]

### Antimicrobial susceptibility testing

Antimicrobial susceptibility testing (AST) for all *S. aureus* isolates were done on Mueller-Hinton agar (HiMedia) by disc diffusion (Kirby–Bauer) technique as per the CLSI (Clinical and Laboratory Standards Institute) guidelines. Isolate inoculum with the turbidity of 0.5 McFarland-standard ($1.5 \times 10^8$ CFU/ml) in peptone water was prepared and lawn-culture on Mueller Hinton agar (MHA) and allowed to dry then antibiotics discs with different potency were placed on MHA by sterile forceps. Determination of methicillin-resistant *Staphylococcus aureus* (MRSA) was determined by using cefoxitin 30 µg discs. After incubation, the zone of inhibition was measured by unaided eye and size of ≤21 mm was considered as resistant and ≥22 mm as sensitive.[8]

### Mupirocin-resistant *Staphylococcus aureus* (Mup RSA) Detection

Mup resistance among *S. aureus* was assessed using 5 µg and 200 µg mupirocin discs by Kirby–Bauer disc diffusion method. Isolates with zone > 14 mm for 5 µg as well as 200 µg discs were considered as sensitive, isolates with zone < 14 mm for 5 µg but > 14 mm for 200 µg disc were considered as MupRL, and isolates with zone < 14 mm for both 5 µg and 200 µg discs was considered as MupRH.[9]

### Minimum inhibitory concentration detection by Epsilometer (E) test

E-test was conducted by Kirby Bauer disc-diffusion technique according to CLSI guidelines with mupirocin strip (MupEzy, Himedia). Lawn culture was prepared on MHA medium surface. Himedia E-strip with mupirocin antibiotic varied from 0.064-1240 µg/ml was placed on MHA, perfectly by gently pressing using a sterile forceps. The plates were then incubated aerobically at 35°C for 24 hours. After incubation plates were examined for the minimum inhibitory concentration (MIC). Isolates with MICs > 512 µg/ml were considered as MupRH, those with MICs 8-256 µg/ml were considered as MupRL and with <4 µg/ml were considered as mupirocin sensitive.[9]

## RESULTS

A sum of 265 *S. aureus* was isolated from numerous samples. Among these, 111 isolates (42%) were MRSA. Highest *S. aureus*(60%) were obtained from pus samples followed by blood samples as described in Table 01.

**Table 1: Distribution of *S. aureus* isolates in different samples.**

| Samples | S. aureus (%) | Methicillin-Resistant S. aureus | Methicillin-susceptible S. aureus |
|---|---|---|---|
| Pus | 160 (60) | 78 | 82 |
| Blood | 37 (14) | 12 | 25 |
| Genitourinary specimens | 34 (13) | 10 | 24 |
| Respiratory specimens | 24 (09) | 08 | 16 |
| Miscellaneous | 10 (04) | 03 | 07 |
| **Total** | **265** | **111** | **154** |

The overall occurrence of mupirocin resistance was 13% among all *S. aureus* isolates. Mupirocin resistance was found 19% in MRSA and 09% in MSSA. MupRH and MupRL-strains were 9% and 4% respectively. Out of 265 isolates, majority isolates (87%) showed less than 4 µg/ml MIC. 10 (4%) isolates were found to have MIC between 8-256 µg/ml followed by 25 (9%) isolates were showed MIC more than 512 µg/ml as described in Table 2 and 3.

**Table 2: Distribution of Mupirocinresistant *S. aureus*.**

| Isolate (265) | Mupirocin Sensitive (MupS) | Low-level Mupirocin resistance (MupRL) | High-level Mupirocin resistance (MupRH) |
|---|---|---|---|
| **MRSA (111)** | 90 | 8 | 13 |
| **MSSA (154)** | 140 | 2 | 12 |

**Table 3: MIC of Mupirocin against *S. aureus***

| E-test Minimum Inhibitory Concentration(MIC) range (µg/ml) | No. of isolates (265) |
|---|---|
| Sensitive (< 4) | 230 |
| Low-level resistance (8-256) | 10 |
| High-level resistance (>512) | 25 |

Antibiotic susceptibility testing (AST) was done to all *S. aureus* strains. Comparison of antibiotic sensitivity pattern was done for three groups (MupS, MupRL, MupRH). Overall, all three groups were 100% sensitive to Teicoplanin, Linezolid and Vancomycin. All antibiotics showed good sensitivity against all group isolates except Penicillin as described in Table 4.

**Table 4: Antibiotic sensitivity (%) pattern of Mupirocin sensitive and resistant S. aureus isolates**

| Antibiotics (µg) | MupS isolates | MupRL isolates | MupRH isolates |
|---|---|---|---|
| **Penicillin (10)** | 30 | 27 | 29 |
| **Erythromycin (15)** | 50 | 45 | 47 |
| **Cotrimoxazole (1025/23.75)** | 55 | 56 | 50 |
| **Gentamycin (10)** | 70 | 78 | 82 |
| **Ciprofloxacin (5)** | 35 | 40 | 37 |
| **Amoxyclav (20/10)** | 80 | 77 | 82 |
| **Clindamycin (2)** | 79 | 80 | 76 |
| **Tetracycline (30)** | 69 | 65 | 64 |
| **Teicoplanin (30)** | 100 | 100 | 100 |
| **Linezolid (30)** | 100 | 100 | 100 |
| **Vancomycin** | 100 | 100 | 100 |

## DISCUSSION

Mupirocin topical preparations were first available in 1985. Since then mupirocin has been widely used for management of colonization and infection of *S. aureus* in both medical personnel and patients. Soon after 2 years (1987) of mupirocin introduction, First mupirocin resistant S. aureus isolate was reported from the UK. Globally mupirocin-resistance was increased in MRSA and MSSA as irrational, uncontrolled, prolonged and multiple courses of this drug are the main reasons for the development of resistance.[10]Inadequate hand- hygiene and management of MRSA patients are the main reasons for the increasing prevalence of MRSA around the world. The present study showed a 42 % prevalence of MRSA. Very hogh prevalence was reported 72% compared to current study[11] whereas a study done in Vellore documented 5% prevalence only.[12]

The occurrence of mupirocin-resistance in *S. aureus* strains varied concerning hospitals, patient population and geographic region. The present study revealed that the prevalence of mupirocin resistant was 13%. A study done documented 17.3% prevalence in Madhya Pradesh region of India.[13] Another research done in south India showed 1% prevalence which was very low compared to our study.[14] Our study showed that occurrence of mupirocin-resistance was high in MRSA (19%) compared to MSSA (09%). Rudresh MS et al. reported 22% and 26% prevalence of mupirocin-resistance in MRSA and MSSA respectively.[13] Researchers from Uttar Pradesh found out 18% occurrence of mupirocin-resistance in MRSA which was concordance to present study.[9] Prevalence of mupirocin-resistance MRSA (21%) which was at a higher side compared to our study.[14] The overall prevalence of MupRH and MupRL in *S. aureus* was 9% and 4% respectively. A study from Madhya Pradesh found the prevalence of MupRH and MupRL were 15% and 10% which were higher than our research.[13] On another hand Singh Amit K *et al.* demonstrated only 2% prevalence of MupRH *S. aureus* isolates and did not find any MupRL isolated.[16] MupRH and MupRL in MRSA were 14% and 8% respectively. MupRH and MupRL in MSSA were 8% and 1% respectively. Rudresh MS et al.[13] reported 18% MupRH and 4% MupRL in MRSA whereas 17% MupRH and 9% MupRL in MSSA which were contradictory to our finding. Chaturvedi et al. documented 10% high and 8% low-level mupirocin-resistance.[9] A researcher from Maharashtra showed 6% high and 15% low-level mupirocin-resistance in MRSA which was not relatable to our study as the present study showed a higher prevalence of MupRH than MupRL in *S. aureus*.[15] Teicoplanin, vancomycin and linezolid was found 100% effective antibiotics against all *Staphylococcal aureus* strains. Apart from these antibiotics, antibiotic susceptibility pattern of mupirocin-susceptible and mupirocin-resistant*S. aureus* had some variations. Overall mupirocin-resistant *S. aureus* strains showed less sensitivity to antibiotics than mupirocin-susceptible strains. There was no significant difference were observed between these two groups of isolates.

## CONCLUSION

In summary, the present study showed a high occurrence of high level (9%) and low level (4%) mupirocin resistance in clinically isolated *S. aureus* which is a serious concern to prevent the spread of mupirocin resistance *S. aureus* strains in community and hospitals. Therefore carrier identifications, routine testing, infection control guidelines, surveillance and mupirocin prophylaxis are very crucial components for lowering the mupirocin resistance in *Staphylococcus* species.

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