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Original Research Article

New insights: mupirocin resistance among methicillin-resistant *Staphylococcus aureus* (MRSA) infection in southern Indian region

Umme Hani[1], Masood Ahmed Tahashildar[2]*, Anil Kumar[3]

[1]*AQuity Solutions India Private Limited, Bengaluru, Karnataka, India*
[2]*Dept. of Microbiology, J. N. Medical College and Dr Prabhakar Kore Basic Science Research Center, KLE Academy of Higher Education and Research, Belagavi, Karnataka, India*
[3]*Dept. of Public Health, J. N. Medical College, KLE Academy of Higher Education and Research, Belgaum, Karnataka, India*

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ABSTRACT

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) remains to be the most concerned pathogen with enhanced multi-drug resistance in clinical set-ups. With an immediate need to control MRSA infection, there is a steep rise in the use of mupirocin as a decolonization regime.
Materials and Methods: A total of 65 MRSA samples were analysed in the present study. *Staphylococcus* infection identified by standard conventional phenotypic methods. The antibiotic susceptibility pattern of mupirocin (5 μg/ml) was found using Kirby Bauer's disc diffusion method and the minimum inhibitory concentration (MIC) determined using MIC E-test strips of mupirocin.
Results: All the bacterial strains presented with MIC value less than 4 μg/ml, 23 isolates falls in the range of 0.05 μg/ml and 0.19 μg/ml, 12 strains MIC ranged between 0.125 and 0.640 μg/ml. However, five MRSA isolates showed no zone against mupirocin E-strip.
Conclusions: In present study, 92% of isolates were sensitive to mupirocin, this gives hope that mupirocin can be promising in the elimination of MRSA strains, a major concern in clinical practice. Also, the use of 5μg mupirocin discs is economical as compared to mupirocin E-strips, mupirocin discs can be used in a low resourceful clinical setups. However, our study revealed no difference in sensitivity for both the E-strip and disc method.

1. Introduction

Staphylococcus aureus is a well-known ubiquitous microorganism that able to colonize the anterior nares and skin surface, normally cause no infection in healthy individuals. Still, if invades the systemic circulation, can cause various serious infections. Currently antibiotic therapy remains difficult because of the circulation of multi-drug resistant methicillin-resistant *Staphylococcus aureus* (MRSA) strains. MRSA has been recognized as a major mode of origin of multi-drug resistant among nosocomial pathogens, causing high risk infections in patients.[1]

Decades after, *Staphylococcus aureus* remains to be a notoriously dangerous organism against human individuals. The rate of community-acquired as well hospital-acquired *staphylococcal* infection has increased drastically, with negligible impact on overall mortality.[2] The success of *S. aureus* as a human pathogen with its ability to impact with wide range of implications as a result of dominant virulence factors and toxins. The increased resistance of this *S. aureus* to broad-spectrum antimicrobial agents, addition as a prevalent nosocomial pathogen is of great

* *Corresponding author*.
E-mail address: connect.masudahmedofficial@gmail.com (M. A. Tahashildar).

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threat for global health sector. The resistant phenotypes mostly associated with the persistence of *S. aureus* in the hospitals leads to the emergence of resistant strains against methicillin.[1,3]

Studies pertaining to Indian set up including present study reveals all the MRSA isolates found to be sensitive to vancomycin. But, antibiotics such as Cotrimoxazole, Erythromycin, Gentamicin, Penicillin and Cephalosporin found to be resistant, correlating to the present study.[4–6] In late nineteen century wide range antibiotics were effective in treating bacterial infections. But the emancipation of the clinical strains resistance toward broad antibiotics and emergence of bacterial population with rise in antimicrobial resistance is possible due to various factor such irrational use of antimicrobials and drugs usage in animal feed as an enhancers.[7,8] At present, resistance is firmly established towards penicillin for the most clinical *S. aureus* isolates. Resistance against Beta-lactam antibiotics such as methicillin and penicillin causing MRSA infections too difficult to treat. MRSA strains related to hospital infection predominantly is of multi-drug resistant, causing reserved drug to be the only final option.[9]

A promising action plan taken into consideration to avert hospital related *staphylococcal* infections by using mupirocin, a decolonizing regime.[10] With an urgent need to curb MRSA infection, there is a possibility with increased use of mupirocin against MRSA infection as nasal decolonization regime. To determine the usage of mupirocin as a decolonization regime in clinical setting, there is a need to commiserate the clinical significance, pathogenesis, and epidemiology of resistance towards mupirocin, this may be a leaping step for the controlling emergence of MRSA strains.[9,10] The increased irrational use of some antibiotics added with the endemic outbreaks because of the presence of resistant MRSA strains (low level and high level) causing the emergence of resistance against mupirocin. However, the spread of low-level resistance is becoming significant and it is less possibly has major impact on clinical practice.[10] Implementations are formulated in order restrict the rise in mupirocin resistance in MRSA strains should express the vitality of monitored use of mupirocin in clinical practice. The goal of the present study is to understand the susceptibility and resistance pattern among the clinical isolates of MRSA strains to mupirocin and to ascertain the minimum inhibitory concentration (MIC) against MRSA strains using E-strips.

2. Materials and Methods

2.1. Study design

Cross sectional study design.

2.2. Place and duration of study

1. Place: KAHER's Dr Prabhakar Kore Basic Science Research Center, KLE Academy of Higher Education and Research, Belagavi, Karnataka, India -590010.
2. Duration: The duration of the study was of 8 months, from January 2023 to August 2023.

2.3. Inclusion criteria

All the samples subjected for the microbiological analysis presenting with MRSA infection.

2.4. Exclusion criteria

Samples with other bacterial isolates other than MRSA infection.

2.5. Sample size and sampling

Purposive sampling technique used in present study, and sample size taken into consideration based on the presence of MRSA infection.

2.6. Statistical analysis

Statistical analysis done with the help of biostatician to determine the significance.

A total of 65 MRSA samples were identified and analysed in the present study in KAHER's Dr Prabhakar Kore basic science research centre, Belagavi. Samples such as ear swabs, nasal swabs, pus, endotracheal (ET) aspiration, blood and urine collected from hospitalized patients. The *staphylococcus* infection identified by using standard culture methods and biochemical reactions. Antimicrobial susceptibility pattern of mupirocin (5 μg/ml) determined using Kirby Bauer's disc diffusion method using discs impregnated with standard antibiotics (vancomycin, linezolid, daptomycin, gentamycin, erythromycin and clindamycin) and the MIC is determined by MIC E-test strips of mupirocin (0.064-1024 mcg/ml); MIC ranged from 8 to 256 μg/ml taken to be low resistance and isolates with sensitivity of 512 μg/ml considered as high resistant. Strains with reading less than 4 μg/ml considered as sensitive after MRSA strains were identified by using VITEK automated system by using antibiotic oxacillin at the concentration of 4μg/ml.

3. Results

Out of 65 MRSA strains shown drastic variability in a distribution of the staphylococcal infection as per site, ward and type of sample collected (Table 1).

Antimicrobial susceptibility showed the MIC value of 0.5μg/ml to vancomycin of all 65 samples as per CLSI guidelines, which is considered to be sensitive. Linezolid 2μg/ml was sensitive to all MRSA isolates. Antimicrobial

Table 1: Distribution of the *staphylococcal* infection as per site, ward and type of sample collected from the patient

Parameter	Number	Percentage
Type of sample		
Pus	53	81.5
Blood	6	9.2
ET Swab	5	7.7
CSF	1	1.5
Ward		
Surgery	18	27.7
Geriatric	16	24.6
Surgery ICUs	12	18.5
Private wards	9	13.8
Orthopaedics	5	7.7
ENT	4	6.2
Burns ICU	1	1.5
Clinical Diagnosis		
Diabetes Mellitus	18	27.7
Breast abscess	10	15.4
Sepsis	9	13.8
Infected wound	5	7.7
Non healing ulcer	3	4.6
Swellings	3	4.6
Carbuncle	2	3.1
Furuncle	1	1.5
Gangrene	1	1.5
Other infections	13	20.0
Total	65	100

agents such as gentamycin, erythromycin as well as clindamycin reported to be sensitive against MRSA isolates. The resistance towards mupirocin determined by Kirby Bauer's disc diffusion test using mupirocin disc (5 μg/ml), zone of inhibition observed in all the MRSA isolates except five (8%) samples and remaining other sixty (92%) samples shown sensitivity zone with more than 18mm (Table 2). The MIC determined by using mupirocin E-strip on Muller Hinton agar. All isolates found to have MIC of < 4 μg/ml, 23 isolates between 0.05 μg/ml and 0.19 μg/ml, 12 isolates MIC ranged between 0.125 μg/ml and 0.640 μg/ml. However, five MRSA isolates not found to be present with any zone against mupirocin E-strip (0.0064 - 1024 μg/ml). (Table 2)

Present study report that the majority of the MRSA isolates coincide with surgical ward followed by geriatric ward. The clinical history revealed that the majority of the MRSA isolates were obtained from the individuals with Diabetes Mellitus, breast abscess and Sepsis. All the five mupirocin resistant strain were isolated from the pus sample.

4. Discussion

In present study out of 65 MRSA isolates five were resistant to mupirocin. The antibiotic resistance pattern among these five samples correlated with emergence of resistance for mupirocin in S aureus isolates detected in various parts of world. This brings to grave concerns towards antibiotic therapy, as the most effective drugs are at the brink of development of resistance. In present work 92% of bacteria were sensitive to mupirocin, which is a helpful finding. However, various studies shows the evident interrelation between development of low rate of mupirocin resistance and reduced usage.[11]

One study revealed that 5μg mupirocin discs resistant towards all MRSA isolates (n=25). MIC breakpoint range suggest heterogeneous variability towards methicillin resistance. The mupirocin low level resistance using 5μg discs in MRSA isolates present with no clinical relevance. This pattern of resistance is drastically at rise in United Kingdom and south East Asia. A Study with a duration of 10 year at SJMCH laboratory, revealed that the resistance towards mupirocin is of 8.3% to 10% when 5μg mupirocin disc was used against MRSA isolates.[12]

Another study carried out for a period of three months in a tertiary care hospital to detect the occurrence of high level and low level mupirocin resistance (MuL) among staphylococcus isolates, in which 5 μg and 200 μg mupirocin discs were used by means of agar dilution method. The rate of high level mupirocin resistance (MuH) detected to be 2% among MRSA and 28% methicillin resistance CONS species. The suggested strains with low level resistance mupirocin can be effectively treated with use of mupirocin, however the high level resistance towards mupirocin need to eradicate with other treatments.[13] The utilization of topical application of mupirocin, the elimination of MRSA strains in healthcare workers studied earlier. Additionally, some previous studies carried out previously in which decimation of MRSA infection in 25% patients by using mupirocin was evident and 18% of them treated with placebo amalgamated with chlorohexidine baths. This study revealed that application of mupirocin intra nasally is effective in expunging of MRSA infection among patients.[14]

Present study accord with one of the study carried out in India which shows similar results of mupirocin resistance among 5% isolates in which three found to be high level mupirocin resistant isolates and two strains found to be low level resistance strains. But the present work discloses the complete resistant among five MRSA isolates possibly because of point mutation in ileS genes.[15]

In present study 92% of isolates were sensitive to mupirocin which still gives hope that mupirocin is promising in elimination of MRSA strains. MRSA predominantly found in individuals with diabetes and breast abscess. Hence, extermination of such strains is essential added with preventive and control measures among such individuals.

Table 2: Sensitivity of MRSA isolates againstmupirocin disc and mupirocin strips

Type of Sample	MRSA Isolates	Mupirocin Disc		Mupirocin Strips		p value*
		Sensitive N (%)	Resistance N (%)	Sensitive N (%)	Resistance N (%)	
Pus	53	48 (90.6%)	5 (9.4%)	48 (90.6%)	5 (9.4%)	0.000
Blood	6	6 (100%)	0 (0.0%)	6 (100%)	0 (0.0%)	NA
ET Swab	5	5 (100%)	0	5 (100%)	0	NA
CSF	1	1 (100%)	0	1 (100%)	0	NA
Total	65	60 (92.3%)	5 (7.7%)	60 (92.3%)	5 (7.7%)	NA

P value* significant < 0.005

5. Conclusions

Present work revealed that the use of 5μg mupirocin disc economical as compared to mupirocin E-strips. Mupirocin discs can be used in low resourceful clinical set up. However, present study gives evidence of no difference in sensitivity for the both E-strip and disc method.

6. Sources of Funding

None.

7. Conflict of Interest

None.

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Author biography

Umme Hani, Transcribe Officer

Masood Ahmed Tahashildar, Doctoral Research Scholar https://orcid.org/0000-0003-2043-9152

Anil Kumar, Doctoral Research Scholar

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