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Antimicrobial susceptibility pattern and mupirocin resistance among methicillin-resistant *Staphylococcus aureus* isolated from skin and soft-tissue infection patients attending a tertiary care hospital in North India

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ABSTRACT

Background: Antimicrobial susceptibility among bacterial isolates varies from center to center. Mupirocin is a topical antibacterial antibiotic used to treat wound infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA). **Aim and Objectives:** This study was conducted to know the prevalence of high and low levels of mupirocin resistance along with antimicrobial susceptibility in MRSA isolates from skin and soft-tissue infection in patients admitted to a tertiary care hospital in North India. **Materials and Methods:** A total of 97 non-repetitive isolates of MRSA from various pus samples over a period of 1 year were included in this study. These strains were identified as per standard laboratory protocols given by the Clinical Laboratory Standards Institute. High- and low-level mupirocin resistance of the isolates was tested by using mupirocin discs of 200 µg and 5 µg, respectively. Mupirocin strips of 256 µg and 512 µg were used for the E-test to detect low-level and high-level mupirocin resistance, respectively. The isolates were reported as sensitive to mupirocin, with minimum inhibitory concentrations of <4 mg/L. **Results:** Overall, 9.27% of mupirocin resistance was found, of which 2.06% of isolates were high-level resistant to mupirocin, while 7.21% had low-level resistance. All MRSA strains were susceptible to vancomycin, followed by linezolid (94.84%), teicoplanin (91.75%), and fusidic acid (88.65%). **Conclusion:** Regular monitoring, good infection control practices, and proper awareness about utilizing mupirocin therapeutically and prophylactically may help prevent the emergence of mupirocin resistance in health-care facilities.

Key words: Methicillin-resistant *Staphylococcus aureus*; Antibiotic susceptibility; Mupirocin resistance; North India

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INTRODUCTION

The wound is an abrasion of the skin, one of the most significant barriers to establishing bacterial pathogen infections in internal tissues. Infection can occur when germs overcome this barrier.[1] The wound infection affects the skin and soft tissue, as these advances can overlap.[2] Vancomycin and linezolid are recommended to treat methicillin-resistant *Staphylococcus aureus* (MRSA) infections, whereas mupirocin is used to treat skin and soft-tissue infections and decolonize carriers.[3] The drug mupirocin is used topically to treat infections affecting the skin and soft tissues caused by MRSA. Mupirocin has been authorized for MRSA nasal colonization treatment. It prevents bacterial protein synthesis.[4,5] Mupirocin resistance has changed due to the irrational use of antibiotics in MRSA infections among patients and its transmission among health-care staff. Based on the minimal inhibitory concentrations,

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mupirocin resistance phenotypes are characterized as low level or high levels.[6] Minimum inhibitory concentrations ranging from 8 mg/L to 256 mg/L are low level, and >512 mg/L are called high level. In most cases, the plasmid-mediated gene mupA confers high-level resistance by encoding a transfer RNA synthetase with low mupirocin affinity.[7,8] Mupirocin sensitivity test is routinely not done, rather uncommon.[9] The ability to detect and differentiate between the two groups has clinical implications. Low-level mupirocin resistance can be addressed by prescribing a high dosage, while high-level mupirocin resistance limits its use in the clinic.[10] The resistant of mupirocin to MRSA is a major source of concern, as it may result in the loss of a critical treatment option for MRSA control. Resistance to mupirocin is linked to greater use in closed inpatient settings.[11] Therefore, the goal of this study was to see how often there is low-level and high-level mupirocin resistance among MRSA infections of the skin and soft tissue.

Aims and objectives

This study was conducted to know the prevalence of high and low levels of mupirocin resistance along with antimicrobial susceptibility in MRSA isolates from skin and soft-tissue infection in patients admitted to a tertiary care hospital in North India.

MATERIALS AND METHODS

This research was carried out in the Department of Microbiology, Santosh Medical College, Ghaziabad, along with the collaboration of the Department of Microbiology of the Mayo Institute of Medical Sciences, Barabanki, from January 2018 to December 2018. The study was approved by the Institutional Ethics Committee.

A total of 97 MRSA isolates were studied from pus samples collected from skin and soft-tissue infections. Isolation and identification were done by standard bacteriological protocols.[12] Antibiotic sensitivity tests and MRSA detection were done by the Kirby-Bauer disk diffusion method as per the latest CLSI-M100 guidelines.[13] The MRSA isolated from skin and soft tissue were checked for mupirocin susceptibility; for that, 0.5 McFarland suspensions of isolates were prepared and lawn cultured in a Mueller-Hinton agar plate. The mupirocin disc (5 μg and 200 μg) and E-strip (HiMedia, Mumbai, India) were used, and the results were interpreted as shown in the table given below.

Antibiotic disc concentration	Zone of inhibition	Interpretation
5 μg 200 μg	≥14 mm	Sensitive
5 μg 200 μg	<14 mm ≥14 mm	Low-level resistance
5 μg 200 μg	<14 mm	High-level resistance

RESULTS

Out of the total 97 cases, 58 (59.8%) were males and 39 (40.2%) were females. Maximum cases were found in the 21–40-year age group among both genders, followed by 28 (28.9%) cases in the 41–60-year age group and 24 (24.7%) cases in the 0–20-year age group. Only 2 (2.1%) cases were found in the above 60-year-old age group (Table 1).

Departmental distribution data showed that isolation was highest in the department of surgery 27 (27.84%) followed by orthopedics 24 (24.74%), ear, nose, and throat (ENT) 21 (21.65%), and casualty, medicine, obstetrics, and gynecology. 5 (5.09%) each, pediatrics 4 (4.09%), and the least common from the intensive care unit (ICU) and medicine ICU at 3 (3.09%) cases each (Table 2).

On studying the pattern of antibiotic resistance of MRSA isolates, the maximum isolates 80 (82.47%) were resistant to erythromycin, followed by 65 (67.01%) to ciprofloxacin and cotrimoxazole, 51 (52.58%) to rifampicin, 50 (51.55%) to gentamicin, 37 (38.14%) to clindamycin, 34 (35.05%) to doxycycline, 33 (34.02%) to tetracycline, 08 (8.25%) to teicoplanin, and 5 (5.15%) to linezolid. No isolate was found to be resistant to vancomycin (Table 3). Overall, mupirocin resistance was found in 9 (9.28%) isolates, out of which 7 (7.22%) isolates had low-level resistance, while high-level resistance was found in 2 (2.09%) isolates. Eleven (11.34%) isolates were resistant to fusidic acid (Table 4).

Table 1: Demographic distribution of methicillin-resistant *Staphylococcus aureus* isolates

Age groups (years)	Male		Female		Total	
	No.	%	No.	%	No.	%
0–20	16	16.5	8	08.2	24	24.7
21–40	24	24.7	19	19.6	43	44.3
41–60	16	16.5	12	12.4	28	28.9
>60	2	02.1	00	00.0	02	02.1
Total	58	59.8	39	40.2	97	100.00

Table 2: Department-wise distribution of MRSA isolates

Department	Number	Percentage
Casualty (IPD)	05	05.15
ENT (OPD+IPD)	21	21.64
SICU (IPD)	03	03.10
Medicine (OPD+IPD)	05	05.10
MICU (IPD)	03	03.10
OB and GY (OPD+IPD)	05	05.10
Orthopedics (OPD+IPD)	24	24.74
Pediatrics (OPD+IPD)	04	04.10
Surgery (OPD+IPD)	27	27.87
Total	97	100.00

ENT: Ear nose throat, MRSA: Methicillin-resistant *Staphylococcus* aureus, OPD: Out-patient department, IPD: In-patient department, SICU: Surgical intensive care unit, MICU: Medical intensive care unit, OB: Obstetrics, GY: Gynecology

Table 3: Antimicrobial resistance pattern among MRSA isolates

Antibiotic	Number	Percentage
Penicillin	97	100.00
Cefoxitin	97	100.00
Erythromycin	80	82.47
Ciprofloxacin	65	67.01
Cotrimoxazole	65	67.01
Rifampicin	51	52.58
Gentamicin	50	51.55
Clindamycin	37	38.14
Doxycycline	34	35.05
Tetracycline	33	34.02
Teicoplanin	08	08.25
Linezolid	05	05.15
Vancomycin	00	00

MRSA: Methicillin-resistant *Staphylococcus* aureus

Table 4: Mupirocin and fusidic acid resistance distribution (n=97)

Resistance	Number	Percentage
Low-level resistance only	7	7.22
High-level resistance	2	2.06
Fusidic acid	11	11.34

DISCUSSION

In the present study, a total of 97 MRSA-positive pus samples were included, out of which 58 (59.8%) were from male patients and 39 (40.2%) were from females. Our findings are similar to a study conducted by Mathanraj et al., from south India, who reported a higher incidence of MRSA infection in male patients.[14] Although Ghaznavi-Rad et al from Indonesia have reported no significant difference in gender predilection in isolation of MRSA from cases.[15]

The bacteria *S. aureus* is the most common cause of surgical site infections (SSIs). The organism usually colonizes human skin and mucus.[16] In the present study, MRSA isolates were found most commonly in surgery (27.84%), followed by orthopedics (24.74% and ENT (21%). These findings are similar to a previous study by Srinivasan et al., who reported 80% of MRSA isolates from surgical wards.[17] The MRSA isolated from surgery in this investigation was 27.8%, which corresponds to the findings of Esmat et al.,[18] from Sohag, who reported a prevalence rate of 20% of *S. aureus* in cases of SSIs. MRSA prevalence has ranged from 29% to 35% in several American and European hospitals, whereas as per the current Indian Network for Surveillance of Antimicrobial Resistance (INSAR) group's report, the prevalence varies from 26.8% to 74.7% in Indian hospitals.[19]

As per the latest annual report of INSAR, multidrug resistance among MRSA strains was very common and variable between different centers. 91.8% of isolates were resistant to ciprofloxacin, followed by 75% to erythromycin, 39.2% to cotrimoxazole, 35.8% to clindamycin, and 15.1% to tetracycline. No isolate was resistant to vancomycin and tigecycline, while 9.9% of isolates showed high levels of resistance to mupirocin, followed by 0.9% to linezolid and only 0.5% to teicoplanin.[19]

Our results are a bit different from the latest INSAR report, as we have found 82.5% of isolates resistant to erythromycin, followed by 67% resistant to ciprofloxacin and cotrimoxazole, 38.1% resistant to clindamycin, and 34% resistant to tetracycline. We found all isolates sensitive to vancomycin only, while 8.25% were resistant to teicoplanin and 5.5% were resistant to linezolid. A similar high prevalence of multidrug resistance has been reported by Bhattacharya et al., from Tirupura,[20] Kaur and Chate from Pune,[21] Rudresh et al., from Indore,[22] and Bhattacharya et al., from Kolkata,[23] who found that all *S. aureus* isolates, including MRSA, were linezolid and vancomycin sensitive in their research.

Mupirocin is a topical antibacterial medication used to treat skin infections and prevent MRSA colonization in both patients and health-care workers. Shortly after introducing mupirocin into clinical practice, the first report of mupirocin-resistant *S. aureus* appeared in 1987 in the U.K.[24] In this study, the prevalence of mupirocin resistance was 9.27%, low-level resistance was 7.27%, and high-level resistance was 2.06%. To date, mupirocin medication has been used for the treatment of infections caused by *Staphylococcus* species. Mupirocin resistance has been reported in several countries throughout the world, including Spain (11.3%), the United States (13.2%), Trinidad and Tobago (26.1%), China (6.6%), India (6%), Turkey (45%), and Korea (5%).[25]

High-level mupirocin resistance among MRSA isolates varies from center to center and has been reported from

0% by Rajkumari et al., from Kolkata[26] to 38.46% by Krishnan et al.,[27] while low-level mupirocin resistance has been reported from 0% by Rajkumari et al., from Kolkata[26] to 18.2% by Rudresh et al., from Indore.[22] The results of this investigation are modest when compared to literature reports of 0–18.2% low-level resistance and 0–38.46% high-level resistance.[22] MRSA isolates were susceptible to vancomycin (100%), followed by linezolid (94.84%), teicoplanin (91.75%), and fusidic acid (88.65%). The emergence of higher rate of resistance against teicoplanin and fusidic acid, compared to the latest prevalence rates of 0.3–2.4%[19] and 7.49%,[23] respectively, is worrisome and warrants screening of MRSA isolates in our setup for timely treatment, prevention, and control.

Limitations of the study

The limitation of our study has been the low sample size, and a larger study is needed to reconfirm the findings of our study.

CONCLUSION

The highest number of MRSA isolates was isolated from the surgery department, followed by orthopedic and ENT departments, hinting that the prevalence of MRSA is relatively more common in the surgical departments due to poor environmental cleaning and infection control practices in the Indian setting. The prevalence of high- and low-level mupirocin resistance is moderate, but a higher resistance rate against teicoplanin and fusidic acid warrants regular screening of MRSA isolates.

Hence, it can be concluded that as the antimicrobial susceptibility patterns of various pathogens vary from center to center, screening *S. aureus* isolates for multidrug resistance is highly warranted, as it will help clinicians start empirical antimicrobial therapy as per the prevalent antimicrobial susceptibility patterns of circulating isolates in their setup.

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BLC- Concept, design, Definition of intellectual content, Literature survey, Implementation of study protocol, data collection, data analysis, manuscript preparation; **SS-** Literature survey, preparation of tables, data analysis, review manuscript and article submission.

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