ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 10 | October - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

THE EMERGENCE OF MUPIROCIN RESISTANCE AMONG THE CLINICAL ISOLATES OF MRSA IN TERTIARY HEALTH CARE HOSPITAL OF NORTH EAST INDIA.

Microbiology

Dr. S. Damrolien
Dr. Ksh. Mamta Devi* *Corresponding Author
Dr. Kh. Sulochana Devi

KEYWORDS

INTRODUCTION:

Staphylococcus aureus, a major cause of hospital acquired infections, remains a problem in health care worldwide, causing a wide range of infections such as pneumonia and bacteraemia and their sequelae result in prolonged hospital stayed and a significant economic burden, especially in the case of methicillin-resistant S. aureus (MRSA).These strains show resistance to different variety of antibiotics, thus limiting the treatment options to very minimal agents such as vancomycin, Teichoplannin and linezolid.[1] Carriage of MRSA in nose, axilla, perineum and hands of patients and health care personnel is an important risk factor for the spread of MRSA. Decolonization from the site of carriage is one of the modalities for prevention of MRSA infections in healthcare settings. The only approved antibiotic for decolonisation of MRSA and methicillin-susceptible S. aureus (MSSA) both in patients and healthcare personnel is mupirocin (pseudomonic acid A).[2] Mupirocin (pseudomonic acid A) derived from *Pseudomonas fluorescens* is an important topical antibiotic ointment for the nasal decolonization of MRSA in carriers. It acts by binding specifically to the bacterial isoleucyl- tRNA synthetase (IRS) enzyme and inhibits its protein synthesis. Along with its use as a decolonising agent in health care personnel and patients, it has also been used for treatment of staphylococcal skin and soft tissue infections.[3] However due to the increased use of this antibiotic outbreaks of MRSA resistant to mupirocin is increase, although the frequency of resistance is still low.[4]

Traditionally, mupirocin susceptible strains are defined as those with a minimum inhibitory concentration (MIC) of ≤2 µg/ml while those having a MIC of ≥4 µg/ml were considered resistant, and for disk diffusion zone diameter of ≥14 mm with a 5-µg disc was considered as susceptible while zones of ≤13 mm as resistant.[5] However, recently mupirocin-resistant strains are grouped into two distinct categories: low level (MuL) with MICs of 8–256 µg/ ml, and high level (MuH) with MICs ≥512 µg/ml, while mupirocin-sensitive isolates were those with MIC of ≤4 µg/ ml.[6]

MuL and MuH strains cannot be differentiated. However it can be performed by concomitant use of 5 µg and 200 µg mupirocin disks. MuH strains have been found to be associated with failure of mupirocin as a decolonising agent as well as for treatment of skin and soft tissue infections.[7]

Two types of resistance to mupirocin have been described, with high-level and low-level mupirocin resistance being associated with the plasmid-mediated mupA gene and chromosomal point mutations, respectively. The high-level mupirocin resistance phenotype can be transferred by conjugation between different staphylococcal strains or species.[8]

Treatment with mupirocin is not likely to be effective in the presence of high-level mupirocin resistance and there is some evidence to suggest that low-level resistance may also predict treatment failure.[9] Decolonization regimens, including the eradication of MRSA carriage with topical antimicrobial and antiseptic agents, have been used variably in the clinical setting. Mupirocin has been the mainstay of decolonization therapy as it is the only topical antibiotic approved for the eradication of MRSA nares colonization in the United States.[10]

However, decolonization with mupirocin remains controversial as eradication appears to be short-term, is not achieved in all patients, and does not consistently prevent subsequent infections.[11] Some studies suggest that *mupA* gene which is known to encode for mupirocin resistance is transferred from *Staphylococcus epidermidis* to MRSA during mupirocin prophylaxis. It has been suggested that mupirocin resistant coagulase-negative *Staphylococcus* spp. (CoNS) might be an important source of the *mupA* determinant in MRSA. The increasing prevalence of transferable mupirocin resistance among CoNS species could be an important threat to the future use of mupirocin against MRSA.[12]

It was therefore the intent of this study to identify independent predictors associated with mupirocin-resistant MRSA among the clinical isolates in our tertiary care hospital.

MATERIALAND METHODS

This is 4 years retrospective study conducted in the Department of Microbiology at RIMS Imphal. *Staphylococcus aureus* isolates were recovered from clinical specimens from the patients admitted to wards as well as patients attending OPD's of RIMS Hospital Imphal during 4 years study periods from 1st October 2016 to 30th September 2020.

Isolation and Identification

All the clinical specimens except urine were inoculated onto Blood Agar and Mac Conkey agar media whereas urine samples were inoculated on Cysteine-lactose electrolyte deficient (CLED) agar media and incubated at 37^{0}C aerobically. The growth is identified as *Staphylococcus aureus* according to the standard laboratory operating procedures.[13]

Detection of MRSA and High level mupirocin resistant

MRSA was detected by using cefoxitin 30microgram disc as per CLSI guideline (Clinical and Laboratory Standards Institute). Zone of inhibition less than or equal to 21 was considered as resistant and reported as MRSA High level Mupirocin resistance testing was done by disc diffusion with disc concentration of 200µg. Zone diameter of > 14 mm was taken as susceptible for mupirocin and isolates with zone diameters < 14 mm were considered to be high-level mupirocin resistant strains.[14]

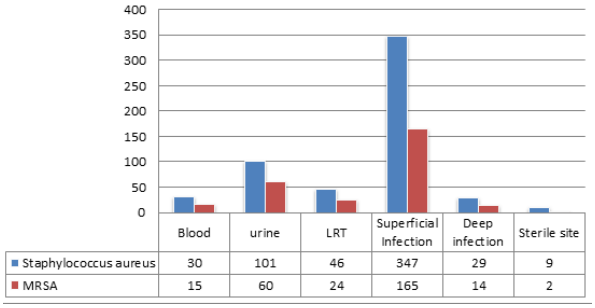
Antimicrobial susceptibility testing of MRSA

Antimicrobial susceptibility testing was done according to the CLSI standards by disc diffusion method for the following antibiotics: ciprofloxacin (5 µg), clindamycin (2 µg), cotrimoxazole (1.25/23.75 µg), doxycycline (30 µg), erythromycin (15 µg), gentamicin (10 µg), linezolid (30 µg), mupirocin (200 µg), penicillin (10 units), and vancomycin (30 µg). D zone test was done do determine inducible resistance to clindamycin. Vancomycin susceptibility was done by agar dilution method.[14]

RESULTS

A total of 562 non-duplicate *Staphylococcus aureus* were obtained from various clinical samples during this 4 years study period i.e 1st October 2016 to 30th September 2020. Out of 562 *Staphylococcus aureus*, 282 (50.2%) isolates were MSSA and 280 (49.8 %) isolates were *MRSA*. Out of 280 isolates of *MRSA* 40 (14.1%) were high level mupirocin resistance **(Fig:2)**

Fig 1: Specimens wise distribution of Staphylococcus aureus and MRSA



Out of 562 *Staphylococcus aureus* 280 (49.8 %) isolates were *MRSA* .MRSA were isolated in highest from samples of Superficial infection 165 (29.3%) followed by Urine 60 (10.7%) and lower respiratory tract samples 46 (8.2%). Distribution of *Staphylococcus aureus* and MRSA on the basis of source of specimens is listed in **Fig 1.**

Table 1: Description of different type of specimens

	Specimens types
Blood	Blood from Central and Peripheral catheter
Lower respiratory tract (LRT)	BAL, Sputum, Lung aspirate, Endotrachael aspirate (ETA) and Lung tissue
Superficial Infection	Skin and Soft Tissue, Pus/Exudate, Wound swab, Superficial Biopsy and Tissue
Deep infection	Abscess aspirate, Pus aspirate, Deep Biopsy and Tissue
Sterile site	Fluid from sterile space, Abdominal/Ascitic fluid, pancreatic drain fluid, pericardial fluid, peritoneal fluid and pleural fluid.

Fig 2: Prevalence of mupirocin resistance in MRSA strains: Out of 280 MRSA, 40(14.1%) isolates were high level mupirocin resistants.

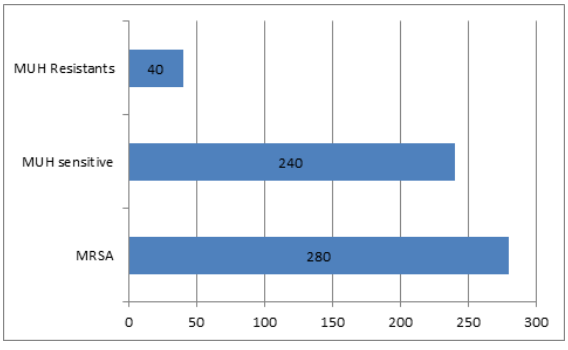


Table 2: Antimicrobial susceptibility profile of MRSA

Antibiotics	MRSA (n=280)	MRSA (OPD) n=92	MRSA (ward) n=178
Ciprofloxacin	77 (27.7%)	20 (22.2 %)	54 (30.6 %)
Clindamycin	177 (63.5%)	74 (81.3%)	97 (54.8%)
Erythromycin	47 (16.9%)	19 (21.1 %)	26 (14.5 %)
Linezolid	265 (94.8%)	88 (96.6%)	167 (94.2%)
Mupirocin high level	240 (85.9%)	86 (94.1%)	147 (83 %)
Teichoplannin	244 (87.4%)	84 (92%)	151(84.8%)
Tetracycline	221 (79.2%)	80 (87.6%)	134 (75.3%)
Co-trimethoprim	151 (54%)	57 (61.8%)	91 (51.5%)
Vancomycin	280 (100%)	92 (100%)	178 (100%)

Table 2 shows the antimicrobial susceptibility profile of MRSA in OPD and Ward isolates. In this study, it is observe that MRSA isolates in OPDs is more sensitive to various antibiotics than MRSA Isolates in wards. High level mupirocin sensitivity in OPD and Ward isolates were 94.1% and 83% respectively. The following antibiotic sensitivity were ciprofloxacin (27.7%), Clindamycin (63%), Erythromycin (16.9%), Linezolid (94.8%), Teicoplannin(87.4%) Tetracycline (79.4%), Co-trimoxazole(54%), Vancomycin (100%)

DISCUSSION:

Health care associated infection cause by MRSA is increasing in the past few years because of the improper hand hygiene and handling of MRSA carrier patients. Along with increase prevalence of MRSA mupirocin resistance also increase among staphylococci isolates in many parts of the world.[15]

In this study, out of 562 Staphylococcus aureus 280(49.8%) were MRSA which is comparable with the finding of study conducted in South India by *B. Madhumati et al*[16] i.e.54% were MRSA and out of which 24% were mupirocin resistant and a similar study was conducted in central India by *Parul Chaturvedi et al*[17] shows that mupirocin resistance among MRSA was 18.3% but in this study prevalence were slightly lower only 14.1% of MRSA shows mupirocin resistant. This may be due to decrease used of mupirocin ointment for treatment of skin and soft tissue infection and also for decolonization of MRSA in carriers among the health care workers in our Hospital. In this study Antimicrobial susceptibility pattern shows that, MRSA isolate from OPDs are more sensitive to different variety of antibiotics than MRSA isolates from ward and this finding is consistent with most of the Indian study.[18]

CONCLUSION:

This study has demonstrated a high prevalence of MRSA among the staphylococcus aureus isolates and mupirocin resistance among the MRSA is still low. therefore it is highly recommend to used mupirocin ointment for treatment of infection cause by MRSA and also for decolonization of MRSA in the nasal carrier among the health care workers. Furthermore it is also recommended that routine testing of MRSA for high level mupirocin resistance be conducted at the earliest and assists in the control and spread of mupirocin-resistant MRSA. Infection control practices such as hand hygiene should be encourage as far as possible and antimicrobial stewardship programmes are also equally important to address excessive or inappropriate antimicrobial usage. In case of mupirocin resistant strains of MRSA alternate agents to mupirocin must be considered as per sensitivity reports to prevent spread of resistant strains. Detection of MRSA in a healthcare worker usually leads to a 7-day chlorhexidine-based baths and topical 2% mupirocin ointment application along with absence or relocation from duty till two negative culture reports are documented. Hence, it would be advisable to screen all isolates obtained from nasal carriers with mupirocin prior to start of therapy such that MuH strains may be treated with other alternatives like fusidic acid, neomycin etc.

Acknowledgment:
Our Sincere thanks to Mr.Moirangthem Herokumar Data entry operator and Mr. Rameswor Singh, Lab. Technician AMR project funded by ICMR for their technical support and assistance.

Financial support and sponsorship: Study was conducted as a part of RIMS AMR project funded by ICMR.

Conflict of Interest: Nil

REFERENCES

1. Xavier Malaviolle, Claire Nonhoff, Olivie Denis, Sylvianne Rottiers and Marc J. Struelens. Evaluation of disc diffusion methods and Vitek 2 automated system for testing susceptibility to mupirocin in Staphylococcus aureus. Journal of Antimicrobial Chemotherapy. 2008; 62: 1018–1023.
2. Caffrey AR, Quilliam BJ, LaPlante K. Risk factors associated with mupirocin resistance in meticillin-resistant Staphylococcus aureus. J Hosp Infect 2010;76:206–10.)
3. Singh Amit K, Venkatesh Vimala, Singh Mastan. Mupirocin resistance in clinical isolates of Staphylococcus aureus in a tertiary care hospital set up in north. Int J Med Res Health Sci. 2013; 2(4): 840-847.
4. Schmitz FJ, Jones ME. Antibiotics for treatment of infections caused by MRSA and elimination of MRSA carriage. What are the choices? Int J Antimicrob Agents 1997;9:1-19.
5. Fuchs PC, Jones RN, Barry AL. Interpretive criteria for disk diffusion susceptibility testing of mupirocin, a topical antibiotic. J Clin Microbiol 1990;28:608-9.
6. Eltringham I. Mupirocin resistance and methicillin-resistant Staphylococcus aureus (MRSA). J Hosp Infect 1997;35:1-8.
7. Hurdle JG, O'Neill AJ, Ingham E, Fishwick C, Chopra I. Analysis of mupirocin resistance and fitness in Staphylococcus aureus by molecular genetic and structural modeling techniques. Antimicrob Agents Chemother2004;48:4366-76.
8. Shahsavan S, Emaneini M, Khoshgnab BN, Khoramian B, Asadollahi P, Aligholi M, et al. A high prevalence of mupirocin and macrolide resistance determinant among Staphylococcus aureus strains isolated from burnt patients. Burns 2012;38:378–82.
9. Walker, E. S., J. E. Vasquez, R. Dula, H. Bullock, and F. A. Sarubbi. 2003. Mupirocin-resistant, methicillin-resistant Staphylococcus aureus: does mupirocin remain effective? Infect. Control Hosp. Epidemiol. 24:342–346.
10. GlaxoSmithKline. Mupirocin Calcium Ointment, 2% (Bactroban Nasal) Package Insert.Research Triangle Park, NC: GlaxoSmithKline 2007.
11. van Rijen MM, Bonten M, Wenzel RP, Kluytmans JA. Intranasal mupirocin for reduction of Staphylococcus aureus infections in surgical patients with nasal carriage: a systematic review. J Antimicrob Chemother 2008; 61: 254-61.
12. Hurdle JG, O'Neill AJ, Mody L, Chopra I, Bradley SF. In vivo transfer of high-level mupirocin resistance from Staphylococcus epidermidis to methicillin-resistant Staphylococcus aureus associated with failure of mupirocin prophylaxis. J Antimicrob Chemother 2005;56:1166-8.
13. Baird D. Staphylococcus. Cluster forming gram positive cocci. Chapter 11. In: Collee

JG, Fraser AG, Marmion BP, Simmons A, editors. Mackie and McCartney Practical Medial Microbiology. 14th ed. New York: Churchill Livingstone; 1996. p. 245-58.
14. Performance Standards for Antimicrobial SusceptibilityTesting; 20th Informational Supplement, Clinical and Laboratory Standards Institute (CLSI) M100-S20: Vol. 30,No.1. Wayne, PA: Clinical and Laboratory Standards Institute;2010.
15. Chaves, F., J. Garcı´a-Martı´nez, S. de Miguel, and J. R. Otero. 2004. Molecular characterization of resistance to mupirocin in methicillin-susceptible and -resistant isolates of Staphylococcus aureus from nasal samples. J. Clin. Microbiol. 42:822–824) .
16. B. Madhumati*, Vijaya Rajendran and K. Ashwin : Prevalence of Mupirocin Resistance in Methicillin Resistant Staphylococcus aureus Strains isolated from a Tertiary Care Hospital International Journal of Current Microbiology and Applied Sciences ISSN: 2319-7706 Volume 7 Number 05 (2018)
17. Parul Chatuvedi, Amit Kumar Singh, Snehanshu Shukla, Loveleena Agarwal. Prevalence of Mupirocin Resistant Staphylococus aureus Isolates among Patients admitted to Tertiary Care Hospital. N Am J Med Sci. 2014 Aug;6(8):403-407.
18. Hare Khrishna Tiwari, Darshan Sapkota and Malaya Ranjan Sen. High prevalence of MDR MRSA in tertiary care hospital of Northern India. Infect Drug Resist: 2008;1:57-61.