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Original Research

Nasal Staphylococcus Carriage and Mupirocin-Methicillin Resistance Among Healthcare Workers in a Tertiary Care Hospital.

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Abstract
Background: Healthcare workers (HCWs) colonized with methicillin-resistant *Staphylococcus aureus* (MRSA) act as an important reservoir for nosocomial transmission. Mupirocin is widely used for nasal decolonization, but emerging resistance threatens its long-term value. *Objectives:* To determine the prevalence of nasal carriage of MRSA and of high-level (MuH) and low-level (MuL) mupirocin resistance among HCWs in a tertiary care hospital. *Methods:* A prospective study was conducted over one year among 300 HCWs (doctors, nurses, technicians, office and housekeeping staff) at BGS GIMS, Bangalore. Anterior nasal swabs were cultured on mannitol salt agar, blood agar, and nutrient agar, and *S. aureus* was identified by standard methods. Antibiotic susceptibility was tested by Kirby-Bauer disc diffusion per CLSI guidelines. MRSA was detected using cefoxitin disc diffusion and oxacillin MIC. Mupirocin resistance was determined using 5 µg and 200 µg discs to distinguish MuL from MuH resistance. *Results:* Coagulase-negative staphylococci (CoNS) predominated (75%), followed by *S. aureus* (15%); 9% showed no growth and 1% micrococci. Of 44 *S. aureus* isolates, 10 were MRSA, giving a nasal MRSA carriage rate of 3.33%, with carriage higher among nurses and doctors. *S. aureus* showed the greatest resistance to penicillin (75%) and amoxicillin-clavulanate (70.4%), and the least to linezolid (9%). Among the 10 MRSA isolates, 2 showed low-level mupirocin resistance and none showed high-level resistance; all 34 MSSA isolates were mupirocin-susceptible. Among 122 methicillin-resistant CoNS (MRCONS), 18 were MuH and 4 were MuL. *Conclusion:* Nasal MRSA carriage among HCWs was relatively low (3.33%) but concentrated among nurses and doctors. Mupirocin resistance in MRSA remained low; however, the substantial high-level resistance seen in MRCONS represents an expanding reservoir that could threaten future mupirocin efficacy. Judicious mupirocin use alongside robust infection-control measures is recommended.

Keywords: *MRSA; nasal carriage; healthcare workers; mupirocin resistance; coagulase-negative staphylococci; infection control.*

Introduction

MRSA is a major nosocomial pathogen that causes morbidity and mortality worldwide(1**)**.It has emerged as one of the commonest causes of hospital acquired infection and continues to remain an important factor contributing to failure of management(2**)** **.**Screening for and eradication of MRSA from colonized HCW have been recognised and recommended as an important part of a comprehensive infection control policy(3) .Several studies have identified anterior nares as the etiological niche of Staphylococcal aureus(4,5,6,7)

Staphylococcus resistance to methicillin demonstrated by MRSA strains implies resistance to all antibiotics belonging to the beta lactam group(8).The main concerns of MRSA is the limited number of therapeutic options to treat this infection. The major sources of MRSA in the hospital environment are asymptomatically colonized patients and healthcare workers.Healthcare workers act as links in the transmission of MRSA between patients(9).

In 1940s penicillin was the drug of choice for staphylococcal infections. Very soon resistance to penicillin was reported from various countries. Methicillin was introduced in 1959 to treat infections due to penicillin resistant staphylococcal aureus. Unfortunately in 1960 there was first report of methicillin resistance in Staphylococcus aureus(MRSA) from Europe(10)

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Infections caused by mrsa are associated with worse outcomes, in addition to prolonged hospital stays, higher costs of treatment and increased mortality(11).Nasal colonization with *S. aureus* has been linked to surgical-site infection [12], bloodstream infection [13], and ventilator-associated pneumonia [14]

Knowledge of prevalence of MRSA and its antimicrobial profile is necessary for selection of the appropriate empirical antimicrobial treatment for S.aureus infections(15) In particular, screening for and eradication of MRSA from colonized HCWs have been recognized and recommended as an important part of a comprehensive infection control policy for this organism.(16)

Mupirocin was introduced in clinical practise in 1985 in UK and the use of mupirocin ointment has been progressively increasing worldwide(17)Prolonged, widespread, uncontrolled use and multiple courses of mupirocin are all associated with the development of mupirocin resistance(11,18).

Mupirocin resistance is also common in MRSA and CONS than MSSA and CONS(.19).The first report on staph resistance to mupirocin came 2years after its introduction(20) .The increasing prevalence of MuH in CONS is an important threat to the future use of mupirocin against MRSA. There are no formally defined breakpoints for mupirocin susceptibility. Since mupirocin became available in the 1980s, 2 distinct forms of resistance have been described in association with *S. aureus* [21]. Low-level resistance is mediated by point mutations in the chromosomal *ileS* gene. High-level resistance to mupirocin is conferred by a novel gene, *mupA*, which encodes for an isoleucyl tRNA sythetase enzyme that is not susceptible to mupirocin and can be acquired through plasmid exchange [22].

MuH can be transferred from CONS to SA species. The emergence of MuH in CONS isolates indicates an expanding reservoir of plasmids encoding mupirocin resistance.(23) MuL nasal isolates can still be controlled with mupirocin therapy, as the ointment contains a much higher mupirocin concentration(200micro/ml) than the MuL MIC's, but MuH strains cannot be controlled with mupirocin ointment(24).The emergence of resistance to mupirocin has threatened its value as a nasal decolonizer and therapeutic agent(25,26)

A recent randomized trial of mupirocin use for MRSA decolonization reported a high rate (24%) of mupirocin resistance, emphasizing the need to test for mupirocin resistance before implementing routine mupirocin use.(27)
The present study is to determine MRSA and the prevalence of MUH and MUL among the healthcare workers in our hospital.

Materials and Methods

A prospective study was conducted among healthcare workers at Department of Microbiology, BGS GIMS, Bangalore, Karnataka over a period of 1 Year. The 300 healthcare workers in the study included were doctors, nursing staffs, technicians and class 4 workers .The procedures were explained to their satisfaction and a written consent was taken from all the healthcare workers included in the study. A proforma with age, sex ,department, health status and relevant data was prepared.

Healthcare workers with a history of upper respiratory tract infection, allergies, fever, recent nasal surgery, use of nasal medications and antimicrobial therapy, immunocompromised patients and those with diabetes were excluded from this study. The study was cleared by the institutional ethical committee.

Two samples were collected from the anterior nares using pre-moistened swabs. The swab was inserted into each nostril in turn to a depth of approximately 1cm and rotated 4-5 times both clockwise and counter clock wise. The swabs were immediately transported to microbiology laboratory for further processing. Specimens were inoculated onto Mannitol salt agar(selective media for Staphylococcus aureus),10% sheep Blood agar ,Nutrient agar and incubated for 24 hours at 37 c. Colonies of Staphylococcus aures were identified as per standard microbiological procedures. Isolates which were Beta haemolytic on blood agar, yellow colonies on mannitol salt agar, golden yellow pigment producing colonies on nutrient agar, gram positive cocci in clusters on gram stain, catalase positive, tube coagulase positive, mannitol fermenting were subjected to further processing.

Fig-1: Yellow colonies on mannitol salt agar.

Fig-2: Golden yellow colonies on nutrient agar

Fig-3: Coagulase positive, Mannitol fermented, Urease positive

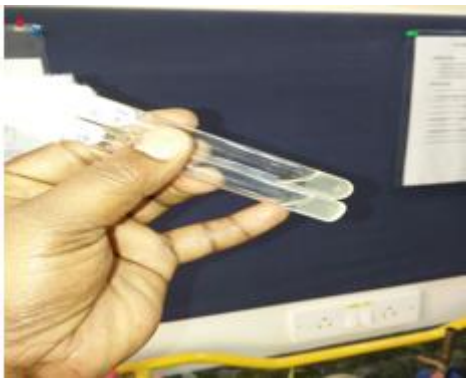
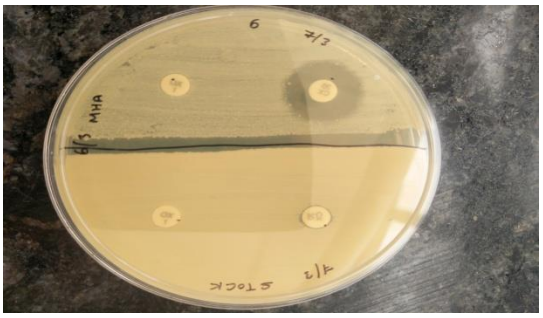


Fig-4: Cogulase positive staphylococcus aureus.

All the Staphylococcus aureus isolates were subjected to in vitro antibiotic susceptibility testing by Kirby Bauer disc diffusion method as per CLSI guidelines on Mueller-Hinton agar. The antibiotic discs used were penicillin (10units), cefoxitin (30mg), chloramphenicol (30mg), ciprofloxacin(5mg), clindamycin(2mg), amoxicillinclavulinicacid(30mg),doxycycline(30mg), erythromycin(15mg),gentamicin(10mg),linezolid(30mg) and vancomycin(30mg),teicoplanin(30mg).Zone diameters were interpreted a sensitive,intermediate and resistant as per CLSI guidelines(27).CLSI has recommended cefoxitin disc diffusion method for detection of MRSA.A 0.5 Mac Farland standard suspension of the isolate was prepared and lawn culture was done on Mueller Hinton agar plate.A cefoxitin disc(30mg) was placed on this plate and incubated at 37c for 18 hours.The zone diameter was measured.An inhibition zone of</= 21mm is considered as methicillin resistant and an inhibition zone of >/=22mm is considered as methicillin sensitive(27).



MIC for oxacillin was tested using Hi Comb MIC strip(Himedia,Mumbai) as shown in fig( ).The interpretive criteria for oxacillin MIC are MIC 2 <-mg is sensitive and MIC >-4mg is resistant(27).

Resistance to mupirocin was detected by Kirby Bauer using 5mg mupirocin discs(Himeda,Mumbai) and 200mg mupirocin discs.A zone diameter of >14mm for 5mg was considered to be susceptible to mupirocin.Isolates that showed a zone diameter of <14mm in 5mg disc and any zone with 200mg disc were considered to be mupirocin low-level resistant(MuL).Isolates with zone diameter <14mm with 5mg and no zone with 200mg disc were considered to be mupirocin high-level resistant(26,27**).**
Statistical analysis was done.

Results

A total of 300 healthcare workers nasal smears were sampled for the study .

Table 1: Sex distribution among the health care workers who were sampled.

Sex	Number (n=300)	Percentage (%)
Male	90	30
Female	210	70
Total	300	100

The above table shows the sex distribution among the health care workers who were sampled of which males were 90/300 ie30% and females were 210/300 ie 70% with a male to female ratio of 3:7.

Table 2: Age distribution among the health care workers who were sampled.		
Age Group	**Total Number (n=300)**	**Percentage (%)**
11 - 20 years	12	4.0
21 - 30 years	126	42.0
31 - 40 years	97	32.3
41 - 50 years	45	15.0
> 50 years	20	6.6
Total	300	100

The highest number of healthcare workers were in the age group of 21-30 years(126,42%) followed by 31-40 years age group(97,32.3%).41-50years age group was 45,15% and 11-20 and >50years age group were 12,4% and 20,6.6% respectively.

Table 3: Distribution of health care workers who were sampled.		
ategory	**Total Number (n=300)**	**Percentage (%)**
Doctors	105	35.0
Nurses	59	19.6
Technicians	21	7.0
Office staff	19	6.3
House keeping	96	32.0
Total	300	100

Among the health care workers who were sampled 105,35% were doctors followed by housekeeping staff who were 96,32%.Nurses formed 59,19.6% followed by technicians21,7% and office staff were 19,6.3%.

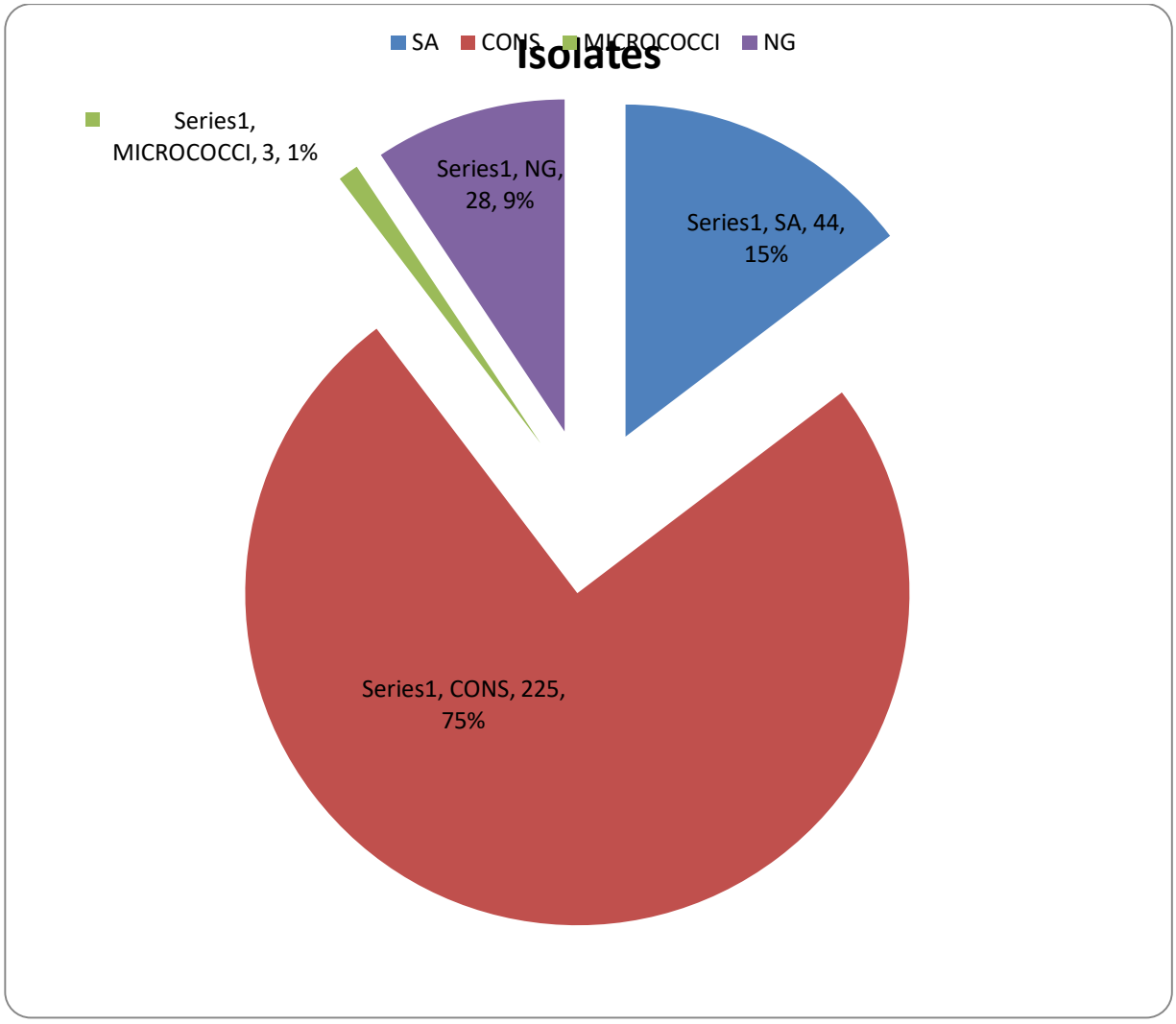


Fig-3:The figure represents coagulase negative staphylococcus isolates were75%,staphylococcus aureus were 15%,no growth were 9% and micrococci was 1%

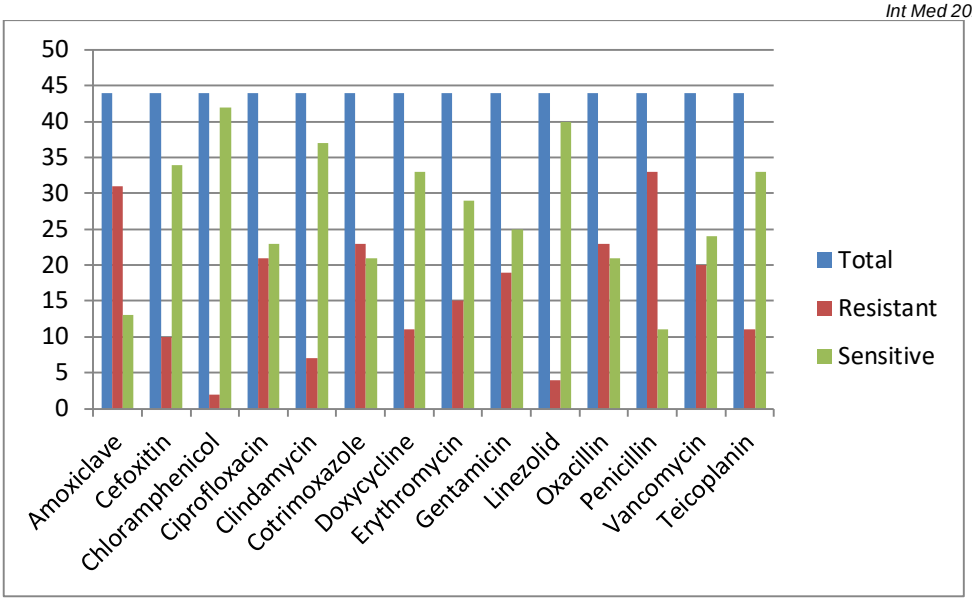


Fig-4: Antibiotic sensitivity pattern of the 44 staphylococcus aureus isolates showed 75%resistance to penicillin,70.4% were resistant to amoxiclav,52.4% to cotrimoxazole and oxacillin,47.7% were resistant to ciprofloxacin,45.4% were resistant to vancomycin,43.1% were resistant to gentamicin,34%were resistant to erythromycin,25% were resistant to doxycycline,22.7 were resistant to cefoxitin,25% were resistant to teicoplanin,15.9% were resistant to clindamicin and 9% to linezolid.

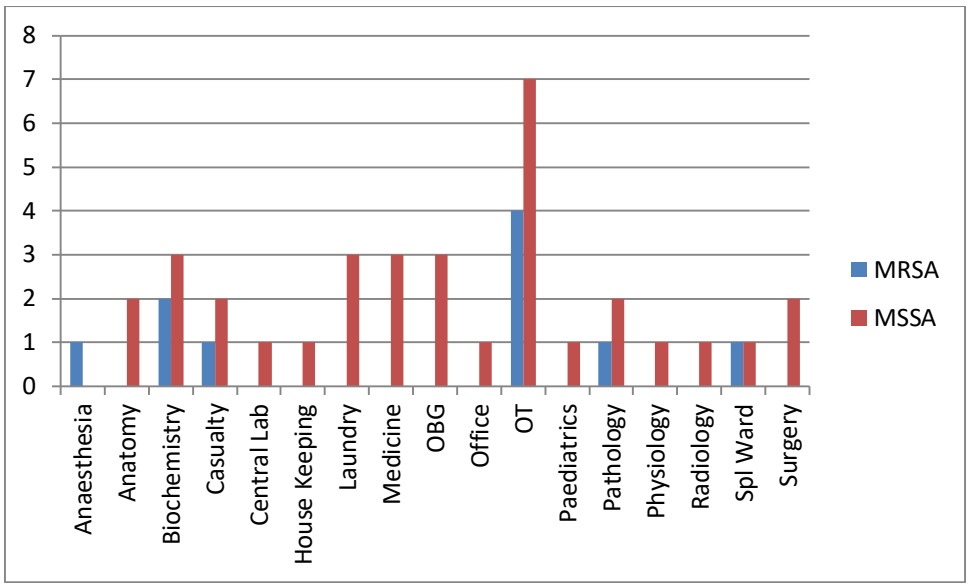


Fig-5: The various wards from departments from which MSSA and MRSA were isolated is shown in Fig-5.4MRSA carriers were from labour ot,2 were from biochemistry and 1 each from anesthesia,pathology,casuality and special ward.

Table 6: High and Low level Mupirocin resistance among Methicillin resistant Staphylococcus aureus			
Total No. Of MRSA	Mupirocin resistant		Mupirocin sensitive
	High level resistance	Low level resistance	
10	0	2	8

Among the 10 MRSA isolates 8were mupirocin sensitive and 2 showed low level mupirocin resistance. There were no high level mupirocin resistant MRSA isolates.

Table 7: High and Low level Mupirocin resistance among Methicillin sensitive Staphylococcus aureus			
Total No. Of MSSA	Mupirocin resistant		Mupirocin sensitive
	High level resistance	Low level resistance	
34	0	0	34

Out of 34 MSSA isolates, all were mupirocin sensitive.

Table 8: High and Low level Mupirocin resistance among Methicillin resistant coagulase negative Staphylococcus species			
Total No. Of MRCONS	Mupirocin resistant		Mupirocin sensitive
	High level resistance	Low level resistance	
122	18	4	100

Among 122 MRCONS,18 were Mup-H and 4 were Mup-L and 100 isolates were Mup-Sensitive.

Discussion

Present study was conducted on 300 healthcare workers to know the prevalence of nasal carriage of MRSA and Mupirocin resistant MRSA isolates in a tertiary care hospital. According to Mathenraj et al,the rate of colonization of MRSA was 1.8% among healthcare workers(9).This is in correlation with the study by Kausalya et al the rate of colonization was 1.33%.In our present study the rate was 3.33% .But in a study done by Bala et al, the rate of colonization was found to be 37.5%.this is high compared to the above studies.

Among the 3.33% of MRSA carriers,4.2% were females and 1.1% were males,but according to Mathanraj et al,male carriers were more common than female carriers.This is in accordance with the study by Kausalya et al where male carrier was 3.37% and female carriers were0.47%.(29).This disparity could be due to the fact that female employees were more in comparison to male employees in our institute.

Among the professional category, according to the study by Radhakrishna M et al(30),the Staphylococcus aureus nasal carriage was particularly high among doctors(32.5%) and housekeeping personnel(26.7%),followed by nursing staff(13.6%). In our study 4 doctors ,5 nurses and 1 housekeeping were MRSA carriers.Our study showed that nasal carriage of MRSA among nurses were higher compared to doctors which is in accordance to the study by Nabi Abdulla el aila et al where the MRSA carriage among the nurses were high(30.4%) followed by doctors(16%) This finding could be explained by the increased physical contact of nurses and doctors with patients(3).

Among the total 10 MRSA isolates,8 were mupirocin sensitive and 2 were mupirocin lowlevel resistant and there were no mupirocin high level resistant isolate.IN a study by Schmitz et al mupirocin low level resistant MRSA isolates were 2 and high level MRSA isolates were 1(31).in Oomen et al (32)and Jaykumar et al(33) the incidence of MUPLR was 0 and MUPHR were 1 and 1 respectively.

It has been suggested that MuL nasal isolates can still be controlled with mupirocin therapy,as the ointment contains a much higher mupirocin concentration(200micrgram/ml) than MuL MIC's,but MuH strains cannot be controlled with mupirocin ointment(34).

Conclusion

Nasal carriage of MRSA is relatively low in our hospital but high among nurses and doctors in comparison to other HCW.This shows that with appropriate implementation of HIC programmes this threat of MRSA among HCW can be brought under control.Overall mupirocin resitance in MRSA species is still low,still a judicious use of mupirocin is recommended to keep the resistance at a bare minimum.

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