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# ANTIMICROBIAL RESISTANCE PATTERN OF STAPHYLOCOCCUS AUREUS AMONG HEALTHCARE WORKERS AT TERTIARY CARE HOSPITAL WITH SPECIAL REFERENCE TO METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS AND VANCOMYCIN RESISTANT STAPHYLOCOCCUS AUREUS

Microbiology

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KEYWORDS

## INTRODUCTION

Hospital acquired infections (HAI) represent a significant epidemiological threat in both developed and developing countries. The Centers for Disease Control (CDC) estimates that HAIs account for an estimated 1.7 million **infections** and 99,000 **associated** deaths each year. Though these can be caused by many gram positive and gram negative organisms present in hospital environment, but predominant organism are: *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumonia, Acinetobacter baumanii, Pseudomonas aeruginosa and Enterobacter* sp. Out of these *Staphylococcus aureus* is one of the principal human pathogens that colonizes healthy individuals as well as causes infections in hospitalized patients, especially in high risk areas like Intensive Care Units (ICUs), Paediatric Intensive Care Units (PICUs), burn wards and surgical post operative wards.[1]

Direct contact is undoubtedly the main means of transmission of hospital infections. Colonization of *Staphylococcus aureus* which is capable of causing a wide range of infections, ranging from mild skin and soft tissue infections to serious life threatening infections, has long been recognized as a major risk factor of hospital acquired infection.[2] Infected and colonized inpatients appear to be the major institutional reservoir, and transient carriage on the hands of healthcare workers appears to be the most important mechanism of serial patient to patient transmission; [3] airborne dispersal and transmission through contacts with contaminated surfaces may also be important. [4]

Infections with Staphylococcus aureus have increased in the past 20 years, and the rise in incidence has been accompanied by a rise in antibiotic-resistant strains particularly, methicillin resistant Staphylococcus aureus (MRSA) and, more recently, vancomycin resistant strains. Risk factors for MRSA carriage include-cutaneous lesions or conditions, sinusitis and rhinitis, chronic otitis external and ear lobe dermatitis, recent urinary tract infection, cystic fibrosis and recent antibiotic intake. Poor infection control practices are implicated in acquisition and transmission of MRSA by staff.[5]

Health-care workers (HCWs) and asymptomatically colonized patients are the major sources of MRSA in the hospital environment. They comprise an important source of hospital acquired infection and its dispersal both in the hospital and in the community. The estimation of MRSA colonization in HCWs can vary widely, depends on country, hospital specialty and setting.

Vancomycin has been used as the drug of choice for methicillin resistant *S. aureus* (MRSA) infections. The rate of infections caused by MRSA has been steadily on the rise worldwide and as a result the consumption of vancomycin has also increased. VRSA carriage is extremely rare and there are reports of only a handful of cases worldwide. Therefore, finding even a handful of cases of VRSA at our hospitals would be an alarming discovery Various strategies exist in controlling the spread of MRSA and VRSA with in healthcare settings. Preventive measures include laboratory surveillance and screening for MRSA, promoting careful hand washing with soap and water rather than antibacterial gels in common use, gowning and gloving by the staff and eradication of MRSA from colonized people.

## MATERIALS AND METHOD

### Study design and settings

A prospective, cross-sectional study was carried out in the Department of Microbiology, Government Medical College, Amritsar, Punjab from January 2019 to November 2020. A total of 250 nursing staff, doctors and housemen/housewomen were included after taking informed written concent and approval from institution ethical committee.

Nasal swabs and hand swabs were collected from HCW's. These swabs were streaked on Mannitol salt agar and blood agar and kept for incubation at 37°C for 24 h. Identification of *S. aureus* was done by standard microbiological procedures. Antimicrobial susceptibility testing of S. aureus isolates was performed by the Kirby-Bauer disk diffusion method as per the CLSI recommendations.[6] The Antibiotic Disc of Ampicillin(10µg), gentamycin(10µg), Amikacin(30µg), cefoxitin(30µg), ciprofloxacin(5µg), teicoplanin(30µg), linezolid(30µg), erythromycin(15µg) and clindamycin(2µg) were placed at recommended distance. All cultured plates were aerobically incubated at 37°C for 24 hours before the zone sizes were recorded.

### Detection of MRSA

Methicillin resistance was determined using cefoxitin 30µg disks using modified Kirby Bauer Disc Diffusion Method on Muller Hinton agar. Isolates which showed cefoxitin disk inhibition zone sized of diameter less than or equal to 21mm were considered as MRSA strains as per CLSI guidelines.[7]

Break points for detection of Methicillin resistance by CLSI

| | Resistant (mm or less) | Intermediate (mm) | Sensitive (mm or more) |
|---|---|---|---|
| *S. aureus* | 21 | -------- | 22 |
| CONS | 24 | -------- | 25 |

### Detection of VRSA

All the strains were tested for Vancomycin resistance by broth macrodilution method and Epsilometer test.

MIC Break points for detection of Vancomycin resistance by CLSI

| Strain | Vancomycin MIC |
|---|---|
| VSSA (Vancomycin sensitive *S. aureus*) | ≤2µg/ml |
| VISA (Vancomycin intermediate resistant *S. aureus*) | 4-8µg/ml |
| VRSA (Vancomycin Resistant *S. aureus*) | ≥16µg/ml |

### D- test for screening of inducible clindamycin resistance

Clindamycin (2ug) and Erythromycin (15ug) antimicrobial disks were placed at a distance of 15mm (edge to edge) from each other. Following overnight incubation at 37°C, a D-shape zone around the clindamycin in the area between the two disks, the isolate was positive for inducible resistance.

S. aureus ATCC 25923, MRSA ATCC 29213 and MSSA ATCC 33591 are used as control strain during antibiotic susceptibility testing.

## RESULT

Out of 250 HCWs included in the study,57.6% were doctors followed by36% nurses and 6.4%housemen/housewomen. 54.4%of them were in the age group of 21-30 with mean age of 31.93±8.49 years and 69.6% were females. Maximum of HCWs were working in wards (67.2%) followed by ICU (20.4%) , labour room and operation theaters (8%), and emergency (4.4%). Maximum of HCWs were from the medicine department (22%), followed by anaesthesia (20.8%) and others.

113 (45.2%) Staphylococcal isolates were obtained from samples of 250 healthcare workers screened. Out of 113 Staphylococcal isolates, 49(19.6%) were identified as Staphylococcal aureus and 64 (25.6%)were coagulase negative staphylococci (CONS). Out of 49 Staphylococcus aureus, 22 (44.2%) were MRSA (FIG 1).

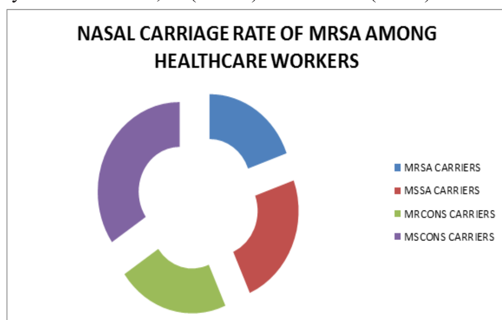


**FIG 1**

The nasal carriage of MRSA among HCWs was 8.8% (22/250). In our study, highest carriage of MRSA was found among the subjects working in Emergency (18.18%) followed by ICU (15.6%), and Wards (7.14%). Maximum MRSA positives were the Housemen/ housewomen i.e. 12.5%, followed by nurses (10%) and doctors (7.63%) for MRSA.

**Table 15:- Antibiotic Senstivity Of Methicillin Resistant Staphylococcus Aureus And Methicillin Sensitive Staphylococcus Aureus**

| ANTIBIOTIC | MRSA (n=22) | %AGE of MRSA | MSSA (n=27) | %AGE of MSSA | P -VALUE |
|---|---|---|---|---|---|
| Ampicillin | 0 | 0 | 8 | 29.62% | 0.005* |
| Erythromycin | 5 | 22.72% | 13 | 48.14% | 0.066; NS |
| Gentamycin | 20 | 90.9% | 26 | 96.29% | 0.434; NS |
| Amikacin | 20 | 90.9% | 23 | 85.18% | 0.543; NS |
| Clindamycin | 11 | 50% | 16 | 59.25% | 0.517; NS |
| Ciprofloxacin | 13 | 59% | 14 | 51.85% | 0.612; NS |
| Teicoplanin | 22 | 100% | 27 | 100% | - |
| Linezolid | 22 | 100% | 27 | 100% | - |
| Vancomycin | 22 | 100% | 27 | 100% | - |

NS: p > 0.05; Not significant; *p<0.05; Significant

Antibiotic susceptibility pattern of MRSA showed that Vancomycin, linezolid and teicoplanin was 100% sensitive, followed by Amikacin 90.9% and Gentamycin 90.9%, Ciprofloxacin 59%, Clindamycin 50% and erythromycin 22.72%. No isolate was sensitive to ampicillin. All the MRSA and MSSA isolates were 100% sensitive to vancomycin, Linezolid and Teicoplanin. MSSA isolates were more sensitive to amikacin and ciprofloxacin as compared to MRSA isolates.

In our study the overall Inducible Clindamycin Resistance was seen in 15.04% with 18.3% of *Staphylococcus aureus* and 12.5% of CoNS isolates showing inducible clindamycin resistance.

Sample collected from hands of healthcare workers showed 24.8% (62/250) culture positivity. Out of the 62 organisms identified, the predominat pathogenic organism was Staphylococcus aueus (19.35%), followed by, Coagulase negative staphylococci (17.74%), Escherichia coli (12.90%) Klebsiella (11.29%), Pseudomonas (4.83%), Acinetobacter (4.83%) and Candida(4.83%).

**ANTIBIOTIC SENSITIVITY PATTERN OF THE BACTERIAL ISOLATED FROM HANDS**

| ANTIBIOTIC | S. AUREUS (n=12) | CoNS (n=11) | E. COLI (n=8) | KLEBSIELLA PNEUMONIA (n=7) | PSEUDOMONAS AERUGINOSA (n=3) | ACINETOBACTER BAUMANI (n=3) |
|---|---|---|---|---|---|---|
| **Ampicillin** | 6(50%) | 3(27.27%) | 4(50%) | 3(42.8%) | - | - |
| **Erythromycin** | 8(66.6%) | 5(45.45%) | - | - | - | - |
| **Gentamycin** | 9(75%) | 9(81.81%) | 6(75%) | 5(71.4%) | 2(66.66%) | 2(66.66%) |
| **Amikacin** | 8(66.6%) | 8(72.72%) | 7(87.5%) | 6(85.7%) | 2(66.66%) | 2(66.66%) |
| **Clindamycin** | 6 (50%) | 5(45.45%) | - | - | - | - |
| **Ciprofloxacin** | 6 (50%) | 6(54.54%) | 5(62.5%) | 6(85.7%) | 1(33.33%) | 2(66.66%) |
| **Teicoplanin** | 12 (100%) | 11(100%) | - | - | - | - |
| **Linezolid** | 12 (100%) | 11(100%) | - | - | - | - |
| **Cefoxitin** | 7(58.3%) | 8(72.72%) | - | - | - | - |
| **Vancomycin** | 12(100%) | 11(100%) | - | - | - | - |
| **Piperacillin-tazobactam** | - | - | 8(100%) | 76(100%) | 3(100%) | 3(100%) |
| **Imipenem** | - | - | 8(100%) | 7(100%) | 3(100%) | 3(100%) |

## DISCUSSION

The recent years have witnessed an increase in resistance of *Staphylococcus aureus* to many antimicrobial agents. MRSA has remained a major cause of nosocomial disease worldwide, including India. Person to person spread of MRSA is traditionally associated within hospital facilities. The present study was conducted on 250 healthcare workers who were in close contact with the admitted patients, with the aim of determining the carriage of MRSA and VRSA among healthcare workers and also to study the antibiotic susceptibility profile of all the staphylococcal isolates.

In the present study, 45.2% staphylococcal nasal carriage among health care personnel was observed. Similar study done by *Gupta et al* showed carriage rate of 51% which is in accordance to our study.[8] The higher carriage rate among active health care workers predispose for direct transmission to the patients. Being anterior nares carriage, they are easily transmitted by coughing, sneezing, even through the hands.

Carriage of Staphylococcal aureus from anterior nares in the present study was found to be 19.6%. Khaililie *et* al have reported a lower nasal carriage rate of 12.67%.[9] Similarly Rita Khanal *et al* studied nasal carriage of methicillin resistant Staphylococcus aureus among HCW's at a tertiary care hospital in Western Nepal and found the carriage rate of Staphylococcus aureus to be 15.7%.[10]

In our study, the carriage of MRSA among HCW's was 8.8% which was comparable to study done by Rakhi Dixit*et al* and Goyal *et al*.[11,12]

As the emergency department is a site of high healthcare worker–patient contact, high patient turnover, potentially substantial crowding, and many infected patient wounds that are being drained, explored, and dressed. In our study highest carriage of MRSA was found among subjects working in emergency (18.18%) followed by ICU (15.6%) and wards (7.14%), which was in concordance to study done by Khatri *et al*, showed MRSA carriage among HCW's to be 12.5% from emergency.[13]

Housemen/housewomen were harbouring maximum MRSA (12.5%) followed by nurses (10%) and doctors (7.63%) which was similar to study done by Verwers *et al*.[14]

In our study, Antibiotic susceptibility pattern of MRSA showed that Vancomycin, linezolid and teicoplanin was 100% sensitive, followed by Amikacin 90.9% and Gentamycin 90.9%, Ciprofloxacin 59%, Clindamycin 50%. No isolate was sensitive to ampicillin. A study by Salim *et al* and Fomda *et al* reported that all MRSA isolates were 100% resistant to ampicillin[15,16]. Erythromycin proved to be 22.72% sensitive in MRSA isolates in our study. A sensitivity ranging from 20 to 30% was reported in other studies.[17,18,19] The high level of resistance

to ampicillin and erythromycin could be due to their easy availability, indiscriminate and uncontrolled usage. 100% sensitivity to Vancomycin, teicoplanin and linezolid in our study was similar to the findings of Adwan *et al*.[20] All the MRSA isolates in our study showed 90.9% sensitivity to amikacin and gentamycin comparable to study by Ansari *et al* and Prates *et al*.[21]

In our study, MSSA isolates were more sensitive to amikacin and ciprofloxacin as compared to MRSA isolates. This was in agreement with the studies conducted by Askarian *et al* and Vidhani *et al*.[22,17]

Inducible clindamycin resistance in our study was found to be 15.04% which was similar to study conducted by AM Ciraj *et al* showed 13.11% of ICT.[23] In our study Among Staphylococus aureus and Coagulase Negative Staphylococci, ICT was 18.3% and 12.5% respectively comparable to study conducted by Mahesh C B *et al.*[24]

Sample collected from hands of healthcare workers showed 24.8% culture positivity which in concordance with the study conducted by Ranweer *et al* in Ajmer which also showed 26% culture positivity.[25] Various studies have shown contamination of the hands of HCWs ranging from 3.78% to 25%.[26,27,28] Low culture positivity from the hands of HCW s in our study as compared to various studies can be explained by good hand hygiene practices of HCW s in our hospital and due to samples taken during period of COVID-19 where hand sanitization of HCW s was more frequently and thoroughly done.

## CONCLUSION

Present study highlighted increase incidence of multidrug isolates among healthcare workers. Routinely screening of HCWs for MRSA carriage may help in reduction of MRSA prevalence in patients, decreased risk of spread to close contacts, reduction of glycopeptides use and long term cost savings. So it should be monitored as a routine protocol in medical colleges to prevent spread of resistant strains from hospital to patients. Hand washing and decolonization of MRSA carriers are effective measures to reduce the incidence of MRSA infections in health care settings.

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