Indian Journal of Basic and Applied Medical Research; March 2020: Vol.-9, Issue- 2. P. 254 - 261
DOI: 10.36848/IJBAMR/2020/12215.51345

Original article

Study of MRSA in tertiary hospital, Intensive Care Unit

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ABSTRACT:

Introduction: Due to development of methicillin resistant *S.aureus* (MRSA), treatment of community and hospital-acquired infections has become problematic. Indiscriminate use of multiple antibiotics, prolonged hospital stay, intravenous drug abuse, carriage of MRSA in nose are important risk factors. Currently, treatment options for MRSA are limited to very few and expensive drugs like Teicoplanin and Vancomycin.

Material and methods: This study was done in Intensive Care Unit of Wanless Hospital, Miraj. We recorded demographic characteristics and data regarding current and previous hospital admissions in 40 patients. Relevant samples were collected for culture and antimicrobial sensitivity testing. Patients were managed as per standard treatment protocols. Changes were made as per results of AST patterns. Hospital stay and outcome of each patient was noted.

Results: Majority of study population were aged from 51-60 years (33.3%), with male predominance (73.4%). Previous history of hospitalization was observed in 13.33%. Prevalence of MRSA was 33.3%. MRSA was isolated from Clinical specimen in 82.35% and from Screening sample in 17.64%. MRSA was sensitive to Penicillin, Ampicillin, Erythromycin, Imipenem and Vancomycin in 8.2%, 3.4%, 5.1%, 38.1% and 26.9% cases respectively. MRSA was mostly isolated from Throat swabs (56%) followed by Blood (51%). 35% had history of previous broad spectrum antibiotics. Prevalence of MRSA was observed most in 41-50 years (50%) followed by 51-60 years (31%) and above 70 years (19%). The difference was statistically significant. Prevalence of MRSA was significantly more in females (56.25%) as compared to males (43.75%). MRSA prevalence was higher in previously hospitalized patients (25%) though statistically insignificant. Prevalence of MRSA was significantly higher in patients with Previous history of intake of broad spectrum antibiotics (75%).

Conclusion: Theoretically, Vancomycin is still the drug of choice for MRSA. But our study shows increasing resistance of MRSA to Vancomycin also. We recommend frequent monitoring of susceptibility patterns of MRSA and formulation of a definite antibiotic policy, which may help in decreasing incidence of MRSA infection.

Keywords: MRSA, ICU, MANAGEMENT

INTRODUCTION

Methicillin resistant *Staphylococcus aureus* (MRSA) is endemic in India and is a dangerous pathogen for hospital acquired infections. It is a common problem in health care facilities, sports facilities, clinics, and the community worldwide. It causes significant morbidity and mortality[1] with elevated health care costs and an increased financial burden on society. [2] The prevalence of MRSA has increased over the last 10 years; Infections caused by MRSA are associated with longer hospital stays.[3,4]

The MRSA strains associated with hospitals are referred to as *hospital-acquired MRSA* (HA-MRSA) and are the most common cause of hospital-acquired infections.[2, 4, 5, 6] MRSA is the leading cause of skin and soft tissue infection in patients reporting to emergency departments for treatment,[7] with a rising rate in primary care clinics [8] and intensive care units.[4] Invasive MRSA-related conditions most commonly reported include septic shock (56%), pneumonia (32%), endocarditis (19%), bacteremia (10%), and cellulitis (6%).[1] Strains associated with the community are referred to as *community-acquired MRSA* (CA-MRSA) and are also present in people who serve as asymptomatic carriers.[9]

Hospital-acquired MRSA has a high prevalence in Australia,[10] North Africa, the Middle East, and East Asia [3] and has been reported in 25% or more. Methicillin was first introduced in 1959−1960, and, within a year, methicillin-resistant isolates were reported [11]. Methicillin resistance is conferred by the *mecA* gene, which encodes a penicillin-binding protein (PBP2A) with decreased affinity for *β*-lactam antibiotics. *mecA* is part of a mobile genetic element called the "staphylococcal cassette chromosome (SCC) *mec*." SCC*mec* is flanked by cassette chromosome recombinase genes (*ccrA*/*ccrB* or *ccrC*) that permit intra- and interspecies horizontal transmission of SCC*mec*. The initial reservoir of SCC*mec* is unclear but may have been a coagulase-negative staphylococcal species .[12-14]

AIMS AND OBJECTIVES

1. To study the prevalence of MRSA among patients admitted in Medical ICU.
2. To study antibiotic sensitivity pattern among MRSA isolates.
3. To study the short term outcome among these patients.

MATERIAL AND METHODS

This prospective, observational study was conducted over two years (from September 2017 - September 2019) in the Department of Medicine at Wanless Hospital, Miraj, Maharashtra, which is a 450-bedded tertiary care centre. 40 patients above 18 years of age from both genders with clinical suspicion of hospital acquired infection were included in this study after taking written, informed consent. Patients aged below 18 years and those with MRSA infection at the time of admission to hospital were excluded.

Based on the previous literature, the prevalence of admitted patients acquiring MRSA was approx. 11% [*Ahmad S et al. Prevalence of Methicillin-Resistant Staphylococcus Aureus (MRSA) in Intensive Care Unit of CPEIC, Multan. Medical forum monthly. 2018*]. Sample size was calculated using formulae:

$$\mathbf{n = Z_{\alpha}^2\ (5\%)\ p\ (1\text{-}p)\ /\ E^2}$$

where n=sample size

Z = Level of significance (at 95% confidence level, its value is 1.96)

P = probability (0.11)

Q = 1-p (1-0.11=0.89)

E= Absolute error (taken as 10%)

$n = (1.96)^2 * (0.11)* (0.89) / (0.1)^2$

n =40 (approx.)

So, final sample size was taken as 40 suspected cases of MRSA, admitted in Intensive Care Unit of our hospital.

We recorded demographic characteristics (age and sex), previous hospital stays, history of surgery or antimicrobial therapy, date of hospital admission, date of ICU admission, severity at ICU admission, presence at ICU admission of breaks in the skin and history of invasive procedures.

Blood samples were collected for culture and antimicrobial sensitivity (AST) patterns from all suspected patients. The patients were managed as per standard treatment protocols followed at our hospital. Changes were made as per results of AST patterns. The hospital stay and outcome of each patient was noted.

Samples for MRSA isolation were collected both by conventional methods, as well as by automation for sterile body fluid in BACT/ALERT 3D. All samples that were collected were routinely cultured on Blood Agar, McConkey's Agar and Nutrient Agar. Identification of bacteria and antibiotic sensitivity testing (MIC) was done by VITEK-Z compact which helped in detection of B-lactamase production, Oxacillin screening for MRSA as well as obtaining the MIC for Cefoxitin.

All the collected data was entered in Microsoft Excel sheet and then transferred to SPSS software ver. 22 for analysis. Qualitative data was presented as frequency and percentages and analyzed using chi-square test.

RESULTS

Most of the study population belongs to the age group of 51 to 60 years (33.3%) followed by 41 to 50 years (26.7%), 61 to 70 years (26.6%) and more than 70 years (13.4%). There was male predominance (73.4%) amongst study population as compared to females (26.6%). Previous history of hospitalization was observed in 13.33% of study population. Prevalence of MRSA was 33.3 % amongst study population. MRSA was isolated from Clinical specimen in 82.35% of study population and from Screening sample in 17.64%. MRSA was sensitive to Penicillin, Ampicillin, Erythromycin, Imipenem and Vancomycin in 8.2%, 3.4%, 5.1%, 38.2% and 26.9% of study population respectively. MRSA was most commonly isolated from Throat swabs in 56%, followed by Blood in 51%, Sputum in 44%, Urine in 39% and pus in 25%. Previous history of intake of broad spectrum of antibiotics was observed in 35% of study population. Prevalence of MRSA was observed most commonly in 41 to 50 years (50%) followed by 51 to 60 years (31%) and more than 70 years (19%) and the difference was statistically significant. Prevalence of MRSA was observed most commonly in female (56.25%) as compared to males (43.75%) and the difference was statistically significant. Prevalence of MRSA was higher in patients with previous history of hospitalization (25%) though statistically insignificant. Prevalence of MRSA was significantly higher in patients with Previous history of intake of broad spectrum of antibiotics (75%).

DISCUSSION

Methicillin, the first β-lactamase stable semi-synthetic penicillin, was introduced in 1960.[15] MRSA was detected soon after methicillin came into clinical use in 1961.[16] Mucin appears to be the critical surface that is colonized in a process involving interactions between staphylococcal protein and mucin carbohydrate.[17]

Many of these MRSA isolates are becoming multidrug resistant and are susceptible only to glycopeptide antibiotics such as vancomycin.[18] Low level resistance even to vancomycin is emerging at present.[19] The prolonged hospital stay, indiscriminate use of antibiotics, lack of awareness, receipt of antibiotics before coming to the hospital etc. are the possible predisposing factors of MRSA emergence.[20] Serious endemic and epidemic MRSA infections occur globally as infected and colonized patients in hospitals mediate the dissemination of these isolates and hospital staff assists further transmission. [21] The development of resistance to multiple antibiotics and control of disease transmission by MRSA isolates in hospitals/communities have been recognized as the major challenges as the bacterial population that expresses the resistance phenotype varies according to the environmental conditions. [22]

In the present study, most of the study population belongs to the age group of 51 to 60 years (33.3%) followed by 41 to 50 years (26.7%), 61 to 70 years (26.6%) and more than 70 years (13.4%). In the present study,

prevalence of MRSA was observed most commonly in 41 to 50 years (50%) followed by 51 to 60 years (31%) and more than 70 years (19%) and the difference was statistically significant. Similar study conducted by Dechen C Tsering et al., reported that Extremely significant higher MRSA positive cases was observed from ages less than 30 years. [23]

In the present study, there was male predominance (73.4%) amongst study population as compared to females(26.6%). In the present study, prevalence of MRSA was observed most commonly in female (56.25%) as compared to males (43.75%) and the difference was statistically significant.

In the present study, previous history of hospitalization was observed in 13.33% of study population. In the present study, prevalence of MRSA was higher in patients with previous history of hospitalization (25%) though statistically insignificant. Similar study conducted by Dechen C Tsering et al., reported that there was no significant difference of MRSA positivity with a previous history of hospitalization.[23]

In the present study, prevalence of MRSA was 33.3 % amongst study population. This findings was in agreement with the study conducted by Dechen C Tsering et al., in which prevalence of MRSA was 52 % amongst study population. The overall MRSA prevalence in our study was 42 per cent in 2008 and 40 per cent in 2009.[23] The prevalence of MRSA in a study by Gopalakrishnan R et al., reported as 40-50 per cent. *S. aureus* constituted 17 per cent of catheter related blood stream infections (CRBSIs) in that centre.[24] A high prevalence of MRSA (35% in ward and 43% in ICU) was observed from blood culture specimens in a study by Wattal C et al.[25] In the present study, MRSA isolation rates from ICU and wards were higher than that seen among outpatients. Patel *et al* reported a change in the blood stream infections with *S. aureus* emerging as the predominant pathogen in recent years.[26] In a study by Arora S et al., the prevalence of MRSA was 46 per cent and MRSA isolates were found to be more resistant to other antibiotics than MSSA. Significant difference was observed in case of erythromycin, ciprofloxacin, gentamicin and amikacin.[27]

In the present study, MRSA was isolated from Clinical specimen in 82.35% of study population .and from Screening sample in 17.64%.This findings was in agreement with the study conducted by Dechen C Tsering et al., in which 111 (38.14%) MRSA from 291 S. aureus from 827 clinical specimens and 41 (20.92%) MRSA were isolated from 196 carrier screening samples. The prevalence of MRSA was significantly different among various clinical specimens. [23]

In the present study, MRSA was sensitive to Penicillin, Ampicillin, Erythromycin, Imipenem and Vancomycin in 8.2%, 3.4%, 5.1%, 38.1% and 26.9 % of study population respectively. These findings were in agreement with the study conducted by Dechen C Tsering et al., in which among 111 (38.14%) MRSA screened from clinical specimens, 7.22% were sensitive to Penicillin, 4.81% to Ampicillin, 4.12% to Erythromycin, 35.40% to Imipenem, and 20.27% to Vancomycin. The resistance pattern was very high for Vancomycin which was an alarming finding. However , from 41 (20.92%) MRSA screened from carriers all were sensitive to Vancomycin and Imipenem.[23] Similarly in the study by Rajaduraipandi K et al reported that out of 906 strains of S. aureus isolated from clinical samples, 250 (31.1%) were found to be methicillin resistant. However , all strains of clinical and carrier subjects were sensitive to Vancomycin.[28] A Sachdev D et al., reported that the incidence of MRSA was 15.87%. All the MRSA strains isolated, however, were found to be sensitive to Vancomycin.[29] Researchers in other part of the globe also observed that many of these MRSA isolates were becoming multidrug resistant and were susceptible only to glycopeptide antibiotics such as Vancomycin. Low level resistance even to vancomycin was emerging. [19]

Similarly in the study conducted by K Rajaduraipandi et al., reported that almost all the 250 MRSA strains (99.6%) screened from clinical specimens were resistant to Penicillin, 93.2% to Ampicillin, 63.2% to Co-trimoxazole, 62% to Gentamicin, 60.8% to Cephalexin and 60.0% to Erythromycin. However, all (100%) MRSA strains recorded sensitivity to Vancomycin, which was followed by 97.6% to Linezolid. In general, all MRSA strains were resistant to 8.0 ± 0.3 drugs, in which 63.6% isolates proved multidrug resistance. Higher percentage of intermediate resistance was noted against antibiotics such as erythromycin, Ofloxacin, amikacin, cephotaxime and ciprofloxacin. [28]

Majumder et al., from Assam had reported 23.2% of the MRSA isolated from clinical specimens to be multidrug resistant.[30] Anupurba from Uttarpradesh had reported a higher percentage of multidrug resistant MRSA. [20] Vidhani from Delhi reported even a higher percentage of multidrug MRSA but from high risk patients admitted in burns and orthopedic units.[31]

Similarly Umashankar Nagaraju et al., observed a high rate of resistance to commonly used antimicrobials, such as penicillin, erythromycin, and co-trimoxazole even in MSSA isolates.[32] Similar findings of high resistance to commonly used antimicrobials in MSSA isolates has been reported from North India by Sardana *et al*. MDR *S. aureus* was observed in 13.98% patients, which is similar to another study which reported it to be 16.9%.[33]Antimicrobial resistance is an unavoidable consequence of the selective pressure of antimicrobial exposure. [34] Indiscriminate use and over-counter availability of different antibiotics may be the reason for such a high resistance in these MSSA isolates. Infection with drug-resistant bacteria is favored by drug abuse, underlying illness, and previous hospitalization and antimicrobial treatment.

In the present study, MRSA was most commonly isolated from Throat swabs (56%) followed by Blood (51%) , Sputum (44%), Urine (39%) and pus (25%). This findings was in agreement with the study conducted by Dechen C Tsering et al., in which 61.90% of these were from throat swabs followed by sputum (56.52%), blood (50%), urine (45.83%), and pus (27.05%).[23]

In the present study, previous history of intake of broad spectrum of antibiotics was observed in 35% of study population. In the present study, prevalence of MRSA was significantly higher in patients with Previous history of intake of broad spectrum of antibiotics (75%). Similar study conducted by Dechen C Tsering et al., reported that previous history of intake of broad spectrum of antibiotics. [23]

CONCLUSION

There is a progressive increase in MRSA positivity and multi-drug resistance in strains of Staphylococci. Theoretically, vancomycin is still the drug of choice for MRSA infections. But our study shows increasing resistance of these strains to vancomycin also. The major reservoir of methicillin resistant staphylococci in hospitals is colonized/infected inpatients and colonized hospital workers. The field practitioners should be judicious enough in terms of use of antimicrobials so that the growing problem of antibiotic resistance of organism isolated does not reach a level of public health concern in this part of India. We recommend that frequent monitoring of susceptibility patterns of MRSA and the formulation of a definite antibiotic policy may be helpful in decreasing the incidence of MRSA infection. The dissemination of this information will help the treating clinicians for the primary care level physicians.

ACKNOWLEDGEMENTS:

1. Dr. E.J.David, M.D.(Med), DNB(Med), Professor and Head of the Medicine Department, Wanless Hospital, Miraj, Dr. P.M. Kulkarni, M.D. Med, Chief consultant, Department of Medicine, and Dr. Nathaniel Sase MD (Med), DM (Neuro), Director, Wanless Hospital, Miraj for their sincere guidance, continuous encouragement and timely suggestions which have made this effort possible.
2. Dr. Amanda Pereira, Dr. Amol Chandgude, Dr. Komal Kulkarni, Dr.Santosh Kumbhar, Dr. Shirin Mashalkar for their constant support.

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Date of Submission: 22 January 2020
Date of Peer Review: 13 February 2020
Date of Acceptance: 26 March 2020
Date of Publishing: 30 March 2020
Author Declaration: Source of support: Nil , Conflict of interest: Nil
Ethics Committee Approval obtained for this study? YES
Was informed consent obtained from the subjects involved in the study? Yes
For any images presented appropriate consent has been obtained from the subjects: NA
Plagiarism Checked: Urkund Software

DOI: 10.36848/IJBAMR/2020/12215.51345