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ORIGINAL ARTICLE

Community Associated- Methicillin Resistant Staphylococcus aureus in skin and soft tissue infections

MANDELIA C*, SHENOY S**,

ABSTRACT

Introduction

Methicillin-Resistant Staphylococcus aureus (MRSA) is well recognized as a major cause of nosocomial infections worldwide. Infections due to MRSA have become increasingly common among healthy members of the community with no other known risk factors for acquiring HA-MRSA infection. They are termed CA-MRSA and differ significantly from HA-MRSA in their virulence and epidemiological properties. In this study, we detected the infections caused by CA-MRSA and studied their anti-biotic sensitivity pattern. **Settings and Design** : A prospective study which included 60 subjects attending the Surgery OPD with ailments like abscesses, carbuncles, osteomyelitis and skin infections in whom MRSA infection was newly identified in the microbiology laboratory and who fulfilled the inclusion & exclusion criteria for CA-MRSA..

Materials and Methods: The specimens were cultured in the laboratory and identified as Staphylococcus aureus and subsequently, as MRSA using standard methods. Anti-biotic sensitivity pattern of these MRSA was studied using the modified Kirby Bauers disc diffusion method. Antibiotics used were Amoxyclav, Gentamicin, Netilmycin, Erythromycin, Trimethoprim + Sulfamethoxazole, Ciprofloxacin, Clindamycin, Linezolid and Vancomycin. Statistical Analysis was done using SPSS Version 11.5 and association was found by using chi square test. **Results:** A total of 60 CA-MRSA strains were isolated in Skin and Soft Tissue Infections (SSTIs), these strains were highly susceptible to Vancomycin (100%), Clindamycin (93.3%) and Linezolid (96.7%), moderately susceptible to Gentamicin (75%) and Netilmycin (90%) and a low susceptibility was recorded to Ciprofloxacin (18.3%) and Cotrimoxazole (31.7%), indicating the emergence of resistance to these valuable antibiotics. The results indicate that Vancomycin, Linezolid and Clindamycin, are to be used as 'Reserve Drugs' for resistant cases. **Conclusion:** A high proportion of resistance was found among CA-MRSA isolates. Susceptibility to Gentamicin, Ciprofloxacin and Cotrimoxazole was much lower than what was previously reported. This suggests that, the face of CA-MRSA has changed in both, epidemiological and microbiological features and calls for the formulation of specific treatment guidelines to prevent emergence of resistance to currently used drugs.

Key Words: Community- associated MRSA, Skin and soft tissue Infections, Antibiotic Sensitivity, Drug Resistance.

Key Messages:

- CA-MRSA is mostly associated with skin and soft-tissue infections and a high proportion of resistance was found among the isolates.
- Detection of CA- MRSA infections and resistance to commonly used antibiotics, helps to prevent the treatment failure.

*III MBBS, Kasturba Medical College, Mangalore
 **Professor and Head, Dept. Of Microbiology,
 Kasturba Medical College, Mangalore

Department(s) and institution(s) :
 Department of Microbiology, Kasturba Medical
 College, Mangalore

Guarantor:
 Dr. Shalini Shenoy
 Professor and Head,
 Dept. Of Microbiology,
 Kasturba Medical College, Mangalore
 Email address: shenoysshalini@gmail.com

Corresponding Author:
 Chetan Mandelia
 404, Main Block, KMC Men's Hostel, Kaprigudda,
 Mangalore, Karnataka, India
 Phone numbers: +91 9845508568
 Facsimile numbers: 0824 2428183
 E-mail address: chetanmandelia@gmail.com

Introduction

Community Associated–Methicillin Resistant *Staphylococcus aureus* (CA-MRSA) infections are an emerging problem in India and many parts of the world. These infections originate in communities as opposed to Hospital associated–Methicillin resistant *Staphylococcus aureus* (HA-MRSA)[1].

CA-MRSA differs from HA-MRSA in several important ways. These include, the lack of traditional risk factors associated with MRSA among patients, a bacterial susceptibility pattern with resistance to fewer classes of anti-microbial drugs, and the inclusion of specific virulence factors[2]. Historically, MRSA has been linked to patients in hospitals or nursing home settings, but outbreaks have been reported among previously healthy members of the community, further increasing the awareness of CA-MRSA[3]. In these outbreaks, environmental sources, such as sharing of clothing, sports equipment, towels, balms, lubricants, razors and soaps; improper care of skin trauma, direct skin-to-skin contact with MRSA lesions and crowded living conditions, such as military recruits, sports teams, inmates of jails, were identified as possible risk factors[3]. Due to its changing epidemiology,

CA-MRSA may become a serious problem for the clinicians in the near future.

In this study, we studied the infections caused by CA-MRSA and their anti-biotic sensitivity pattern.

Materials and methods

A prospective study was conducted in the Department of Microbiology, Kasturba Medical College, Mangalore. After obtaining permission from the Institutional Ethics Committee, pus samples were collected from 60 patients attending the Surgery OPD with ailments like abscesses, carbuncles, osteomyelitis and skin infections who fulfilled the criteria of absence of risk factors for CA-MRSA like prior hospitalization, out patient visit, antibiotic exposure in the past 12 months, chronic illness, IV drug use and close contact with health care personnel. Demographic data and other relevant history were collected from the eligible patients using a pre-tested semi structured questionnaire after obtaining the informed consent. Drained pus sample or a swab from the depth of the skin lesion was collected and transported to the laboratory within 30 minutes.

In the laboratory, pus or swab was cultured on to 5% sheep blood agar incubated at 37°C for 24 - 48 hours. Growth was identified by colony morphology, Gram staining, Catalase and Coagulase test. MRSA was detected by agar screen method using Muller- Hinton agar containing 4% NaCl and 6µg /ml of Oxacillin incubated at 35°C. The isolates grown on Oxacillin screen agar were considered as MRSA[4].

Anti-biotic sensitivity pattern of these MRSA strains were studied using modified Kirby Bauers disc diffusion method and interpretation was done as per CLSI guidelines. Antibiotics (Hi Media Pvt. Ltd, Mumbai) used were Amoxyclav (20/10 µg), Gentamicin (30µg), Netilmycin (30 µg), Erythromycin (15µg), Trimethoprim+Sulfamethoxazole (25 µg), Ciprofloxacin (5 µg), Clindamycin (2 µg), Linezolid (30 µg) and Vancomycin (30 µg). Minimum inhibitory concentration for Vancomycin was detected by broth micro-

dilution method for two resistant isolates and MIC values less than 2µg/ml was considered as sensitive.

The collected data was fed into the computer in Excel, and analysis was done using Statistical Package for Social Sciences (SPSS) Version 11.5 and association was found by using chi square test.

Antibiotic	Susceptible	Resistant
Ciprofloxacin	11 (18.3%)	49 (81.7%)
Erythromycin	31 (51.7%)	29 (48.3%)
Gentamicin	45 (75%)	15 (25%)
Netilmycin	54 (90%)	6 (10%)
Amoxyclav	17 (28.3%)	43 (71.7%)
Cotrimoxazole	19 (31.7%)	41 (68.3%)
Clindamycin	56 (93.3%)	4 (6.7%)
Vancomycin	60 (100%)	0
Linezolid	58 (96.7%)	2 (3.3%)

Table/Fig 1: Antibiotic Susceptibility of CA-MRSA Strains (N=60)

Results

The study sample consisted of 60 subjects, which included 27(45%) males and 33(55%) females. The mean age was 33.28 yrs with a std. deviation of 14.80. Majority of the infections (83.3%) were deep abscesses, while the rest (16.7%) were superficial skin infections. Pus samples were collected from abscesses and skin swabs were taken from the superficial infections.

Table 1, shows the antibiotic susceptibility of the CA-MRSA strains to various antibiotics. It was found that the CA-MRSA strains showed high sensitivity to Vancomycin (100%) - Two resistant strains showed MIC less than 2 / µg/ml, therefore considered as sensitive, Linezolid (96.7%), Clindamycin (93.3%) and Netilmycin (90%), while Ciprofloxacin (18.3%), Amoxyclav (28.3%) and Cotrimoxazole (31.7%) showed relatively low sensitivity.

Table 2, shows the differences between the antibiotic susceptibility of CA-MRSA strains causing deep abscesses and superficial skin

infections. Significant difference (p=0.035) in susceptibility was observed for Cotrimoxazole, it showed 60% susceptibility for superficial infections in contrast to only 26% for deep abscesses.

A comparison between the three highest susceptibility drugs, i.e. Vancomycin, Linezolid and Clindamycin revealed that there was no cross-resistance between them. Only 1 strain was found to be resistant to both Clindamycin and Linezolid, but it was sensitive to Vancomycin.

Antibiotic	Sensitive		Resistant	
	Abscess	Skin Infection	Abscess	Skin Infection
Ciprofloxacin	9(18%)	2(20%)	41(82%)	8(80%)
Erythromycin	26(52%)	5(50%)	24(48%)	5(50%)
Gentamicin	38(76%)	7(70%)	12(24%)	3(30%)
Netilmycin	45(90%)	9(90%)	5(10%)	1(10%)
Vancomycin	50(100%)	10(100%)	0(0%)	0(0%)
Clindamycin	47(94%)	9(90%)	3(6%)	1(10%)
Linezolid	48(96%)	10(100%)	2(4%)	0(0%)
Amoxyclav	14(28%)	3(30%)	36(72%)	7(70%)
Cotrimoxazole	13(26%)	6(60%)	37(74%)	4(40%)

Table/Fig 2: Shows the comparison between the antibiotic susceptibility of CA-MRSA Strains causing deep abscesses and superficial skin infections. The p value for Cotrimoxazole is 0.035, which is statistically significant.

Discussion

The findings of our study have confirmed our clinical impression that CA-MRSA has spread in our community. Most of the CA-MRSA infections were skin and soft-tissue type. We found that 83.3% of the infections were deep abscesses while 16.7% were superficial skin infections. The deep abscesses included abscesses on various parts of the body viz. gluteal abscess, thigh abscess, axillary abscess, perianal abscess, chest-wall abscess, scalp abscess, wound infections, infected ulcers etc. These findings are consistent with various studies showing that CA-MRSA is most likely to cause skin and soft tissue infections (SSTIs) [5],[6]. Skin and soft tissue infections by CA-MRSA can be treated with antibiotics like Erythromycin, Cotrimoxazole and Clindamycin. In our study, Erythromycin susceptibility of CA-MRSA strains was 51.7%, at par with the study done by Wylie et al [9] and Naimi et al [5] where susceptibility was 40% and 44% respectively. This is in contrast to the 7% susceptibility noted by Huang et al [6]. A large difference was noted in the susceptibility to Trimethoprim-Sulfamethoxazole (Cotrimoxazole) by us compared to studies done elsewhere. In our study, only 31.7% CA-MRSA strains were sensitive to Cotrimoxazole, while various other studies have noted susceptibility ranging between 90-100% [5,6,9]. Susceptibility to Ciprofloxacin was 18.3%, which is quite low as compared to 79% noted by Naimi et al [5], 88% observed by Wylie et al [9] and 53% seen by Huang et al [6]. This may be attributed to the inadvertent use of Cotrimoxazole and Ciprofloxacin for various infections. Gentamicin susceptibility was seen in 75% strains, which is low as compared to 87% observed in a study conducted in Manitoba, Canada [9] and 94% seen in Minnesota [5]. Huang et al [6] reported 100% susceptibility to Gentamicin. In our study, susceptibility to Netilmicin was 90%, which is higher compared to Gentamicin (75%). High degree of susceptibility was shown to Vancomycin (100%), Linezolid (96.7%), and Clindamycin (93.3%). The emergence of low level Clindamycin and Linezolid resistant

Staphylococcus aureus in the community is a matter of concern. Clindamycin susceptibility was reported to be 89% by Wylie et al [9] and 96% by Huang et al [6], which is similar to the findings of our study, whereas 100% susceptibility to Vancomycin among CA-MRSA strains is maintained as reported by Huang et al [6], Wen-Tsung Lo et al [7] and Conly & Johnston [8].

Though, we did not perform the susceptibility testing for Rifampin, it has excellent CA-MRSA coverage. Various studies have reported susceptibility of up to 100% with Rifampin [6]. The problem with Rifampin is that, it must be used in a combination regimen, or resistance quickly emerges. [10]

The antibiotic susceptibility of CA-MRSA strains obtained from abscesses and skin infections was similar for all the antibiotics except Cotrimoxazole, which showed significant differences. While only 26% of strains obtained from abscesses were susceptible to Cotrimoxazole, 60% of strains obtained from superficial skin infections were susceptible to it ($p=0.035$).

Overall, a high proportion of resistance was found among CA-MRSA isolates, suggesting that the face of CA-MRSA has changed in both epidemiological and microbiological features. This calls for the formulation of specific treatment guidelines to prevent emergence of resistance to currently used drugs.

There were several limitations to our study. Firstly, due to the inclusion of only lab-reported MRSA positive subjects, we were unable to estimate the true prevalence of CA-MRSA infection in the general population. Secondly, although patients were carefully interviewed, there is a risk of misclassifying MRSA acquisition due to incomplete history of hospital-related exposures and failure to elicit an accurate history of injecting drug use. Thirdly, due to limited resources, we did not test for the existence of the Panton-Valentine leucocidin gene harbored among CA-MRSA isolates. Despite limitations, this study can contribute to our expanding understanding of CA-MRSA.

Scope for Future Research

CA-MRSA is emerging as an important public health problem. The infections are on the rise in epidemic proportions. More community based surveillance studies are required, to determine the specific risk factors associated with acquisition and transmission of CA-MRSA, and to establish preventive measures within the community.

Name: _____ Age: _____
 Sex: MALE / FEMALE Date of visit: / /2009
 Occupation: _____ Address: _____

1) Reason for your visit to this department?

2) Is this your first visit to this department? Yes / No (If NO, why have you visited earlier?)

3) Did you have any recent hospitalization? (within 1 – 12 months) Yes / No (if yes, why?)

4) Did you have any recent out patient visit? (within 12 months) Yes / No (if yes, why?)

5) Did you have any recent Nursing home admission? (within 12 months) Yes / No (if yes, why?)

6) Did you have any recent Antibiotic treatment? (within 1 -12 months) Yes / No (if yes, why?)

7) Do you suffer from any long term illness? (End stage renal disease, malignancy, Diabetes mellitus etc.) (If yes from what?)

8) Do you take any medicines by injection? Yes / No

9) Were you in contact with people having any of the above mentioned conditions? Yes / No

Table/Fig 3: CA-MRSA in Skin and Soft tissue Infections - Questionnaire

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