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REVIEW

Community Associated Methicillin-Resistant Staphylococcus aureus (CA-MRSA) —An Emerging Pathogen: Are We Aware??

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ABSTRACT

Methicillin-Resistant Staphylococcus aureus (MRSA) is one of the most important causes of nosocomial infections all over the world. Once prevalent in health care setup Hospital acquired MRSA (HA-MRSA) for more than 40 years, MRSA has migrated to the community in recent years. Community associated MRSA (CA-MRSA) has evolved as a novel emerging pathogen in patients who had no contact with the health care setup. The epidemiological, molecular and microbiological differences between community associated and hospital acquired MRSA, necessitate different strategies to prevent, control and treat these two types of infection.

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Introduction

Staphylococcus aureus can cause mild skin infections to potentially life threatening infections e.g. surgical site infection, osteomyelitis, bacteriaemia etc. In the preantibiotic era, mortality due to *Staphylococcus aureus* was 90%. With the discovery of penicillin in 1928, the infection due to *Staphylococcus aureus* was controlled for a certain period. In 1942, penicillin was described as the magic bullet against *Staphylococcus aureus*, but by 1945, 12-22% *of Staphylooccus aureus* species had become resistant to penicillin by producing β-lactamase. In 1959, Methicillin was introduced, which could resist β-lactamase. But in 1961, *Methicillin resistant Staphylococcus aureus* (MRSA) appeared in U.K [1]. MRSA has become a major nosocomial pathogen, worldwide. For more than 40 years after its initial recognition, the reservoir of MRSA was infected and colonized patients in hospital [2], and were termed hospital acquired MRSA (HA-MRSA).

Why Is MRSA In The Limelight??

It has been found that MRSA causes most of the nosocomial infections (20% to 80%) in different health care set ups [3]. MRSA infection is also a leading cause of the increased cost of treatment and increased hospital stay, leading to increased working day loss. Moreover, MRSA is resistant to most of the commonly used antibiotics. The mechanism of resistance to methicillin was uncovered in 1981 with the identification of an altered protein, penicillin binding protein 2a (PBP2a), which is encoded by the *mec*A gene [4]. The mobile *mec*A gene complex resides within a genomic island, the *Staphylococcal* cassette chromosome mec (SCC mec) [4].

After being confined to the health care setup earlier, MRSA has now migrated into the community. The terminology has become

very inconsistent with MRSA causing infection in the community [5].

Community-onset (CO) MRSA

Infection with MRSA diagnosed or index culture collected in community. The established risk factors of MRSA infection were recent hospitalization, surgery, dialysis, long term cure, indwelling catheter or precutaneous medical device and history of MRSA infection in the recent past.

Community-Acquired MRSA

This term is used for community onset MRSA (CO-MRSA) infections in patients without established risk factors, but it is difficult to establish how the acquisition occurred.

Community-Associated MRSA (CA-MRSA):

Community onset infections in persons without established risk factors.

In a recent and dramatic evolutionary development, community associated MRSA (CA-MRSA) has emerged as an important public health problem [6]. Community-Associated MRSA (CA-MRSA) shares some characteristics with HA-MRSA strains, but also differ in antimicrobial susceptibility and virulence.

The main differences between HA-MRSA and CA-MRSA are as follows: [7] [Table/Fig1] Molecular definition of HA-MRSA and CA-MRSA was given by different workers. An isolate was classified as an HA-MRSA strain if the SCC mec type was other than type IV [8]. An isolate was classified as a CA-MRSA strain if SCC mec type IV was present.

(Table/Fig 1)

HA-MRSA	CA-MRSA
Recent health care exposure	No history of health care exposure
Skin and soft tissue infections less common	Skin and soft tissue infections more common
Antibiotic resistance to many drugs e.g. Gentamicin,Clindamycin & Fluoroquinolones	Antibiotic resistance to fewer drugs
Resistance genes SCC mec types I,II,III	Resistance genes SCC* mec types IV, V
PVL# toxin gene rare	PVL toxin gene common

*SCC- Staphylococcal Cassette Chromosome
#PVL- Panton Valentine Leucocidin

The CA-MRSA strains carry the Panton Valentine Leukocidin (PVL) -toxin gene commonly. Vandenesch et al have found that PVL-MRSA strains are widely distributed in some communities [9]. They also have the risk of transmission in hospitals. Panton Valentine Leukocidin (PVL) Toxin is a necrotizing cytotoxin. It is associated with abscesses and severe pneumonia. It can also be found in some *Methicillin-Sensitive Staphylococcus aureus* (MSSA) isolates. PVL toxins can damage membranes by the synergistic actions of two non-associated secretory proteins S and F [9]. PVL is also lytic for a wide variety of cell lines.

In CA-MRSA, the risk factors for community transmission are the 5Cs: [10]

- Crowding
- Skin to Skin Contact
- Cuts or abrasions
- Contaminated items and surfaces
- Lack of Cleanliness

Outbreaks of CA-MRSA in the community are characterized by serious skin/soft tissue infections or necrotizing pneumonia. CA-MRSA outbreaks are first detected as clusters of abscesses or “spider bite”. CA-MRSA outbreaks have been reported in people who are involved in competitive sports like football, wrestling, fencing etc, or in schools, dormitories, military barracks, prisons and daycare centers [5]. CA-MRSA skin or soft tissue (SST) infections have also been reported in a state prison in Mississippi in 2000 [11] and amongst military trainees

in 2001-2002 [12] and in a detention center in 2004 [13].

In 2005, Kazakova et al reported CA-MRSA abscesses among professional football players at sites of turf burn [13],[14]. They came across a very important finding that trainers providing wound care did not follow hand hygiene, towels were frequently shared amongst the players and weight training equipment was not regularly cleaned. Outbreaks of CA-MRSA have also been reported in several states of USA, with licensed and unlicensed tattooing [5].

Pam Webb, in his report, had shown the differences in the prevalence of the involvement of different body sites in HA-MRSA versus CA-MRSA infections [15].

[Table/Fig 2] From this study, it is very evident that CA-MRSA predominantly causes skin and soft tissue (SST) infections. The common presentations for CA-MRSA skin infections are boils, abscesses, furuncles, carbuncles,etc. In the United States, CA-MRSA skin infections are often misdiagnosed as "spider bite" and this misdiagnosis unnecessarily delays proper treatment of the infection and facilitates it's spread.

(Table/Fig 2)

SITE	HA-MRSA	CA-MRSA
Skin & soft tissue	36%	74%
Respiratory	22%	6%
Urinary tract	20%	1%
Blood stream	9%	4%

Hence the questionon to how to deal with skin and soft tissue infections in the community automatically arises. The CA-MRSA guidelines ofAugust 2007 state that any unusual skin lesions or draining wound is potentially infectious to others and the first rule is to prevent transmission, whereas the second rule is to evaluate and refer [16].

The prevention of CA-MRSA involves four simple steps:

- ✓ Maintain hand hygiene
- ✓ Keep wounds clean and covered
- ✓ Don't share personal items like towels and razors
- ✓ Clean environmental surfaces regularly

The second rule states that any unusual skin lesions have to be evaluated by a health care provider for prompt treatment. Increased awareness among healthcare providers and monitoring close contacts of CA-MRSA patients are also necessary to control CA-MRSA infection.

Generally CA-MRSA is resistant to all β-lactam agents including cephalexin, amoxicillin-clavulanate and ceftriaxone. Many of these strains are also resistant to erythromycin, clarithromycin and azithromycin, trimethoprim-sulphamethoxazole and doxycycline. They are also susceptible to vancomycin, linezolid and daptomycin. Almost all the strains of CA-MRSA are sensitive to topical mupirocin ointment.

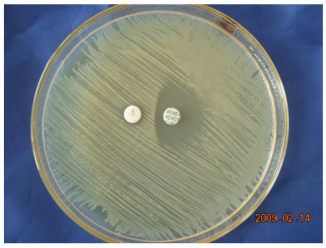
CA-MRSA from an abscess is best treated by surgical drainage. A culture from the lesion should be grown and studied for proper antibiotic therapy. For inpatients, treatment by drainage of the abscess and injection by 1mg/Kg qd vancomycin is the gold standard. In some health care set ups for treating CA-MRSA, 4mg/Kg qd daptomycin (cubicin) is used, as it may have an antitoxic effect. For outpatients, CA-MRSA is treated by surgical drainage of the abscess and treatment with trimethoprim-sulphamethoxazole or doxycycline and or rifampicin orally. Otherwise, second generation fluoroquinolones i.e. levofloxacin, gatifloxacin and rifampicin may also be used. [17],[18]

Though most of CA-MRSA strains are sensitive to clindamycin, as per guidelines, clindamycin should never be given empirically in CA-MRSA infection if the patient is a child and is critically ill, or if the patient is an adult and is mild to moderately

ill, is without D-zone test results or if the patients is an adult and is critically ill [19].

Positive D-zone tests indicate inducible clindamycin resistance (*erm*-mediated) and these can be done by putting clindamycin (2µg) discs 15mm away from the edge of the erythromycin(15µg) disc, as per NCCLS guidelines, 2004 [20]. Inducible resistance to clindamycin is manifested by flattening or blunting of the clindamycin zone of inhibition (giving D-shape) which is adjacent to the erythromycin disc.

[Table/Fig 3] The importance and significance of the D-zone test is that, without the D-zone test, all MRSA strains with inducible clindamycin resistance would have been reported as clindamycin sensitive by routine antibiotic sensitivity tests, resulting in treatment failure [21]. Hence, the D-zone test has become a standard operative procedure (SOP) for any MRSA strains isolated in the laboratory.



(Table/Fig 3) Showing positive D-zone test routinely done in our laboratory.

So, there are three main factors of concern for CA-MRSA [10]

1. CA-MRSA is the leading cause of skin and soft tissue infections in adults in the community
2. CA-MRSA spreads more readily than HA-MRSA
3. CA-MRSA has the potentiality to spread in a health care setting

In India, there still is apaucity of available literature regarding Community-associated MRSA (CA-MRSA) which is emerging as a pathogen worldwide, since 2001. Reliable data on the prevalence of CA-MRSA infection in India is lacking. In two small studies, 1.4% and 11% of community-acquired pyoderma were found to be caused by MRSA [22],[23]. Kabir et al from India, have reported in 2007 , 11.8% of CA-MRSA [24]. Moreover, there is a wide communication gap between the private practitioners and laboratory staff in India, which may be the cause of not reporting skin and soft tissue infections due to CA-MRSA.

To conclude, we must say that as Clinicians and Microbiologists, we must be aware of the fact that CA-MRSA is a novel emerging pathogen and MRSA strains which were only restricted to healthcare setups few years back, have encroached into the community. For proper treatment of the patients, we must try to detect CA-MRSA strains.

So the war is on! Our opponent is now not only *Staphylococcus aureus* as it was 40 years ago, but also hospital acquired MRSA (HA-MRSA), Community associated MRSA (CA-MRSA) and MRSA *coagulase negative Staphylococci* (MRSA-CoNS) have been included in the list.

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