IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
ISSN: 2278-3008. Volume 3, Issue 6 (Sep-Oct. 2012), PP 11-18
www.iosrjournals.org

A Review on Community Acquired Methicillin Resistant *Staphylococcus aureus* an Emerging Infectious Disease

Murtaza Mustafa, [I.] IM. Yusof [2]MN.Malehah[1]
1 School of Medicine University Malaysia Sabah, Kota Kinabalu, Sabah Malaysia.
2 Ministry of Health Malaysia, Sabah, Kota Kinabalu, Sabah, Malaysia.

Abstract: *Methicillin resistant Staphylococcus aureus (MRSA) has emerged as a community acquired infection in the past decade. Molecular studies showed that HCA-MRSA and CA-MRSA represent different organisms that produced different clinical syndromes .MRSA infection is associated with high morbidity, mortality, longer hospital stay and economic burden worldwide. All over the world, the dissemination of a few distinct clones of CA-MRSA has resulted in an increase in skin and soft tissue infections and necrotizing pneumonia, without defined risk factors. There has been link to fluroquinolone (FQ) exposure to epidemic CA-MRSA strains obtained from subjects with nasal colonization. Low socioeconomic status may be one common link among the identified high-risk groups, although many patients with CA-MRSA infections have no risk factor. CA-MRSA isolates are characterized by the presence of SCCmec type IV or type V. S.aureus clones ST30, ST80, CC75 and ST 93 has been documented in some countries. These clones are likely to provide insights into the emergence of methicillin resistant strains of S.aureus. CA-MRSA is readily disseminated in the hospitals and may cause outbreaks of infection .It is suggested that the use of the few effective antibiotic agent should be restricted .Despite these measures, the spread of this organism may not be contained.*

Keywords: *MRSA, CA-MRSA, HCA-MRSA, S.aureus.*

I. Introduction

Staphylococci were first observed in suppurative lesions and classified as *monococcus* by Bilroth in 1874,and renamed as *Staphylococcus* (from Greek *Staphyle*, a bunch of grapes) by Ogston in 1883 [1,2]. The modern era of antimicrobial therapy began in 1940s with the introduction of penicillin and first beta lactamase such as cephalosporin's and semisynthetic methicillin became available in the late 1950s.First MRSA was described at about same time [3]. In United States the prevalence rate of MRSA increased from (2.1 %) in 1975 (35 %) in 1991[4].It is now as high up to 60 % in certain centers in the United States [5]. The MRSA prevalence rate varied worldwide. Western pacific region, (46 %) United States (34.2 %), Latin America (4.9 %) Europe (26.3%) and Canada, (5.7%). Methicillin resistance varied greatly among countries within a region .In western pacific countries ,prevalence of MRSA ranged from (23.6 %) in Australia to more than (70 %) in Japan and Hong Kong ,in china (89.2%).In European centers, these percentage varied from less than (2%) in the Netherland to(54.4%) in Portugal [6,7]. The MRSA originally confined to the hospital environment, now MRSA has emerged as a community-acquired infection over the last decade [8,910].The.*Community acquired* MRSA (CA-MRSA) is different from hospital-acquired MRSA from both epidemiological and molecular points of views. Case-definition studies showed that hospital or health care MRSA (HCA-MRSA) and CA-MRSA represented different organisms that produced different clinical syndromes [11, 12]. HCA-MRSA was associated with risk factors that included recent hospitalization or surgery, living in a nursing home, or carrying an indwelling catheter or device .It produced mostly hospital- related pneumonia and bacteremia. CA-MRSA was not associated with any risk factors and produced primarily skin and soft tissue infections, and sometimes rapidly fatal necrotizing pneumonia. Recently, it was also described as responsible for necrotizing fasciitis and bone and joint infections [13, 14]. In addition, HCA- MRSA was multi resistant and highly clonal, whereas CA-MRSA was pauciresistant and seemingly more polyclonal, except for an extremely successful USA300 clone that has become highly prevalent in the United States [15, 16, 9]. CA-MRSA also different from HCA-MRSA,CA-MRSA strains carry genes for the Panton Valentine leuckocidin (PVL).CA-MRSA isolates carry smaller *Staphylococcal* chromosomal cassette (SCC*mec*) elements most commonly SCC*mec* type IV or type V. These smaller elements also carry the mecA gene. Whereas HCA-MRSA carry SCCmec belonging to type I, II, or 11 [17]. This paper reviews CA-MRSA and its relevance in medical practice. The emergence of new acquired penicillin binding protein, encoded by *Staphylococcal* chromosome cassette mecA (SSC*mec*) two clones, sequence type ST93, and clonal complex CC75, and other clones which are reported from many countries.

II. Methicillin Resistance

Methicillin resistance is not mediated by penicillinase but the newly acquired penicillin- binding protein 2 A (PPBA), encoded *by Staphylococcal chromosome Cassette mecA* [18]. The few staphylococci that express borderline methicillin resistance from the expression of penicillinase are not clinically relevant. Because of low beta-lactam affinity, PBP2A can take over the cell wall assembly when normal staphylococcal PBPs are blocked by these compounds [17]. Provision of this adequate substrate to PBP2A requires the functionality of numerous accessory genes implicated in the normal wall building machinery ,including 14 more accessory determinants, some of which (*femABC and femhB*) are responsible for adding the glycine residues critical for PBP2A function. Any alteration in these elements decreases the expression of methicillin resistance in spite of the fact that PBP2A is present [19, 20].

Resistance to nafacillin, methicillin and oxacillin is encoded and regulated by a sequence of genes found in a region of the chromosome called staphylococcal cassette chromosome *mec* (SCC*mec*). A gene on this locus encodes a low affinity penicillin binding protein (PBP2A) that is responsible for the resistance. There are several different SCC*mec* types. Types 1, 11, and 111, are associated with hospital- acquired infections and may contain genes encode resistance to other antimicrobials as well. SCC*mec* type 1V has principally been found in CA-MRSA strains that tend to be less resistant, more transmissible, and responsible for outbreaks over the last decade in the United States and some countries in Europe [21]. One of theCA-MRSA,USA300 strain extremely successful clone that has become highly prevalent in the United States[9].Strain of *S. aureus* with intermediate susceptibility to vancomycin have been isolated in Japan ,United States and several other countries. These are known as vancomycin-intermediate *S. aureus* or "VISA" .They generally has been isolated from patients with complex infections who received prolonged vancomycin treatment therapy. Often there has been vancomycin treatment failure [21].

III. Community Acquired MRSA

The infections occurring among outpatients or among inpatients with an MRSA isolate obtained earlier than 48 h after hospitalization would be considered CA-MRSA [22].CA-MRSA has now become the most frequent cause of skin and soft tissue infections acquired in the community [23].Groups with high intensity physical contact are particularly affected. This includes competitive athletes, children in daycare centers, military recruits, injection drug users, jailed inmates, and men who have sex with men [24].CA-MRSA also can cause severe sometimes fatal invasive disease, such as necrotizing pneumonia, bacteremia or necrotizing fasciitis [25, 26]. Moreover, CA-MRSA has started to spread from the community into hospital, where outbreaks of health care-associated hospital onset infections with typical CA-MRSA have occurred [27]. Even if compared with HCA-MRSA,CA-MRSA retained susceptibility to many non-beta lactam antibiotics; the rapid increase of such infections will become a serious public health challenge [28].

Researchers in Australia have revealed the burden of disease due to *S. aureus* and CA-MRSA continues to be high in indigenous communities. Pyoderma was found in(38 %) of children in Northern Territory(NT) and western Australian (WA) communities with *S aureus* recovered from (59 %) of pyoderma lesions and methicillin- resistance detected in 23 % of these lesions [29].Researchers also observed that CA-MRSA has two clones, sequence type ST 93 and clonal complex CC75 are of particular interest and provide insight into the emergence of CA-MRSA from indigenous populations. ST 93, known as the Queensland clone, was first described in a Caucasian group of patients in Queensland [30].Subsequent studies, though have led to the conclusion that it has probably emerged from indigenous communities [31]. Remarkably, CC75 has recently also been found in Cambodia and possibly Malaysia and Indonesia [32]. CA-MRSA also been reported in Greece, Korea and in Taiwan [33, 34].

IV. Clinical Manifestation

Staphylococcus aureus is one of the most common bacterial pathogens in hospital –acquired and community acquired infections [12]. Its prevalence rate increased from (0.74%) of all inpatients admitted to U.S .hospitals in 1998 to (1 %) in 2003 (annual increasing rate from (7 % to 11%), corresponding to a total of nearly 300,000 patients with *S.aureus* in U.S. hospitals in 2003. *S.aureus* infection is associated with substantial morbidity and mortality. Infected patients had, on average, three times longer hospital stay, three times greater charges ,and a five times greater risk of hospital death (11.2 % versus 2.3 %) The annual impact in the Unites States at least 12,000 inpatients deaths and $ 9.5 billion excess costs [35, 36]. *S.aureus* is responsible for an array of infections where it is either present on the infection site or acts at a distance by secreting of toxins. The SENTRY antimicrobial surveillance program, which collects data from United States, Canada, Latin America, Europe, and the Western Pacific, reported the following distributions of *S.aureus* infections: 1.SSTI,(39.2 %) 2, Lower respiratory tract infections (23.2 %) 3, Blood stream infections including infective endocarditis(22. %) 4,(15.6%) other infections including urinary tract, brain, and abdominal cavity [37]. *S.aureus* is the leading cause of nosocomial infection, particularly in the case of surgical site infections (15.5 % to 30 %) catheter related bacteremia, and ventilator associated pneumonia (20.5 % to 28 %) [38, 39]. In the community, it is also

one of the first causes of native valve (31.6 %), and prosthetic valve endocarditis (23% of cases), and osteomyelitis (50 % to 70 %) cases [40]. and the second cause of community-onset bacteremia after *Escherichia coli* (15 % to 23 .5 %) [40]. *S.aureus* skin and soft tissue infections are commonly classified according to the anatomic structure involved, such as (1) infection of the epidermis: impetigo (2) infection of superficial epidermis: folliculitis (3) infection of the deep dermis: furuncles, carbuncles and hydradenitis suppurated and (4) infection of subcutaneous cellular tissues: erysipelas [27].

V. Predisposing Conditions for S. Aureus Infection

Population based studies have consistently identified male gender very young and elderly individuals as at high risk for *S.aureus* infections. Moreover, two studies showed that the most important risk factor is necessity for dialysis ,either peritoneal (relative risk) [RR],(150 to 204,95%CI) or hemodialysis, (RR,257 to 29,95%CI).Other conditions that increase the risk of invasive *S.aureus* infections include diabetes (RR,7), cancer (RR,7.1 to 12.,95%CI), rheumatoid arthritis (RR,2.2 to 9.2), HIV infection (RR23.7), intravenous drug use (RR,10.1,95%CI), or alcohol abuse (RR,8.2,95%CI) [36].

Rare but classical predisposing factors encompass chemostatic defect and defect in phagocytosis. Inheritable chemotactic defects include Job's syndrome,Chediak-Higashi syndrome, Wiskott-Aldrich syndrome, and Down syndrome. Job's syndrome is a condition that involves recurrent eczema with repeated skin infections and cold abscesses. *Chediak-Higashi syndrome* is defined clinically by albinism and recurrent *S.aureus* infections and cytologically by giant granules in phagocytic and other cells. However, one of the most important factors that independently add to all these predisposing conditions is chronic *S.aureus* nasal carriage .Whether they are in the hospital or in the community; patients mostly become infected with their own carriage strain. Thus screening of patients at high risk for *S.aureus* nasal or cutaneous carriage and decontaminate positive cases with mupirocin ointments or other means as part of control of MRSA disseminated [41]. Most decontamination regimens recommend a 1-week daily total body washing with chlorohexadine –based soap, plus mupirocin application. Use of systemic antibiotic (e.g.trimehoprim- sulfametoxazole + rifampin) must be restrained to particular situations. Control cultures should be made thereafter. Routine antibiotic testing must be performed to detect emergence of resistance to decolonization agent. About 5 % of heath care workers become colonized with MRSA; clinical disease develops in approximately 5 % of these workers .Eradicating MRSA carriage from health care workers might thus be performed as well. However, health care workers most frequently act as vectors of transmission, not as main source of MRSA .Regarding nasal carriers local disinfection appears more successful than systemic antibiotics, because of emergence of resistance and significant failure rate [42].

VI. CA-MRSA as a Pathogen

There are several hypotheses to explain the emergence and entrenchment of CA-MRSA isolates have been proposed. None of these hypotheses definitively explain the observed epidemiological data. The emergence of new CA-MRSA isolates occurred in the late 1990s in tandem with the increasing use of fluroquinolones (FQs), some have suggested that the relationship between the phenomena might be more than a coincidence.The increase use of FQ has been associated the elimination of methicillin sensitive *S.aureus* (MSSA) strains from the colonization of the nasal mucosa which might predispose one to colonization by MRSA strains[43]. Other ideas have been proposed to link FQ exposure to epidemic CA-MRSA strains obtained from subjects with nasal colonization were exposed to a sub inhibitory concentration of FQ .In a microarray analysis, this resulted in the increased expression of 53 open reading frames of the exposed CA-MRSA isolates, including mecA ,suggesting that beta –lactam, resistance may be increased by FQ exposure [44]. Moreover the restriction of FQ use in the health care setting has been shown to decrease the rate of MRSA isolation and FQ use has been identified as a risk factor for MRSA infection in hospitalized patients [45,46].

The United States which has uniquely experienced epidemic CA-MRSA infections, was only country recommending the childhood conjugate pneumococcal vaccination (Prevnar) for routine use for several years. Moreover the recommendation for the use of Prevnar in 2002 in Canada may have retrospectively correlated with a rise in CA-MRSA infections there. Conversely CA-MRSA was already commonly reported from Australia in January 2005 at the time of the addition of Prevnar to the National Immunization Program Schedule for the routine vaccination of children younger than 2 years of age .Prevnar was introduced as a recommended routine vaccine in September 2006 in The United Kingdom ,where CA-MRSA has continued to be rare [47]. In Netherland a negative correlation was found between colonization by the vaccine serotypes of *S.pneumoniae* and *S.aureus* in children who had recurrent otitis media.*S.aureus* became a more cause of otitis media in children after Prevnar vaccination [48]. Some researchers have postulated that decreased pneumococcal may provide a new ecological niche for colonization with CA-MRSA strains this is supported by evidence that the cocarriage of *S.pneumoniae and S.aureus* was found rarely among 790 healthy children in Israel in 2002 a country with few CA-MRSA infections[49]. Controversy still surrounds the notion that Prevnar is associated with increasing MRSA colonization in a given population; some authors have not found evidence to support the contention that colonization with *S.aureus and S.pnerumoniae* is uncommon [50].

VII. Staphylococcus Chromosome Casstte(SCmec) Elements in CA-MRSA

Nearly all MRSA strains contain the SCC*mec* element, which is uniformly integrated into a specific *S.aureus* chromosomal site known as *orfx*.SCC*mec*, which was likely acquired from a coagulase-negative staphylococcus species, carries the mecA gene, which encodes penicillin binding protein 2a (PBP2), a cell wall trnspeptidase,,which in conjunction with native PBP2, allows continued cell wall synthesis in the presence of beta lactams [51,52]. There are nine types of SCC*mec* (types I to VIII and VI) have been defined, which can be distinguished by the type of *ccr* gene complex that mediates the site-specific excision and insertion of SCC*mec* cassette out of or into the bacterial genome and the class of of *mec* complex that they bear. The large SCC*mec* types I to III are present in HCA-MRSA strains and were likely transferred to *S.aureus* from a commensal staphylococcal species on a few occasion [53, 54]. The smaller SCC*mec* types IV or V, however are believed to have been transferred to methicillin-susceptible backgrounds frequently, with the resultant emergence of novel, fit MRSA strains bearing the type IV or V elements [17, 55]. The presence of SCC*mec* type IV element, which lacks genes conferring non- beta-lactam antimicrobial resistance, may account for the decreased likelihood that CA-MRSA strains are MDR. Several subtypes of SCC*mec* type IV that very dependent on the typing system used have been described. An international committee of experts in 2009 formulated a consensus nomenclature for SCC*mec* types [56].

VIII. Virulence Factors in CA-MRSA

The experimental and epidemiological studies have confirmed a number of putative virulence factors in CA-MRSA strains, particularly in USA300. PVL is a two-component *S.aureus* pore-forming protein encoded by the *lukF-PV and lukS-PV* genes The genes encoding PVL ,which can spread from strain to strain by bacteriophages, were previously believed to be present in fewer than (5%) of unselected clinical *S.aureus* strains in mid 1990s, although the genes were transiently found in circulating ST30 clone in Japan in 1979 to 1985[57].

PVL and CA-MRSA Infections. In the United States, after the mid-1990s, carriage of the PVL genes has been closely linked to infections caused by CA-MRSA strains in numerous epidemiological studies. Approximately 60 to 100 % of CA-MRSA (by various definitions) have been shown to carry PVL .For example, in 2000, large study from Minnesota found that 77 % of patients with infections caused by CA-MRSA isolates were PVL^+ ,but only (4%) of HCA-MRSA isolates were PVL^+ [58]. While PVL has been strongly linked epidemiologically to prevalent CA-MRSA strains, it is not known with certainly how they contribute to their fitness and/or virulence or if they are merely a marker for other fitness or virulence determinants.PVL strains carrying *SCCmec* type IV,V,or VI[59]. In the United States, PVL genes have been almost universally detected among CA-MRSA strains causing SSTIs and *S.aureus* invasive disease as community acquired necrotizing pneumonia, severe sepsis and other sometimes fatal infections [60, 61]. Among patients with *S.aureus* pneumonia, higher mortality and a increased likelihood of sepsis, hemoptysis, and pleural effusion were documented for cases caused by PVL^+ strains[62]. In Australia, the first reports of community-onset MRSA infections in 1993 were caused by strains that lacked PVL genes. Subsequently, however a polyclonal surge of largely PVL^+ MRSA infections occurred among previously healthy young adults and children; each newly described PVL^+ *SCCmec* type IV-bearing community strain identified in country had a distinct geographic distribution. Studies from many countries in Europe also documented the emergence of PVL^+ SCC*mec* type IV-bearing CA-MRSA strains in multiple *S.aureus* backgrounds, although CA-MRSA infections occur far less commonly there than in the United States [63].PVL^+ strains also been found in Taiwan, Korea and China [64-66].

IX. Molecular Analysis of CA-MRSA

In the 1990s several *S.aureus* genetic backgrounds were responsible for initiating the CA-MRSA epidemic, but only one well characterized genetic background, USA300, emerged as the most prevalent strain in the contiguous 48 states in the United States [67, 68]. The MRSA strains with different genetic backgrounds carrying SCC*mec* type IV or V have been identified as etiological agents of infections among previously health people in different part of the world. These clones, like USA 300, tend to be PVL^+ and have been associated with distinctive SSTIs resembling spider bites and necrotizing pneumonia [69]. The main background genotypes of CA-MRSA strains other than USA300 are ST1, ST80, ST30, ST59, CC75, and ST93.

ST1. USA400 is the pulsotype of the strain ofST1 CA-MRSA that predominated among CA-MRSA clones in the United States when first recognized in the late 1990s.The genotype of a prototype strain, MW2, has been sequenced[70]. USA400 was also identified in community in 1999 to 2002 in Saskatchewan, Canada, and in 1995 to 2000 in Manitoba, Canada [71,72]. An ST1 strain carrying SCC*mec* type IV that has been usually susceptible to most non-beta lactam drugs and has been found most commonly to cause SSTIs has been described. This strain lacked PVL genes and circulates in the community in Australia, particularly in Western and South Australia and England in Australia it is designated WA-MRSA-1[73, 74].

ST80.CA-MRSA infections have remained infrequent in Western Europe relative to the United States.ST80 is likely the most common PVL^+, SCC*mec* type IV-bearing ST MRSA strains causing such

infections. PVL^+ MRSA strains bearing SCC*mec* type IV have been reported by many Western European nations as an increasing common cause of skin infections in the community in Austria [69]. Other European countries have also reported similar strains.ST80 was a rare cause of sporadic invasive infections in France in 2006 to 2007 and accounted for 3.6% of 111 MRSA isolates collected during a national survey of patients with invasive disease. It is not clear why ST80 strains have not spread to North America or why USA300 strains have not spread widely to Western Europe [75].

ST30. ST30 corresponds to phage type 80/81 strains of *S.aureus* that were virulent nosocomial pathogens in the United States during the 1950s and 1960s.These strains were MSSA strains and often carried the PVL genes [76]. The clones 80/81 have long been a common human pathogen in Australia [73]. Since the mid-1990s, MRSA ST30 clones with different pulsotypes and genetic characteristics have been reported from many parts of the world, including the United States, Japan, Latin America, Turkey, the middle East, Egypt, and other countries in Western Europe [77]. ST30 isolates reported from many regions, including PFGE type USA1100 in the United States, carry the genetic determinants of PVL and the SCC*mec* type IV element but these clones have many *spa* types, suggesting continued evolution [77, 78].

ST59.ST59 isolates are prevalent in Taiwan. Strains that are PVL+ have diverse spa types and several SCC*mec* types.PVL+ST59 isolates have also been recovered from patients in Australia, Taiwan, Netherlands, Denmark, England, the United States and elsewhere [78]. In Taiwan, ST59 clones with distinctive SCC*mec* DNA sequence, type V_T and multidrug-resistant phenotype are common[79]. For example PVL^+ ST59 isolates bearing SCC*mec* type V_T accounted for 25% (53/212) of MRSA strains colonizing healthy children in 2005-2006 at medical centers in Taiwanese cities.However,ST59 strains that were PVL negative and carried SCC*mec* type IV accounted for(59 %, 129/212) of MRSA strains from tested children. In a study at 2,500-bed hospital Taiwan University hospital in Taipei in 2001 to 2006(, 92%) of the 30 available CA-MRSA isolates (by CDC criteria) from patients with bacteremia were ST59 strains[80].

ST93.The ST93 Queensland MRSA was first identified in 2000 in Queensland and New South Wales, Australia. It spread rapidly to become the predominant PVL^+ MRSA clone isolated from infections in those regions. In 2004 to 2005, in a national surveillance program in Australia, 87/462 (18.8%) MRSA isolates obtained from outpatients were ST93 strain and all were PVL^+ among PVL^+ MRSA isolates 87/136(63.9%) were ST93 strains and they were isolated in all regions of the country [73]. Despite the high prevalence of this strain in Australia, it has rarely been identified on other continents [81, 82]. It has been associated with severe infections, including necrotizing pneumonia as well as SSTIs [83, 84].

X. Risk Factors in CA-MRSA Infection

Low socioeconomic status may be one common link among many of the identified high-risk groups, although many patients with CA-MRSA infections have no risk factors [85]. In addition to the putative high-risk groups for CA-MRSA infection there has been evidence of CA-MRSA strain transmission among children in day care centers and outbreaks of MRSA SSTIs within families[86,87] among children on camping trip, among IVDUs and individuals exposed to another person with an SSTI by skin- to – skin contact during sexual activity[88-90]. In U.S. Since 2000, there have been an increasing number of reported outbreaks in the neonatal intensive care units caused by CA-MRSA strains. Several neonatal MRSA outbreaks have linked to CA-MRSA strains including USA300 and USA 400[91, 92]. Many medical centers in the United States have documented an increasing burden of CA-MRSA infections in children as a percentage of *S.aureus* infections an absolute increase, or both [93]. CA-MRSA strains and USA300 has been identified as a frequent cause of infection among the athletes [94]. In U.S .emergency department(ED) patient visits for SSTIs increased from an estimated 1.2 million in 1993 to 3.4 million in 2005, an increase from (1.35 %) to (2.98 %) of all ED visits likely reflecting the impact of CA-MRSA. Studies of medically underserved communities in U.S .cities have revealed foci of CA-MRSA SSTIs and frequent asymptomatic MRSA nasal colonization. For example in 1999 to 2000 (2.7 %) of 833 homeless or poor adults harbored MRSA a rate higher than that found in 2001 to 2002 in the general U.S .population[95]. Multiple indigenous populations including Native American(NA),First Nation(Manitoba and Nunavut, Canada),Australian Aboriginal, ,Pacific Islander and Alaska Natives ethnicities, has been associated with high risk of infection with CA-MRSA strains. Many of these groups are disadvantaged in their societies and their association with lower socioeconomic status may be responsible for the increased risk of CA-MRSA infection [96].

XI. Decontamination for Patients Colonized or Infected With MRSA

Protective measures.Keep patient in contact isolation, one or several contaminated patients in single room with restricted access .Use protective gown and gloves. Use protective mask and glasses if risk of projection of contaminated liquids. Clean hands with alcohol solution at glove removal and between cares. Leave disposable in room and discard for sterilization in special containers [27].

Decontamination measures, apply nasal muprocin (2 %) every eight hrs for 5 to 7 days. Apply chlorohexadine-based oral spray 3 to 4 times daily for 5 to 7 days. Take daily shower or clean body thoroughly with

chlorohexadine–based soap for 5 to 7 days. In case of dental prosthesis, clean and soak daily chlorohexadine – based solution for 5 to 7 days [27].

Control Cultures and Decision. Take control swabs of any contaminated sites 48 hrs to 96 hrs after end of treatment .Keep isolation measures until laboratory results .If no MRSA is present in control cultures, consider decontamination .Relief isolation and swab weekly for follow–up cultures .If MRSA is present in control cultures ,pursue isolation measures and repeat whole decontamination scheme[27].

XII Conclusion

MRSA the cause of community acquired MRSA infections worldwide. A few distinct clones of CA-MRSA has resulted in skin and soft tissue infections and necrotizing pneumonia, without risk factors.CA-MRSA isolates are characterized by the presence of SCCmec type IV S.aureus clones CC75 and ST93 has been documented in many countries. To prevent the spread of these organisms the use of certain effective antibiotics should be restricted.

References

[1] Bilroh T.Unterusuchungen iiber die Vegetationsformen von *coccobacteria* septica. Berlin, Reimer, 1874; **244**.
[2] Ogston A .*Micrococcus* poisoning. *J anat Physiol* (London) 1883; **17:**24-58.
[3] Jevons MP."Celbenin" resistant *Staphylococcus*.*Br Med J*.1961; **1**:124-125.
[4] Panililo Al ,Culver DH, Gaynes RP ,*et al* ,Methicillin-resistant *Staphylococcus aureus* in U.S. hospitals,1975-191,*Infect Control Hosp Epidemiol*,1992;**13**:582-586.
[5] Styers D ,Sheehan DJ ,Hogan P, Sahm DF .Laboratory-based surveillance of current antimicrobial resistance patterns and trends among *Staphylococcus aureus :* 2005 status in the United States. *Ann Clin Microbiol Antimicrob*.2006; **5**:2.
[6] Diekema DJ, P faller MA ,Schmitz FJ ,*et al* .Survey of infections due to *Staphylococcus* species: frequency of occurrence antimicrobial susceptibility of isolates collected in the United States, Canada, Latin America, Europe ,and the Western Pacific region for the SENTRY Antimicrobial Surveillance Program,977-1999.*Clin Infect Dis*.2001;**32**:5114-5132.
[7] McGowan J .Antibiotic resistance in hospital organisms and its relation to antibiotic use, *Rev Infect Dis*, 1983; **5**:1033-48
[8] Dufour P, Gillette Y, Bes M, *et a*l. Community acquired methicillin resistant *Staphylococcus aureus* infections in France: emergence of a. clone that produces Pantong Valentine leukocidin .*Clin Infect Dis.*2002;**35**:819-824.
[9] Moran GJ, Krishnadasan A, Gorwitz RJ, *et a*l. Methicillin-resistant *S.aureus* Infections among patients in the emergency department .*N.Engl J Med*.2006;**355**:666-674
[10] Dietrich DW, Auld D, Mermel LA .Community-acquired methicillin-resistant *Staphylococcus aureus* in Southern New England Children.*Pediatrics*.2004; **113**:e347e352
[11] Salgado CD, Farr B, Calfee DP .Community acquired methicillin resistant *Staphylococcus aureus*: a meta- analysis of prevalence and risk factors, Clin *Infect Dis*.2003; **36**:131-139.
[12] Diep B, Stone GG, Basuino **L**, *et al.* The arginine catabolic mobile element and *Staphylococcal* chromosomal cassettee *mec* linkage: convergence of virulence in the USA300 clone of methicillin resistant *Staphylococcus aureus*. *J Infect Dis*.2008; **197**:1523-1530
[13] Nimmo GR ,Bell JM ,Mitchell D, *et al*. Antimicrobial resistance in *Staphylococcus aureus* in Australian teaching hospitals.1989;1999. *Microb Drug Resist*. 2003: **9**: 155-160.
[14] Vandenesch F, Naimi T ,Enright MC, *et al.* Community acquired methicillin-resistant *Staphylococcus aureus* carrying Panton – valentine leukocidin genes : Worldwide emergence. *Emerg Infect Dis.* 2003; **9**:978-984.
[15] Ito T, Okuma K, Ma XX, *et al.* Insights on antibiotic resistance of *Staphylococcus aureus* from his whole genome: genomic island SCC. *Drug Resist Updat*.2003; **6**:41-52.
[16] Chambers HF, Hartman BJ, Thomasz A. Increased amount of a novel penicillin binding protein in a strain of methicillin- resistant *Staphylococcus aureus. J. Clin Invest*.1985; **76**:325-331.
[17] Berglund C, .Siderquist B..The origin of a methicillin-resistant *Staphylococcus aureus* isolate at a neonatal ward in Sweden-possible horizontal transfer of a staphylococcal cassette chromosome mec between methicillin-resistant *Staphylococcus haemolyticus* and *Staphylococcus aureus*.*Clin.Microbiol,Infect*.2008;**14**:1048-1056.
[18] de Jonge BL, Sidow T, Chang YS, *et al*. Altered muropeptide composition in *Staphylococcus aureus* strains with an inactivated fem A locus.*J.Bacteriol*.1993:**175**:2779-2782.
[19] Berger Bachi B. Expression of resistance to methicillin. *Trends Microbiol*.1994; **2**:389.
[20] de Lancaster H, Thomasz A. Reassessment of the number of auxiliary genes essential for expression of high- level methicillin resistance in *Staphylococcus aureus . Antimicrob Agents Chemothe*. 1994; **38**:25902598.
[21] Geo FB, Karen CC.*Staphylococci. In* Jawetz, Melinick & Adelberg's, Microbiology, 25th ed. McGraw Hill, 2010.
[22] Methicillin-resistant *Stphylococcus aureus* infections among patients in the emergency department (2006).
[23] Epidemiology of methicillin resistant *Staphylococcus aureus* (2008).
[24] Lina G, Piemont Y, Godail-Gamot F, *et al*. Involvement of Panton valentine leukocidin-producing *Staphylococcus aureus* in primary skin infections and pneumonia. *Clin Infect Dis*.1999; **29**:1128-1132.
[25] Seybold U, Kourbatova EV, Johnson JG, *et al*. Emergence of community-associated methicillin- resistant *Staphylococcus aureus* USA300 genotype as a major cause of health care associated blood stream infections. *Clin Infect Dis*.2006; **42**:42-647-656.
[26] Miller LG, Perdreau F, Rieg G, *et a*l. Necrotizing fasciitis caused community-associated methicillin-resistant *Staphylococcus aureus* in Los Angeles. *N engl J Med*.2005; **352**:1445-1453.
[27] Fernandez C, Gaspar C, Torrellas A, *et al*. A double blind study ,randomized ,placebo-controlled clinical trial to evaluate the safety and efficacy of mupirocin calcium ointment for eliminating nasal carriage of *Staphylococcus aureus* among hospital personnel .J *AntimicrobChemothe*r.1995;**35**:399-408
[28] Que,YA,Philippe M. *Staphylococcus aureus (including staphylococcal toxic shock*).In Mandell ,Douglas and Bennett's Principles and Practice of Infectious Diseases,7th ed. Mandell GL. , Bennette JE, Dolin R (editors).Churchill Livingstone Elsevier,2010
[29] McDonald M, *et al*. Use of a single- nucleotide polymorphism genotyping system to demonstrate the unique epidemiology of methicillin resistant *Staphyloccocus aureus* in remote Aboriginal communities .*J Clin Microbiol*. 2006; **44**:3720-3727.
[30] Munchkof WJ, et *al* .Emergence of community-acquired methicillin resistant *Staphylococcus aureus* (MRSA) infection in Queensland, Australia. *Int Infect Dis*.2003; **7**:259-267.

[31] Vlack S, *et a*l. Carriage of methicillin resistant *Staphylococcus aureus* in a Queensland Indigenous community. *Med J Aust*.2006; **184**:556-559.

[32] Ruimy R, *et al* .Comparison between geographically diverse samples of carried *Staphylococcus aureus* .*J Bacteriol*.2009; **191**:5577-5583.

[33] Kleisiari C, Panagiotaki E, Totos G, Sofianu D. Prevalence of methicillin resistant *Staphylococcus aureus* (MRSA) isolated from outpatients in Greek hospitals using the surveillance network (TSN) database-Greece.2003;4th Int symp Antimicrob Agent Resist

[34] Jeong HY, Jang SJ, Lee S,*et a*l. Antibiotic resistance of *Staphylococcus aureus* isolated from community in Korea. 2003; 4th Int Symp Antimicrob Agent Resist.

[35] Chih JC, Kuang H, Tzou YL *et al* .Factors associated with nasal colonization of methicillin resistant *Staphylococcus aureus* among healthy children in Taiwan. *J Clin Microb*. 2011; **49**:131-137

[36] National trends in *Staphylococcus aureus* infection rates: impact on economic burden and mortality over 6 –year period (1998-2003). (2007).

[37] Laupland KB ,Church DL, Mucenski M ,*et al* .Population- based study of the epidemiology of risk factors for invasive *Staphylococcus aureus infections* .*J Infect Dis*.2003;**187**:1452-1459

[38] NHSN annual update: antimicrobial - resistant pathogens associated with healthcare- associated infections: annual summary of data reported to the National Healthcare Safety network at Centre for disease Control and Prevention, 2005-2007.(2008).

[39] Hoban DJ, Biedenbech DJ, Mutnick AH, *et al*. Pathogen of occurrence and susceptibility patterns associated with pneumonia in hospitalized patients in North America: results of the SENTRY Antimicrobial Surveillance Study (2000), *Diag Microbiol Infect Dis*.2003; **45**:279-285.

[40] Tice AD, Hoalund PA, Shoultz DA .Risk factors and treatment outcomes in 0steomyelitis.*J Antimicrob Chemother*. 2003; **51**: 1261-1268

[41] Laupland KB ,Gregson DB, Flemons WW,*et a*l. Burden of community- onset bloodstream infection::population based assessment .*Epidemiol Infect*.2007;**135**:1037-1042

[42] Mupirocin ointment for preventing *Staphylococcus aureus* infection in nasal carriers. (2008).

[43] Klutmans J, Van Bellcum A, Verburgh H. Nasal carriage of *Staphylococcus aureus* epidemiology ,underlying mechanisms ,and associated risks. *Clin Microbiol Rev*.1997;**10**: 505-520.

[44] LeBllanc IJ,Pepin K,Toulouse MF,et al.Fluoroquilones and risk for methicillin-resistant *Staphylococcus aureus*,Canada.*Emerg Infect.Dis*. 2006;**12**:1398-1405.

[45] Takano TW,Higuchi T,Otsuka T, *et al*.Novel characteristics of community acquired methicillin-resistant *Staphylococcus aureus* belonging to multi locus sequence type 59 in Taiwan.*Antimicrob.Agents Chemother*.2008;**52**:837-845

[46] Campillo B upeyron C,Richardet JP .Epidemiology of hospital acquired infection in cirrhotic patients: effect of carriage of methicillin-resistant *Staphylococcus aureus* and influence of previous antibiotic therapy and norofloxacin prophylaxis.*Epidemiol Infect*.2001;**127:**443-450.

[47] DziekanGA,Hhan K,Thine G.,*et al*.Methicillin –resistant *Staphylococcus aureus* in a teaching hospital: investigation of nosocomial transmission using a matched case-control study.*J.Hosp.Infect*.2000;**46**:263-270.

[48] Centre for disease Control and Prevention.Progress in in introduction of pneumococcal conjugate vaccine-worldwide,2000-2008.MMWR .Morb Mortl.Wkly.Rep.2008;**57:**1148-1151.

[49] Bogaeret D,Belkum A van, Sluijter A,. *et al*. Colonization by *Streptococcus pneumonia* and *Staphylococcus aureus* in healthy children.*Lance*t.2004;**363**:1871-1872.

[50] Regev-Yochay,Dagan GR,Raz R, *et al.* Association between carriage of *Streptococcus pneumonia* and *Staphylococcus aureus* in children.JAMA.2004;**292:**716-720.

[51] Bogaeret D,Nouwn J,Hermans WM,Belkum A van. Lack of interference between *Streptococcus pneumonia* and *Staphylococcus aureus* in HIV-infected individuals . *J.Infect. Dis*.2006;**194**:!617-1618.

[52] Mongkolarttanothai K, Boyl S,Murphy TV,Daum RS.Novel non mecA-containing Staphylococcal chromosomal cassette composite island containing php4 and tagF genes in commensal Staphylococcal species : a possible reservoir for antibiotic resistant islands in *Staphylococcus aureus .Antimicrob.Agents Chemothe*r.2004;48:1823-1836.

[53] Pinho MG,H de Lencastre,Tomsz A .An acquired and a native penicillin- binding protein cooperate in building the cell wall of drug- resistant *Staphylococci.Proc.Natl.Acad.Sci* USA.2001;98:10886-10881.

[54] Ito TK,Okuma K,Ma,XX, Yuzwa H, Hiramatsn K .Insights on antibiotic resistance of *Staphylococcus aureus* from its whole genome: genomic island SCC.*Drug Resist.Update*.2003;6:41-52.

[55] Ma XX,Ito C, Tiensaitorn M, Jamklang P..*et al*. Novel type of *Staphylococca*l cassete chromosome mec identified in community-acquired methicillin –resistant *Staphylococcus aurerus* strains.*Antimicrob.Agents.Chemother*.2002;**46:**1147-1152.

[56] Daskalaki M,Otero JR,Sanz F,Chaves F. Bateremia due to clonally derived methicillin-resistant ,gentamicin susceptible isolates and methicillin–susceptible ,gentamicin –resistant isolates *Staphylococcus aurerus.J.Clin.Microbiol*.2007;**45**:3446-3448.

[57] **International Working Group on the Classification of Staphylococcal Cassette Chromosome Elements (IWG-SCC).**Classification of Staphylococcal cassette chromosome mec (SCCmec): guidelines for reporting novel SCCmec elements. *Antimicrob.Agents Chemother*.2008; 53:4961-4967.

[58] Ma XX,Ito T ,Chongtrakool P,Hiramatsu K. Predominance of clones carrying Panton-valentine leukocidin genes among methicillin-resistant *Staphylococcus aureus* strains in Japanese hospitals from 1979 to 1985.*J.Clin.Microbiol*.2006;**44**:4515-4527.

[59] Naimi TS,Ledell KH, Como-Sebeti K. *et al.* Comparison of community and health care-associated methicillin-resistant *Staphylococcus aureus* infection.JAMA. 2003;**290:**2976-2984.

[60] Boyl-Vavra S,Ereshefsky B,Wang CC. Daum RS.Successful multiresistant community-associated methicillin-resistant *Staphylococcus aureus* lineage from Taiepi,Taiwan,that carries either the novel Staphylococcal chromosome cassette mec (SCCmec) type VT or SCCmec type IV.*J.Clin.Microbiol*.2005;**4**3:4719-4730.

[61] Boussaud V,Parrot A,Mayaud C,.*et al*.Life threatening hemoptysis in adults with community –acquired pneumonia due to Panton-Valentine leukocidin-secreting *Staphylococcus aureus.Intensive Care Med*.2003;**29**:1840-1843.

[62] Adem PV,Montogomery CP, Hisain AN, *et al.Staphylococcus aureus* sepsis and the Waterhouse-Friderchsen syndrome in children.*N.Engl.J.Med*.2005;**353**:1245-1251.

[63] Gillet Y, Issartel B,Vanhems P,*et al.*Association between *Staphylococcus aureus* strains carrying gene for Panton-Valentine leukocidin and highly lethal necrotizing pneumonitis in young immunocompetent patients.*Lance*t.2003;**359**:753-759.

[64] Rossney AS,Shore AC,Morgan PM,. *et al*. The emergence and importation of diverse genotypes of MRSA harboring the Panton-Valentine leukocidin gene (*pvl*) reveal that *pvl* is a poor marker for community acquired MRSA in Ireland.*2007;J.Clin. Microbiol.***45**:2554-2563.

[65] Huang YC,Lin IH,Chen CJ,Lin Ty.Nasal carriage of methicillin- resistant *Staphylococcus aureus* nasal colonization among Taiwanese children in 2005 and 2006.*J.clin.Microbiol*. 2007 ;**45:**3992-3995.

[66] Park C,Lee DG, Kim SW,.*et al*. Predominance of community-associated methicillin resistant *Staphylococcus aureus* strains carrying chromosome cassette mec type IVA in South Korea. *J.Clin.Microbiol*.2007;**45**:4021-4026

[67] Yu F,Chen Z,Liu C,Zhang X,Lin X,.*et al*..Prevalence of *Staphylococcus aureus* carrying Panton –Valentine leukocidin genes among isolates from hospitalized patients in China.*Clin.Microbiol. Infect.*2007;**14:**381-384.

[68] Furtado N, Mangat PD,Frank A, *et al*. Two clindamycin susceptible (community associated) MRSA epidemics in Chicago,abstr.378.Abstr.46 Annu .Meet.*Infect.dis.Soc.Am.(*IDSA).2006. Toronto, Canada

[69] Hota B, Ellenbogen C ,Hyden MK,. *et a*l. Community associated methicillin-resistant *Staphylococcus aureus* skin soft tissue infections at a public hospital: do public housing and incarceration amplify transmission ?.*Arch.Interm.Med*.2007;**167**: 1026-1033.

[70] Tristan A,Bes AM, Meugnier H,*et al*. Global distribution of Panton –Valentine leukocidin-positive methicillin resistant *Staphylococcus aureus*,2006.*Emerg.Infect.Dis*.2007;**13:**594-600.

[71] Baba T,Takenchi F,Kuroda M, *.et al*. Genome and virulent determinants of high virulence community- acquired MRSA.*Lancet.*2007**;.35**:1819-1827

[72] Mulvey MR,MacDougall L,Cholin B, *.et al.* Community associated methicillin resistant *Staphylococcus aureus*. Canada.*Emerg.Infect.dis*.2005**;11**:844-850.

[73] Wylie JL,Nowiki DI,.Moelecular epidemiology of community –and health care-associated methicillin- resistant *Staphylococcus aureus* in Manitoba,Canada.*J.Clin.Microbiol*.2005;**43:**2830-2836.

[74] Coombs GW ,Nimmo GR,Pearson JC..*et al* .The Australian Group for Antimicrobial Resistance .Prevalence of MRSA strains among *Staphylococcus auresu* isolated from outpatients,2006.*Commun.dis.Intel.* 2009;**33:**10-20.

[75] Otter JA, French Gl. Community- associated methicillin resistant *Staphylococcus aureus* in injecting drug users and the homeless in south London.*J.hosp.Infect*.2008;**69**:198-200.

[76] Dauwalder OG,Lina G,Durang G, *et al* .Epidemiology of invasive MRSA clones in France.2006-200.*J.Clin.Microbiol*.2008;**46**:3454-3458.

[77] Benoit SR,,Estivariz C,,Mogadasy C,.*et al* .Community strains of methicillin –resistant *Staphylococcus aureus* as potential cause of healthcare-associated infections,Uruguay,2002-2004.*Emerg.Infect. Dis*.2008;**14:**1216-1223.

[78] Boyle-Vavra S,Ereshefsky B,Wang CC,Daum RS. Successful multiresistant community associated methicillin –resistant *Staphylococcus aureus* lineage fron Taipei, Taiwan, that carries ether the novel staphylococcal chromosome cassette mec (SCCmec) type VT or SCCmec type IV. *J.Clin.Microbiolol*.2005;43:4719-4730.

[79] Chen CJ, Hsueh PR,Su IH,.*et al.* Change in the molecular epidemiology of methicillin-resistant *Staphylococcus aureus* bloodstream infections in Taiwan.*Diag.Microbiol.Infect.Dis*.2009; **65**:199-201.

[80] TakanoT ,Higuchi W,Otsuka T,.*et al*. Novel characteristics of community-acquired methicillin-resistant *Staphylococcus aureus* belonging to multilocous sequence type 59 in Taiwan. Antimuicrob.Agents.Chemother.2008;52:837-845.

[81] Wang JI,Chen Sy,Wang J,.*et al* Comparison of both clinical features and mortality risk associated with bacteremia due to community-acquired methicillin-resistant *Staphylococcus aureus* and methicillin-susceptible *S.aureus*. *Clin.Infect..Dis.*2008;**46**:799-866.

[82] Nimmo GR,Cooms GW .Community–associated methicillin-resistant *Staphylococcus aureus* (MRSA) in Australia.*Int.J.Antimicrob.Agents*.2008;**31**:401-410.

[83] Ellington MJ ,Ganner M ,Warner M, *.et al.*Firsty International spread and dissemination of the virulent Queensland community associated MRSA strain .*Clin. Microbiol.Infect*. 2009; doi: 10.1111/j.1469.0691.2009.02994.x

[84] Risson DC,0'Connor ED, Guard RW, Schooneveildt JM,Nimmo GR.A fatal case of necrotizing pneumonia due to community associated-methicillin –resistant *Staphylococcus aureus.Med.J.Aust*.2007;**186**:479-480.

[85] Guss J,Kazahaya K..Antibiotic resistant *Staphylococcus aureus* in community- acquired pediatric neck abscesses. *Int.J.PediIatric.Otorhinolaryngol*.2007;**7**1:943-948.

[86] McMullen KM ,Warren DK ,Woeltje KF. The changing susceptibilities of methicillin-resistant *Staphylococcus aureus* at a Midwestern hospital: the emergence of "community associated"MRSA. *Am.J.Infect.Control*.2008;**37:**454-457.

[87] Adcock P, Pastor P ,Medley F ,Patterson J, Murphy T .Methicillin resistant *Staphylococcus aureus* in two childcare centers.*J.Int.Infect.Dis*.1998;**178**:577-580.

[88] Crum NF ,Lee RU, Thornton M, *et al.* Fifteen -Year study of the changing epidemiology of methicillin-resistant *Staphylococcus aureus.Am.J.Med*.2006;**119**:943-951.

[89] Como-Sabetti K ,Harriman K,Juni B, *et al*. Methicillin resistant *Staphylococcus aureus* at Canoe Camp.*Emerg.Infect.Dis*.2006;**12:**1759-1761.

[90] Huang H,Cohen SH ,King JH, *et al.* Injecting drug use and community –associated methicillin resistant *Staphylocoiccus aureus infection.Diagn.Microbiol.Dis*.2008;**60**:347-350.

[91] Roberts JR ,McCawley L ,Laxton M, Trumbo H. Genital community associated methicillin –resistant

[92] *Staphylococcus aureus* infection can be a sexually transmitted disease.*Ann.emerg.Med*.2007;**50**:93-94.

[93] Healy CM, Hulten KG, Palazzi DL, Cambell JR, Baker CJ. Emergence of new strains of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit .*Clin.Infect. Dis*.2004;**39:**1460-1466.

[94] McAdam RM ,Mazuchowski ME,Ellis MW ,Rajnik M. .Spread of methicillin resistant *Staphylococcus aureus* USA 300 in a neonatal intensive care unit.*Pediatr.Int*..2008;**50**.810-815.

[95] Campbell AI, Bryant KA, Stover B ,Marshall GS .Epidemiology of methicillin-resistant *Staphylococcus aureus* at a children's hospital.*Infect.Control.Hosp.Epidemiol*.2003;**24**:427-430.

[96] Nguyen DM,Mascola I,Bancroft E. Recurring methicillin-resistant *Staphylococcus aureus* infections in a football team.*Emerg.Intfect.Dis.*2005;**11**:526-532.

[97] Knehnert MJ,Kruszon-Moran D,Hill HA, *et al.* Prevalence of Staphylococcus aureus nasal colonization in the United States.*J..Infect.Dis*.2006;**193**:172-179.

[98] 96. Tong SY ,McDonald MI,Holt DC ,Currie BJ. Global implications of the emergence of community associated methicillin-resistant *Staphylococcus aureus* in indigenous population.*Clin.Infect.Dis*.2008;**46**:1871-1878.