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Research Article

SKIN AND SOFT-TISSUE INFECTIONS CAUSED BY COMMUNITY-ACQUIRED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS - STUDY OF MRSA FROM KANYAKUMARI GOVT. MEDICAL COLLEGE, ASARIPALLAM

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ABSTRACT

Community acquired infection is different from Hospital acquired infection. Because MRSA is common in Hospital acquired infection, vice versa very rare in Community acquired infection. When MRSA is occurring in Community that to Skin ulcer, it leads for Drug resistance in community. It eill/may sopread to community people. This will leads to drug resistance among common infection. Our idea is to find out any presence of MRSA community among skin ulcer and to identify aetiological factors for Community Acquired Infection in skin ulcer.

INTRODUCTION

Community-acquired methicillin-resistant Staphylococcus aureus (MRSA) infection has become epidemic. Skin and soft-tissue infections (SSTIs) are the most frequent forms of the disease. Obtainment of culture specimens is important for documentation of the presence of MRSA and for susceptibility testing to guide therapy. Purulent lesions should be drained whenever possible. In areas where community-acquired MRSA isolates are prevalent, uncomplicated SSTI in healthy individuals may be treated empirically with clindamycin, trimethoprim-sulfamethoxazole, or long-acting tetracyclines, although specific data supporting the efficacy of these treatments are lacking. In healthy patients with small purulent lesions, drainage alone may be sufficient. In patients with complicated SSTI requiring hospitalization or intravenous therapy, vancomycin is the drug of choice because of the low cost, efficacy, and safety. Linezolid, daptomycin, and tigecycline are also effective, although published studies on the last 2 agents for the treatment of SSTI due to MRSA are more limited. Dalbavancin, telavancin, and ceftobiprole are investigational agents that may expand our therapeutic options for the treatment of SSTI caused by MRSA.

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Methicillin resistant Staphylococcus aureus (MRSA) has been recognized as an important pathogen in nosocomial settings for many years. More recently, serious methicillin resistant S aureus infections from the community have been described in children in Minnesota and North Dakota who have died from these infections in 1997, 1998 and 1999 (Herold, 1998; MMWR, 1999). The children were noted to have matching strains of bacteria despite having no epidemiologic links and no hospital exposure. Since these initial reports, several groups have reported outbreaks of MRSA infections occurring outside of healthcare facilities, involving athletes, military personnel, and inmates in correctional facilities (Lindenmayer, 1998; MMWR, 2003a,b; Pan, 2003; Zinderman, 2004; Kazakova, 2005; Nguyen, 2005; Aiello, 2006) leading to the term community-acquired MRSA (CA-MRSA). CA-MRSA outbreaks in men who have sex with men (MSM) have been recently reported in several US cities, possibly associated with methamphetamine use and risky sexual behavior (Lee, 2005). This review summarizes the current knowledge of the epidemiology, clinical manifestations, diagnosis, and management of CA-MRSA infections with an emphasis on the HIV patient

First recognized in 1960, methicillin-resistant Staphylococcus aureus (MRSA) was considered to be a medical oddity. Now, MRSA is the most common nosocomial bacterial pathogen

isolated in many parts of the world. In the past, community-acquired MRSA (CA-MRSA) infections tended to occur in patients with frequent health care contact or, less commonly, in specific groups of patients, such as intravenous drug users. During the past decade, however, there has been a dramatic change in the epidemiology of community-onset infections caused by MRSA. Young, healthy individuals who lack classic risk factors for MRSA infection are often affected. CA-MRSA infections, which were first described in small series of adult and pediatric patients presenting with skin and soft-tissue infections (SSTIs), pneumonia, or bacteremia have become a significant public health threat in the United States and abroad]. In the United States, a single clone of CA-MRSA (USA 300 ST-8) has become the most prevalent cause of staphylococcal SSTI acquired in the community and has moved into the inpatient setting, causing not only SSTIs but also invasive diseases

CA-MRSA: A Blurred Definition

In the United States, strains of CA-MRSA carry the staphylococcal cassette chromosome (SCC) mec type IV and most carry the gene for Panton-Valentine leukocidin (PVL) from an epidemiologic standpoint; the definition of CA-MRSA is problematic. Most studies have used a time-based definition (e.g., infections recognized within 24–72 h after hospital admission) .However, S. aureus can persist as a colonizer for months or years, leading to misclassification of the source. Indeed, some "community-onset" infections may in fact be caused by hospital-acquired strains and vice versa CA-MRSA is invading US hospitals]. Thus, the distinction between CA-MRSA and hospital-acquired MRSA (HA-MRSA) is blurring. Nevertheless, the presence of SCCmec type IV and the presence of PVL have been useful molecular markers of CA-MRSA strains

Host and Risk Factors for CA-MRSA SSTI

CA-MRSA causes infection in many different hosts, ranging from healthy children and adults to people with underlying diseases and extensive health care contact. CA-MRSA infections have been reported in healthy newborns healthy children], healthy adults pregnant women postpartum women intravenous drug users prisoners homeless persons, men who have sex with men athletes tattoo recipients soldiers .Native American communities and Pacific Islanders .More groups will surely be added to this list. SSTIs caused by CA-MRSA and those caused by HA-MRSA are different in several respects SSTIs due to CA-MRSA predominantly affect children, young adults, and middle-aged adults .The median age for adults infected with CA-MRSA ranges from 20 to 47 years .SSTIs due to CA-MRSA are more frequent among males and nonwhite individuals. Many patients with CA-MRSA infections do not have recognized risk factors for the acquisition of MRSA. Spider bites are commonly reported by patients who have SSTI caused by CA-MRSA .This is not because a spider bite has actually occurred but because the cutaneous lesion of CA-MRSA infection can be similar in appearance to that of a spider bite.

Direct contact with infected patients colonized subjects or a contaminated environment is implicated in the transmission of CA-MRSA infection. Crowding and sharing of personal items appear to be important factors. Transmission has occurred through activities in which direct contact and turf abrasions are common—for example, among football player's wrestlers, and military trainees. Recently, heterosexual transmission was described. Interfamilial spread of CA-MRSA is frequent and most certainly accounts for an increasing number of cases .In 10%–18% of cases; MRSA-infected patients recall having close contact with persons who had similar skin infections (e.g., boils). This percentage is often higher in closed communities. In addition, as with HA-MRSA, previous colonization with CA-MRSA was related to subsequent development of infection.

PVL: A Major Virulence Factor in SSTI?

In contrast to nosocomial strains of MRSA, most strains of CA-MRSA carry genes for PVL. PVL-positive strains of S. aureus are associated with tissue necrosis and abscess formation .However, it is unclear whether PVL is mediating these effects .The role of PVL as a major virulence factor is more established in other infections, such as pneumonia . Other than genes for PVL, CA-MRSA strains may carry exotoxin genes, which may result in significant skin damage .For example, exfoliative toxin genes (eta and etb) have been described in children with impetigo and in patients with toxic-shock syndrome caused by CA-MRSA

Clinical Presentation of SSTI Caused by CA-MRSA

CA-MRSA strains can produce a variety of SSTIs, ranging from impetigo to life-threatening necrotizing fasciitis. Abscesses and cellulitis are the most common lesions .Approximately 50%–75% of patients present with abscesses, and 25%–50% with cellulitis .These infections commonly present as single lesions involving the extremities. Systemic signs of inflammation are variable; fever and leukocytosis are often absent in patients with abscess. Abscesses are frequently accompanied by central necrosis and surrounding cellulitis. Furuncles (boils) are very characteristic are often multiple, and frequently occur in outbreaks.. Lesions can be primarily necrotic and can progress to abscesses and cellulitis. Recurrence is common and is probably related to high rates of MRSA colonization among these patients .Folliculitis caused by CA-MRSA is a less frequent form of presentation, usually with erythe-matous folliculocentric pustules, which can compromise uncommon localizations (e.g., periumbilical) .Impetigo and scalded-skin syndrome due to CA-MRSA (usually in children) are also uncommon forms of the disease .Pyomyositis and myositis due to CA-MRSA are uncommon infections usually involving the lower extremities or pelvis. Pain and fever are almost invariably present. Unlike with viral myo-sitis, an increase in WBC count is common, and creatine kinase levels are often within normal range. Some patients have associated bacteremia and septic shock; muscle drainage is required in most cases.

A subacute form of necrotizing fasciitis has occurred in middle-aged patients, usually associated with a history of intravenous drug use or comorbid conditions, such as hepatitis C or diabetes. Importantly, fewer than half of these patients received a preoperative diagnosis of necrotizing fasciitis. Infrequently, strains of CA-MRSA can produce systemic syndromes affecting the skin, such as staphylococcal toxic-shock syndrome, Waterhouse-Friderichsen syndrome and purpura fulminans.

Requirement of hospitalization for adult patients with SSTIs due to CA-MRSA is variable, ranging from 16% to 44% of cases .The outcomes at 30 days for patients with SSTI caused by CA-MRSA do not appear to be different from those for patients with infections caused by community-acquired methicillin-susceptible S. aureus (CA-MSSA) .In general, the prognosis for patients with SSTI due to CA-MRSA is very good. Death is quite uncommon, and the rate is certainly lower than that among patients infected with nosocomial MRSA .

Therapy for CA-MRSA

Surgical drainage. Surgical drainage is crucial for the cure of furuncles and soft-tissue abscesses and, therefore, is recommended for the treatment of these conditions in all patients .Incision and drainage are required for ~80% of patients presenting to the emergency department with acute, purulent SSTI Patients with abscesses caused by CA-MRSA infection are frequently cured with drainage alone. Separate observational studies noted that a significant proportion of patients who underwent drainage and received inadequate or no antibacterial therapy were cured .A recent randomized clinical trial reported cure rates of >85% for patients who underwent drainage and received placebo, as well as for those who underwent drainage and received cephalexin.

The correlation between abscess size and outcome remains controversial. Children with abscesses that are >5 cm in diameter were more likely to experience failure of incision and drainage therapy without effective antibiotic therapy .Such an association was not observed in adults .Given the lack of prospective studies, clinical judgment should determine for which patients surgical drainage alone is appropriate. For example, healthy, reliable, nondiabetic patients with small lesions and no systemic signs of infection for whom close follow-up can be achieved are certainly candidates for surgical drainage alone.

Antibiotic therapy. Despite the fact that many patients with drainable lesions can be cured with surgical drainage alone, effective antibacterial therapy may improve cure rates even further, especially among patients with large abscesses or cellulitis. Cure rates among patients with SSTI due to CA-MRSA who received active antibacterial therapy were higher than those among patients who received inactive therapy (95% vs. 87%, respectively) .In geographic areas with a high prevalence of CA-MRSA (e.g., >15% of community S. aureus isolates show methicillin resistance), empirical therapy should not be based solely on clinical characteristics. Clinical and epidemiological factors do not adequately discriminate between CA-MRSA and CA-MSSA in patients with SSTI.

For decades, vancomycin has been the standard therapy for patients with SSTI due to MRSA. In addition, vancomycin is the antibiotic most extensively studied in clinical trials involving patients with SSTI. More than 2000 patients with SSTI, including >500 patients with MRSA infection, were given treatment with vancomycin in randomized, controlled trials .Cure rates among evaluable patients infected with MRSA in phase 3, randomized, double-blind trials have ranged from 69% to 90% . Vancomycin has also been shown to be relatively safe.

Linezolid, an oxazolidinone with bacteriostatic activity, can be administered twice a day, either orally or intravenously with identical bioavailability. The efficacy of linezolid therapy for patients with complicated SSTI due to MRSA was studied in an open-label, randomized, controlled trial in which 285 patients in the microbiologically evaluable population had MRSA infection. Although the trial did not find an overall difference in efficacy between patients with complicated SSTI treated with vancomycin versus those treated with linezolid, linezolid treatment was found to be superior to vancomycin treatment in almost all study populations, including the subgroup of patients with MRSA infection .It should be noted that, in this open-label study, vancomycin achieved lower cure rates among patients infected with MRSA (~67%) than were observed in other studies in which the drug was used as a comparator. Another study comparing linezolid therapy with vancomycin therapy for patients with various MRSA infections included 64 evaluable patients with SSTI. Cure rates were 79% and 73% for linezolid treatment and vancomycin treatment, respectively. Finally, in a study of patients with diabetes-associated foot infections, 18 patients with MRSA infection were evaluable, and 13 (72%) were cured .Pediatric studies have provided only limited evidence supporting the use of linezolid therapy for children with complicated and uncomplicated SSTIs due to MRSA.

Daptomycin is a cyclic lipopeptide that is rapidly bactericidal and active against almost all gram-positive cocci, including MRSA .Intravenous daptomycin was approved by the FDA in 2003 for the treatment of patients with complicated skin and skin-structure infections, including those infected with MRSA. Daptomycin treatment was noninferior to vancomcyin treatment in 2 registrational studies involving patients with complicated skin and skin-structure infections. A total of 64 patients with MRSA were microbiologically evaluable .In this group of patients, cure rates for daptomycin treatment and vancomycin treatment were comparable (75% vs. 69.4%, respectively).

Tigecycline is a broad-spectrum glycylcycline designed to avoid both tetK (tetracycline-specific efflux-mediated) resistance and tetM (target modification) class resistance to tetracyclines .Tigecycline was recently approved by the FDA for the treatment of patients with SSTI, including those infected with MRSA. In 2 registrational studies, 65 patients with MRSA were microbiologically evaluable .Cure rates among these patients were 78.4% and 76.5% for tigecycline treatment and vancomycin treatment, respectively. Importantly, most strains of MRSA in these tigecycline studies were SCCmec type IV and PVL positive

Investigational Agents

Dalbavancin is a semisynthetic lipoglycopeptide with a long half-life compatible with weekly dosing Dalbavancin is bactericidal against gram-positive cocci, including MRSA. In a phase 3 study comparing dalbavancin therapy with intravenous or oral linezolid therapy for 14 days, 278 patients with MRSA infection were enrolled and received at least 1 dose of study medication .Although cure rates in these patients were not specifically reported, eradication of MRSA was achieved in 91% of patients who received dalbavancin treatment and in 89% of those who received linezolid treatment.

Telavancin is a lipoglycopeptide with a dual mechanism of action and is rapidly bactericidal against gram-positive cocci, including MRSA .Registrational phase 3 studies comparing telavancin therapy with vancomycin therapy in patients with SSTI included 579 clinically evaluable patients with MRSA

infection. In this group of patients, telavancin treatment showed a trend toward superiority when compared with vancomycin treatment (90.6% vs. 86.4%) . It is of note that this program enrolled the largest number of patients infected with MRSA of any clinical trial and that most strains of MRSA were SCCmec type IV and PVL positive. Oritavancin is a semisynthetic glycopeptide, has a long half-life, and is rapidly bactericidal against gram-positive cocci, including MRSA .Although 2 phase 3 studies of oritavancin treatment were completed some years ago, complete release of the results is still pending. In one of these studies, 33 patients with MRSA infection were clinically evaluable; cure rates were 74% and 80% for oritavancin treatment and vancomycin treatment, respectively.

Ceftobiprole is a broad-spectrum third-generation cephalosporin that is active against both MSSA and MRSA infections .A phase 3 study compared ceftobiprole therapy with vancomycin therapy for patients with complicated skin and skin-structure infections, including 121 patients with MRSA infection in the microbiologically evaluable population. In patients infected with MRSA, cure rates were 91.8% for ceftobiprole and 90% for vancomycin. Other investigational agents active against MRSA are in development, and phase 2 and 3 studies involving patients with SSTI are being conducted. Among these agents are iclaprim, a new selective dihydrofolate inhibitor, and ceftaroline, a new broad-spectrum cephalosporin

Off-Label Agents: Evidence of Efficacy

With the epidemic of CA-MRSA infection, there is an increasing off-label use of antibiotics, such as trimethoprim-sulfamethoxazole (TMP-SMX), clindamycin, and long-acting tetracyclines. Unfortunately, there are no randomized, controlled trials to support the use of these antibiotics for patients with skin infections caused by MRSA. TMP-SMX has not been approved by the FDA for the treatment of S. aureus infections]. However, in vitro data show that TMP-SMX is bactericidal against strains of CA-MRSA .In the early 1990s, a randomized, controlled trial compared TMP-SMX treatment with vancomycin treatment for a variety ofS. aureus infections. In this trial, 32 patients with skin infections caused by S. aureus were evaluated for the efficacy of treatment with TMP-SMX or vancomycin, and all patients with MRSA infection were cured.

In a Boston outpatient clinic, the increasing empirical use of TMP-SMX over time was paralleled by improving rates of clinical resolution for patients with SSTI. TMP-SMX in combination with rifampin was also used successfully for a limited number of patients with CA-MRSA infection .Whether TMP-SMX is effective to treat group A streptococci, also a common cause of SSTI, is not known .When group A streptococci are part of the differential diagnosis, other treatment alternatives (e.g., clindamycin) should be considered.

Although FDA approved for the treatment of serious infections caused by S. aureus, clindamycin is not specifically approved for the treatment of MRSA infection because of the high level of resistance to clindamycin among HA-MRSA strains .With the epidemic of CA-MRSA infection, clindamycin is now commonly used to treat SSTI. Evidence to support the use of clindamycin for patients with SSTI due to CA-MRSA, however, is limited to children. In one observational study, >300 children received empirical intravenous therapy, and 207 were then given an oral formulation; all children were cured, regardless of the antibiotic therapy.

In theory, clindamycin use may have advantages over more-traditional treatments because of the drug's ability to inhibit protein synthesis and, thus, to turn off toxin production in CA-MRSA .The evidence for effective use of long-acting tetracyclines (doxycycline and minocycline) in patients with SSTI due to MRSA is quite limited. In one case series, 15 of 16 patients were cured; 1 discontinued drug use because of an adverse event. Two patients given treatment with minocycline also received concomitant treatment with rifampin. In a different study, 5 patients with CA-MRSA infection were cured with 4–12 weeks of doxycycline therapy. Tetracyclines are not recommended for children <8 years of age or pregnant women. Rifampin is commonly prescribed in combination with other antibiotics for treatment of SSTI due to MRSA. However, there are virtually no data showing a clinical benefit from this practice. Therefore, for most patients with SSTI caused by MRSA, adjunctive therapy with rifampin cannot be recommended.

CA-MRSA strains differ from nosocomial MRSA strains in their susceptibility to different classes of antibiotics .CA-MRSA strains are usually susceptible to TMP-SMX, rifampin, and gentamicin .Most strains are also susceptible to clindamycin .although resistance to the drug is variable and, in some areas, appears to be increasing. Resistance to clindamycin can be inducible (i.e., inducible macrolide-lincosamide-streptogramin B resistance). To detect inducible resistance to clindamycin, a D-zone test should be performed the relationship between inducible resistance to clindamycin and treatment failure is poorly defined

CA-MRSA strains are generally susceptible to tetracyclines. Resistance to the long-acting tetracyclines doxycycline and minocycline is probably overestimated because these drugs usually are not tested in vitro. Many laboratories report only tetracycline-specific susceptibility. In CA-MRSA strains, resistance is mostly associated with tetK , which encodes a tetracycline-specific efflux pump. This pump does not efflux doxycycline and minocycline. Thus, the long-acting tetracyclines may be active even when resistance to tetracycline is detected. Finally, resistance to macrolides and quinolones is common among strains of CA-MRSA .Given the different patterns of resistance between CA-MRSA and HA-MRSA, obtainment of culture samples from patients who present with SSTI should be done.

Decolonization

There are no data to support decolonization (e.g., nasal mupirocin and chlorhexidine body washes) for patients infected with MRSA. An expert panel in collaboration with the CDC has suggested that decolonization may be reasonable in 2 clinical situations: (1) for patients with multiple documented recurrences of MRSA infection and (2) for ongoing MRSA transmission in a closely associated and well-defined cohort of individuals (e.g., a household) .Other recommendations for prevention among patients with SSTI due to CA-MRSA can be found on the CDC Web site

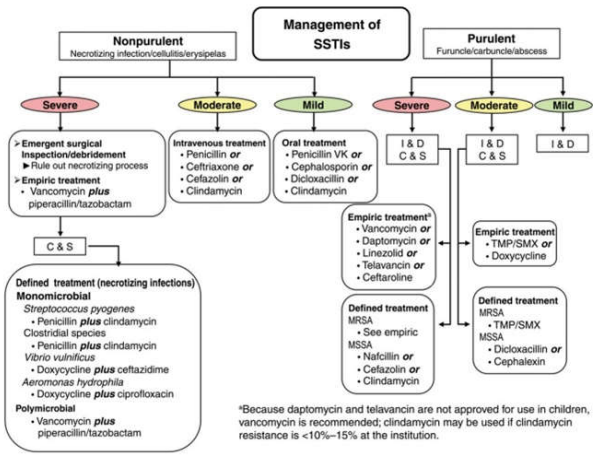

Table 1 Summary of Studies of Community-Acquired Methicillin-Resistant Staphyloccus Aureus Among HIV-Positive Persons

Study	Epidemiologic Trends	Risk Factors for MRSA	Protective Factors against MRSA
Mathews, 2005	6.2-fold increase in cases from 2000–2003 among an HIV cohort at the Owen Clinic, San Diego	• MSM, IDU, or both as HIV transmission risk factors • High HIV viral load • cd4<50 cells/mm^3 • Public bath/sauna use	• TMP/SMX use
Lee, 2005	Cross-sectional study in MSM	• Methamphetamine use • Sexual partner with a skin infection • Recent use of β-lactam antibiotics	• TMP/SMX use • Condom use
Crum-Cianflone, 2006	17-fold increase in cases from 2003–2005 among a HIV cohort in San Diego	• History of syphilis • Low current cd4 count • High maximum viral load	• TMP/SMX use*

Table 2 Clinical Manifestations of Community-Acquired Methicillin-Resistant Staphyloccus AureusInfections

Skin/Soft Tissue Infections
• Abscess
• Furuncle
• Carbuncle
• Folliculitis
• Impetigo
• Paronychia
• Cellulitis (usually in association with one of the above soft tissue infections)
• Wound infection
Other Clinical Manifestations
• Pyomyositis (abscess in a large skeletal muscle)
• Necrotizing fasciitis
• Bone infection (osteomyelitis)
• Joint infections (septic arthritis)
• Bacteremia
• Toxic shock syndrome
• Endocarditis
• Necrotizing pneumonia
• Any type of infection

MATERIALS AND METHODS

Laboratory Methods

Oxacillin susceptibility testing was performed with 5-µg oxacillin disks incubated at 30°C for 24 h on Mueller-Hinton agar, and with 5-µg oxacillin disks incubated at 37°C for 24 h on Mueller-Hinton agar supplemented with NaCl 4% w/v, in accordance with the guidelines of the Comité de l'Antibiogramme de la Société Française de Microbiologie (CA-SF. Susceptibility to cefoxitin was determined without the special conditions used for oxacillin testing [15]. A suspension of organisms adjusted to 0.5× MacFarland standard was diluted 1:100 and inoculated on to Mueller-Hinton agar by streaking over the agar surface. Cefoxitin 30-µg disks were applied and the plates were incubated at 37°C for 24 h. An isolate was considered to be an MRSA strain if the cefoxitin inhibition zone diameter was ≤ 21 mm [3]. *S. aureus* strains ATCC 43300 (heterogeneous oxacillin resistance) and ATCC 25923 (oxacillin-susceptible) were used as quality control strains. Of the 465 isolates tested, 115 were *mecA*-positive by PCR, and 350 were negative The two oxacillin disk methods with agar incubated at 30°C, and with Mueller-Hinton agar supplemented with NaCl 4% w/v incubated at 37°C, agreed with each other, but falsely identified 11 isolates as oxacillin-susceptible (sensitivity 90.4%) and three isolates as oxacillin-resistant (specificity 99.1%) in comparison with PCR. The cefoxitin disk test detected oxacillin resistance correctly in all but four isolates (sensitivity 96.5%), and there were no false-resistant results (specificity 100%). The 11 resistant isolates reported as susceptible by the oxacillin method were different from the four resistant isolates reported as susceptible by the cefoxitin method. Hence, in total, there were 18 discordant results (three with MSSA and 15 with MRSA) between the oxacillin disk methods and the cefoxitin disk method. Combining the results of tests with both cefoxitin and oxacillin would give a sensitivity of 100% and a specificity of 99.1%. The greater reliability of tests with cefoxitin disks confirmed earlier studies which showed that cefoxitin disk tests, without modification to conditions to improve expression of resistance, are as reliable or more reliable than oxacillin disk tests for the detection of methicillin resistance in *S. aureus* [3, 4, 5].

Inclusion Criteria

Op cases coming in surgical op and Dermatovenerology for the first time

Exclusion Criteria

All in patients and repeated OP patients having high antimicrobial therapy

RESULTS

Study period: January 2018 to December 2018
Total cases studied:

Month	No of cases	MRSA Negative	MRSA Positive
January	12	11	1
February	08	08	0
March	12	11	1
April	04	4	0
May	15	14	1
June	10	10	0
July	09	07	2
August	13	11	2
September	06	6	0
October	11	10	1
November	12	10	2
December	13	12	1
	125	113	11

Analysis

Out of 125 cases 113 were found to be Negative MRSA.
11 were found out to positive MRSA
MRSA in community is dangerous

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