

EVALUATION OF ANTIBIOTIC RESISTANCE IN METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUSRusmin Nihala R.^{1*}, Dr. Lita Susan Thomas¹, Dr. Shijikumar P. S.², Dr. Sirajudheen M. K.³ and Sherin A.⁴¹Department of Pharmacy Practice, Jamia Salafiya Pharmacy College, Pulikkal, India -673637.²Department of Pharmaceutical Analysis, Jamia Salafiya Pharmacy College, Pulikkal, India-673637.³Department of Pharmaceutics, Jamia Salafiya Pharmacy College, Pulikkal, India-673637.⁴Department of Pharmaceutical Chemistry, Jamia Salafiya Pharmacy College, Pulikkal, India-673637.***Corresponding Author: Rusmin Nihala R.**

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ABSTRACT

Methicillin Resistant Staphylococcus Aureus is a form of transferable bacterial infection that is resistant to numerous antibiotics. The Aim of the Review is to study the Evaluation of Antibiotic Resistance in Methicillin Resistant Staphylococcus Aureus. Methicillin Resistant Staphylococcus has emerged as a nosocomial pathogen of major worldwide importance and is an increasingly frequent cause of community acquired infection. Staphylococcus Aureus is a well adapted human pathogen, capable of living freely in the environment and spreading from person to person. In recently, Hospital and Community acquired infection with staphylococcus have increased and also increased Antibiotic resistance. These resistant Staphylococcus Aureus can cause various clinical situations. The widespread use of antibiotics have undoubtedly accelerated because of the Evolution of Staphylococcus Aureus, which the multiple resistant gene has become able to survive almost all antibiotic families. All the strains of Staphylococcus Aureus when evaluated show the potent Antibiotic resistant activity against Methicillin. Thus it is resistant to numerous class of antibiotics.

KEYWORDS: Antibiotics, Methicillin Resistant Staphylococcus Aureus, Staphylococcus Aureus, community acquired, Hospital acquired.

INTRODUCTION

Methicillin Resistant Staphylococcus Aureus (MRSA) initially described in the year 1960s, emerged in the last decade as a cause of nosocomial infections responsible for potentially progressive fatal diseases, including potentially progressive pneumonia, osteomyelitis, toxinoses.^[1] Methicillin Resistant Staphylococcus Aureus is a bacterium that effects infections in different parts of the body. It is more difficult to treat than most strains of staphylococcus aureus, because it is resistant to some commonly used antibiotics including methicillin, amoxicillin, penicillin, oxacillins. The symptoms of Methicillin Resistant Staphylococcus Aureus depends on where you are infected. It causes mild skin infections such as wounds, boils. Also cause serious infections n lungs, urinary tract, infected surgical wounds, blood streams. Most of the Methicillin Resistant Staphylococcus infections are not serious, some can be fatal. Many public health experts alarmed the spread of different types of MRSA, because it is difficult to treat, MRSA is some time called as “superbug”. Methicillin Resistant Staphylococcus infection are commonly seen in people who have weak immune system, person who are in hospitals, nursing homes and other health care centers.

Types

Methicillin Resistant Staphylococcus Aureus is a common problem in Health facilities, sports, clinics and the community. MRSA shows that healthy people who have not been hospitalized. This type of MRSA is commonly called community associated Methicillin Resistant Staphylococcus Aureus. The MRSA associated with hospital are referred as Hospital acquired Methicillin Resistant Staphylococcus Aureus.^[2] The infections in patients reporting to emergency department, and intncive care units (ICU).^[3] Europe has high prevalence of Methicillin Resistant Staphylococcus Aureus about 44%. Hospital associated MRSA has high prevalence in North Africa, Australia^[4], Middle east about 25%. Community associated Methicillin Resistant Staphylococcus Aureus has high prevalence in United states, Canada.^[5]

Causes

The Staphylococcal disease is mainly caused by Antibiotic resistant Staphylococcus Aureus, mainly Methicillin Resistant. Staphylococcus is the most common causes of skin infections.

Risk Factors

The Risk factors associated with Methicillin Resistant Staphylococcus Aureus infections are mainly Advanced Age, Previous Hospitalisation, Long Hospitalisation, Stay in intensive care unit, chronic medical illness, Prolonged Antimicrobial use, lack of cleanliness.^[6] The risk factor associated with hospital acquired infections are length of stay in hospital, exposure to people infected with MRSA, exposure to antibiotics. Risk factors for community acquired infection include exposure to an individual with MRSA, skin to skin contact, lack of cleanliness. CA MRSA are more likely to develop skin and soft tissue infection.^[7]

Clinical Presentation

Staphylococcus Aureus is responsible for Broad range of infections in everybody system. Staphylococcus infections are more pyrogenic. The Methicillin Resistant Staphylococcus Aureus infected area will be local tissue destruction, pain, pus production, inflammation, swelling are occur.^[8] Cutaneous skin infections can invade deeper tissues and become expansive. The clinical spectrum of MRSA infections has long been recognized and effective treatment strategies have been developed. Patient with MRSA have not responded to most of the antibiotics used at a time (Beta lactum) although reported to be effective in vitro and in effective invivo. The most common clinical infections caused by MRSA included infections of surgical wounds, pelvic abscesses, osteomyelitis, infections of joints, nosocomial pneumonia.^[9] If a person is infected with MRSA which on radiographs a wood like feelings up on palpitation of the area is noted.

Diagnostic Test For Methicillin Resistant Staphylococcus Aureus

The first step in confirming methicillin-resistant Staphylococcus Aureus is to isolate Staphylococcus Aureus from a blood, tissue or pus culture. If Staphylococcus Aureus is not found in a culture, the individual is unlikely to have MRSA.^[10] The only time a culture would yield a false negative result would be if the patient had recently received several days of anti-staphylococcal medication in the days immediately prior to the culture. You can find the Staphylococcus Aureus in a culture medium, then confirmatory tests can show if the body is resistant to antibiotics. Sensitivity tests do not discriminate between strains of Aquired-MRSA Hospital and Community Aquired-MRSA; and clinically, it is often irrelevant to isolate methicillin-resistant Staphylococcus aureus acquired in the community of methicillin-resistant Staphylococcus aureus acquired in the hospital because sectioning is not governed by the identification of the strain. Cultures are performed when the infection does not respond to sectional isolation with incision and drainage or if the first-line sectional isolation of MRSA plus streptococcus continues to show resistant infection. Cultures can also be obtained when a group of infections is reported, when the local infection is severe, or when there is a systemic infection.

Treatment

The treatment for MRSA will depend on Type and location of the infection, the severity of the symptoms, the antibiotics to which MRSA strains responds. A Doctor will prescribe a medication suitable for the specific infection that occurs. Some people stop taking their medication after the symptoms disappear, but this can increase the risk of the infection coming back and becoming resistant to treatment. When MRSA infection suspected clinical practice guidelines, appropriate medical care should be taken.^[11] If any cellulitis is found antibiotics may be added, usually begins with trimethoprim-sulfamethoxazole. flouroquinolone use is associated with an increased risk of tendinopathy and joint lesions.^[12]

Prevention

For healthy individuals without signs and symptoms of infection, the basic hygiene practices are to prevent MRSA infection. Preventions include Practice good hygiene, Keep your hand clean by washing them thoroughly with soap and water, donot share personal items such as towels, Always take all your antibiotics medicine as prescribed by your doctor, Donot save any antibiotics, and donot use antibiotics that were prescribed for some one else.^[13]

METHODOLOGY

Search Strategy

Pub Med, science direct, wikipedia, journals, books and articles are used for searching the evaluation of antibiotic resistance in Methicillin Resistant Staphylococcus Aureus. The infectious disease, clinical management, and epidemiology and the website of the centers for disease control and prevention were also reviewed. The individual of all age groups, different languages, and all types of study designs are included in this search strategy.

Search Terms

The search terms included in Methicillin Resistant Staphylococcus Aureus, Staphylococcus Aureus. The community acquired and hospital acquired Methicillin Resistant Staphylococcus Aureus epidemiology, skin and soft tissue infection recognition and response, information on Methicillin Resistant Staphylococcus Aureus carriers, pharmacological treatment, clinical hygiene, antibiotic resistant activity against Methicillin Resistant Staphylococcus Aureus.

Review Procedure

From previous studies of evaluation of antibiotic resistance in Methicillin Resistant Staphylococcus Aureus, the studies were found to be heterogeneous, as they were conducted in different countries used different definitions and different methods of collected data. So that the statistical view point is not analyzed, the study have been reviewed based on the parameters like Types, Causes, Risk factors, Clinical manifestation, Treatment and prevention being a narrative review.

Inclusion and Exclusion Criteria

The inclusion criteria included the following

- All individuals with an active surgical site infection,
- Infected skin ulcers,
- Burns,
- Skin abscess
- Diabetic foot ulcers.

The exclusion criteria includes the following

- Lack of informed consent,
- Patients admitted in intensive care units.

RESULT AND DISCUSSION

Bart N. Green MSEd et al. found that the acquired community was more likely to develop compared to the methicillin-resistant *Staphylococcus Aureus* acquired in the hospital. Community-acquired MRSA colonized individuals and their close contacts are more likely to develop skin and soft tissue infections. There is an anterior nostril MRSA rate of 1.5% among un-institutionalized adults in the United States. This rate may be much higher among certain adult populations, such as 3% for U.S. soldiers, 7% for the United States. The incidence of CA-MRSA has recently increased among people who are generally considered to be healthy (e.g. athletes and soldiers), with community tribes being introduced to hospitals and HA-MRSA present in the community. The distinction between Hospital Acquired-MRSA and Community Acquired-MRSA is therefore blurred, and the common settlement of the hospital is likely to become the norm. In clinics where post-operative patients interact with non-operative patients, there is an increased likelihood that both Hospital Acquired-MRSA and Community Acquired MRSA are present. Therefore, doctors must be vigilant for both forms and take appropriate infection control measures. More than 50% of the MRSA strains are resistant to drugs such as macrolides, lincosamides, fluoroquinolones and aminoglycosides. and 30% are resistant to trimethoprim sulfamethoxazole.

The main source of methicillin-resistant *Staphylococcus aureus* infection was isolated from pus samples that constitute 71.6%. According to his data, the patient with a surgical wound had the highest frequency of MRSA (35.6%). Patients with abscess, burns, diabetes had a frequency of 25.4%, 20.3% and 18.6% respectively.

According to their data, the isolation rate of *S. aureus* was 82 (63.1%) of 130 samples. Its finding is similar to a recent finding from a study in Ethiopia. However, the isolation rate was significantly higher in patients younger than 18 years and significantly lower in patients older than 61 years. The age-related variation observed in the frequency of isolation of *S. aureus* has been reported elsewhere. It is true that it should be recognized that the referenced studies used different age groups; Therefore, comparisons are at a general or trend level. More importantly, the factors that contribute to the differences observed remain unclear. In addition, the isolation rate

was higher in the discharge of wounds and abscesses (100%), and the samples of pus and blood had isolation rates of 62.1% and 40.0%, respectively.

CennetRagbetli.et al. implies that a total of 1,116 *Staphylococcus aureus* isolates have been collected from different clinics. Of these isolates, 339 (30.4%) from wounds, 286 (25.6%) from ears, 141 (12.6%) from blood, 90 (8.1%) from tracheotomy material, 85 (7.6%) from urine, 83 (7.4) obtained%) from abscesses and 92 (8.2%) from other clinical samples. All *S. aureus* isolates were identified as sensitive to vancomycin, daptomycin, linezolid and levofloxacin based on the susceptibility test results performed for all years. Resistance rates to nitrofurantoin, quinupristine-dalfopristine and trimethoprim sulfamethoxazole were determined to be 0.3%, 2.4% and 6.1%, respectively. Penicillin (1,033 / 1,033; 100%), erythromycin (183 / 1,034; 17.7%), rifampicin (156 / 1,116; 14%), gentamicin (145 / 1,116; 13.8%) and clindamycin (108/977; 11.1%) were identified as antibiotics with the highest resistance. The total annual methicillin resistance rate of *S. aureus* strains was determined to be 20.1%. Methicillin resistance was highest in 2009 and decreased in the following years. It was found that a higher MRSA rate in 2009 was statistically significant compared to the rates in the period 2010-2013 ($p < 0.01$). No statistically significant difference was found for MRSA isolates between 2009 and 2014 ($p > 0.05$). *Staphylococcus* has proven to be a life-threatening infection factor acquired from hospitals and communities worldwide. The problem of antibiotic resistance in MRSA isolates in hospital infections is associated with high morbidity and mortality. The prevalence of MRSA infections can vary from country to country and between hospitals, and it also varies between different hospital units. The author gives no clear reason for the occurrence of MRSA-induced antibiotic resistance. The author tries to evaluate the resistance induced by MRSA by statistical significance and validation thereof, which is not possible as a narrative check.

Ozkalp and Baybek et. al reported it as 20.6%. In their study, the MRSA rates by year were determined as, respectively, 30%, 19.6%, 16.4%, 12.5%, 18.5%, and 20.8% (2009–2014).^[14] High MRSA rates in 2009 were statistically significant compared to those of other years. They consider this case as a positive reflection of the decrease in MRSA due to proper basic infection control measures, regular implementation of MRSA screening, and decolonization for individuals in high risk group and successful MRSA education programs.

Aydin et al, determined that the strains were resistant to trimethoprim-sulfamethoxazole at a rate of 15.8% and were resistant at a rate of 7.3% to ciprofloxacin.

Eksi. et. Al determined low rates of resistance in methicillin Sensitive *Staphylococcus. Aureus* (MSSA) strains, including a rate of 2.4% for ciprofloxacin and a

rate of 1.6% for nitrofurantoin, and in MRSA strains, they determined low rates of resistance, including 90.8% against ciprofloxacin and 0.8% to nitrofurantoin.^[15] In their study, while resistance rates for norfloxacin, trimethoprim sulfamethoxazole, nitrofurantoin were determined as 10.3%, 6.1%, and 0.3%, respectively, levofloxacin-resistant strains were not detected. Considering the studies examining antibiotic resistance in *S. Aureus* strains.

Ozkalp, Baybek et al. found that the strains showed resistance to penicillin G at the rate of 85.8% and to erythromycin at the rate of 87.2%.

Aydin et al. determined resistance to penicillin at the rate of 92.3%, at 21.5% to erythromycin, and at 14.8% to clindamycin.^[16]

Eksi et al. determined resistance to penicillin at the rate of 87.8%, 6.5% to rifampin, and at 1.6% to gentamicin in MSSA strains. In MRSA strains, they determined resistance at high rates such as 80.8% to rifampin and 85% to gentamicin.

Gursoy et al. determined resistance at the rate of 94% to penicillin, 29% to erythromycin, 19% to clindamycin, 26% to gentamicin, 29% to rifampicin, and 34% to tetracycline in *S. Aureus* strains isolated from blood cultures. In their study, resistance to penicillin was determined at the rate of 100% due to beta-lactamase product.

Tunger et al reported the resistance as 2.3% to daptomycin one of the new antimicrobial agent for the treatment of the infection caused by resistant Gram positive species, is highly effective in the treatment of complicated skin and soft tissue infection. In their studies conducted in Turkey for staphylococcus aureus strain, daptomycin resistance were not observed. In their study, consistent with literature, no resistance was observed in any strains against daptomycin. Patient infected with MRSA were more likely to have had surgery, a previous hospitalization and longer length of stay before infection. All of these factors are known to increase the probability of a patient developing an MRSA infection.

Methicillin has an antibiotic resistant activity against methicillin. Also the most effective antibiotic in *S. aureus* were identified as vancomycin, linezolid, daptomycin, levofloxacin. So it is more effective against MRSA based hospital infection and to reduce the resistant rates.

It is found that surgery, hospitalization and increased length of hospitalisation are the factors leading to the development of Methicillin Resistant Staphylococcus Aureus strains which induce antibiotic resistance. Most of the studies are showing that MRSA strains are showing higher rate of resist Ozkalp and Baybek et al. All reported 20.6%. In their study, the MRSA rates per year were found to be 30%, 19.6%, 16.4%, 12.5%, 18.5% and

20.8% (2009–2014).^[16] High MRSA rates in 2009 were statistically significant compared to other years. They see this case as a positive reflection of the decline in MRSA due to suitable basic measures for infection control, the regular implementation of MRSA screening and the decolonization of people in high-risk groups as well as successful MRSA education programs.

Aydin et al. The strains were resistant to trimethoprim sulfamethoxazole at 15.8% and ciprofloxacin at 7.3%.

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Tunger et al. Reported 2.3% resistance to daptomycin, one of the new antimicrobial agents used to treat infection caused by resistant gram-positive species, which is highly effective in treating complicated skin and soft tissue infections. No resistance to daptomycin was observed in their studies of Staphylococcus aureus strain in Turkey. Resistance to daptomycin was not observed in any strain in their study, in accordance with the literature. Patients infected with MRSA were more likely to have surgery, previous hospitalization, and longer stay before infection. All of these factors are known to increase the likelihood that a patient will develop MRSA infection.

Methicillin has an antibiotic-resistant effect against methicillin. The most effective antibiotic in *S. aureus* was also identified as vancomycin, linezolid, daptomycin, levofloxacin. It is more effective against MRSA-based hospital infections and for reducing resistance rates.

Surgery, hospitalization and extended hospitalization have been found to be the factors that lead to the development of methicillin-resistant Staphylococcus Aureus strains that induce antibiotic resistance. Most studies show that MRSA strains have a higher resistance rate to penicillin and a lower resistance rate to trimethoprim sulfamethoxazole. It is very obvious that MRSA's resistance to antibiotics can be reduced by implementing infection control measures, MRSA screening and MRSA awareness programs so that we can educate both the general public and health professionals. Vancomycin, linezolid, daptomycin and ciprofloxacin have been shown to be very effective in treating MRSA-resistant strains that show the lowest resistance rate to them. The studies found that the studies provide no

preventive measures and no information on the development of methicillin-resistant *Staphylococcus Aureus*-induced antibiotic resistance towards Penicillin and least rate of resistance towards trimethoprim-sulphamethoxazole. It is very evident that the resistance due to MRSA towards antibiotics can be reduced by implementing infection control measures and adopting MRSA screening and conducting MRSA education programs so that we can educate the public as well as the healthcare professionals. Vancomycin, Linezolid, Daptomycin and Ciprofloxacin are found to be very effective in the treatment of MRSA resistant strains which are showing least rate of resistance towards them. It is found that the studies are lacking in providing the preventive measures and the information regarding the involvement of Methicillin Resistant *Staphylococcus Aureus* induced antibiotic resistance.

CONCLUSION

Methicillin-resistant *Staphylococcus aureus* is common in the population and can lead to a harmful and potentially fatal infection. Identifying likely methicillin-resistant *Staphylococcus aureus* skin lesions is straightforward and can lead to early treatment and possibly even prevention of systemic diseases. Using a variety of sample and routine infection control measures to prevent infection and the transmission of MRSA between patients, clinicians and the community.

Patients infected with methicillin-resistant *Staphylococcus aureus* were more likely to have surgery, previous hospitalization, and longer stay before infection. All of these factors are known to increase the likelihood that a patient will develop a methicillin-resistant *Staphylococcus aureus* infection. The two risk factors that posed the greatest risk for developing a methicillin-resistant *Staphylococcus aureus* infection were enteral nutrition and the use of drugs such as levofloxacin. The relationship between antimicrobial use and MRSA is complex, and further studies to address this issue are needed. Most studies agree that prudent use of antimicrobial agents is one of the main steps to reducing growing concerns about antibiotic resistance, alongside good infection control methods.

Methicillin-resistant *Staphylococcus* strain is now widely used in healthcare and the community. Nowadays, the incidence of methicillin-resistant *Staphylococcus aureus* is very high (community-acquired and hospital-acquired MRSA), so the antibiotic incidence and the options for treating methicillin-resistant *Staphylococcus aureus* are lower, and with the emergence of new strains, the options become less even more limited. Further research on MRSA and the evaluation of best practices for the clear detection of MRSA infections are required. Active screening and detection of MRSA will almost certainly lead to a more accurate representation of the prevalence of methicillin-resistant *Staphylococcus aureus*. The *S. aureus* strain will indeed be a very serious development, so the clinician has very few therapeutic options.

The most potent antibiotics in the *Staphylococcus Aureus* strain have been identified as vancomycin, linezolid, levofloxacin and daptomycin. The use of antibiotics when choosing an empirical treatment prevents the reduction and enables multi-resistant bacterial infections.

Some of the strains of *Staphylococcus aureus* show that resistance to drugs like ceftarolin, daptomycin, vancomycin; However, the presence of linezolid and daptomycin resistance in rural areas is a matter of concern.

The increased incidence of antibiotic resistance due to methicillin-resistant *Staphylococcus Aureus* underlines the need for a comprehensive monitoring and containment system for drug resistance.

This information can then be used to develop good methods for infection control and the optimal use of antimicrobial agents in the country. At present, a reassessment of existing infection control methods, the implementation of more effective practices (screening of MRSA carriers, patient isolation or cohort, colonized healthcare workers and pollution) should suffice.

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ABBREVIATIONS USED

MRSA: Methicillin Resistant *Staphylococcus Aureus*, CA: community Acquired, HA: hospital acquired, ICU: intensive care units, US: united states.

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