



ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor: 5.2
IJAR 2017; 3(9): 302-304
www.allresearchjournal.com
Received: 13-07-2017
Accepted: 14-08-2017

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Study of antibiotic resistance pattern in *Staphylococcus aureus* in skin and soft tissue infections: A seven year analysis

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Abstract

Globally, the prevalence of skin and soft tissue infection (SSTI) by *Staphylococcus aureus* are becoming increasingly prevalent in both community and hospital settings. The worse aspect is that certain strains of *S. aureus* are notorious for causing skin and soft tissue infections in health individuals. This is a retrospective study and was conducted a large tertiary referral centre in Mangalore India. We evaluated STI isolates from January 2009 to December 2015 by considering the odd years (5 time points 2009, 2011, 2013 and 2015). Eligible subjects were those who had a skin or soft-tissue culture yielding *S. aureus* and the principal outcome was to ascertain the organism's antimicrobial susceptibilities. The results of our study indicate that the drug resistance pattern varied for the clinically used antibiotics. The most disturbing trend was the development and increase in the resistance to amikacin, cefoxitin, levofloxacin, erythromycin and clindamycin.

Keywords: Skin and soft tissue infection, *Staphylococcus aureus*, drug resistance, antibiotic sensitivity

Introduction

Skin and soft tissue infections (SSTIs) are the most common infectious disease that compiles the patient to seek medical attention^[1]. They can range from mild form like folliculitis to life-threatening necrotizing fasciitis. *Staphylococcus aureus* is the most common bacterial pathogen associated with the SSTI.^[2] The virulence factors produced by the *Staphylococcus aureus*, increases the mortality and morbidity. The emergence of multi drug resistant (MDR) *Staphylococcus aureus* like Borderline Oxacillin resistant *Staphylococcus aureus* (BORSA), Methicillin Resistant *Staphylococcus aureus* (MRSA)^[3], and even Vancomycin Resistant (VRSA), has become the therapeutic challenge for medical faculty. Even though the drugs for the treatment of these multidrug resistant pathogens available, they are costly and toxic. So to combat the emergence of the resistant pathogen, close monitoring of the resistance pattern of the *Staphylococcus aureus* is the need of the hour. Globally, Clinical Microbiologists have reported that with the even in the event emergence of MDR *Staphylococcus aureus* and other pathogens, there are incidents of emergence of drug sensitive pathogens over a period of time in certain settings^[4,5].

Staphylococcus aureus was first described at the end of the 19th century in pus from human abscesses. *S. aureus* is a major pathogen that is responsible for not only severe infections of the skin and skin structures but also life-threatening diseases because of its propensity to form biofilms on artificial materials, difficult-to-treat infections of catheters and other devices^[6]. *S. aureus* was certainly a significant human pathogen prior to the development of antibiotics. For example, in the last century, *S. aureus* was the major bacterial cause of death in the influenza pandemic of 1918, among those who developed secondary bacterial pneumonia^[7]. Following the introduction of antibiotics, *S. aureus* developed resistance to penicillin in the 1940s, and then emerged as an important cause of serious nosocomial infections in the 1950s. With the development and widespread use of chloramphenicol and tetracycline in the 1960s, super infections due to *S. aureus* occurred including staphylococcal enterocolitis^[8].

The incidence of *S. aureus* related infections has increased dramatically since the emergence of methicillin resistant strains and high rates of mortality and morbidity are occurring worldwide [9]. Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of infections in healthcare institutions [10] and more recently in the community [11]. MRSA was first reported in 1961, two years after the introduction of methicillin for the treatment of penicillin-resistant *S. aureus* infections [8-11]. Despite extensive infection control efforts, methicillin resistance among isolates of *S. aureus* has steadily increased around the world and in India. The objective of the current study was to analyze and study the change in sensitivity pattern of the *Staphylococcus aureus* over a period of last 7 years (2009 to 2015) at 5 time points (that is 2009, 2011, 2013 and 2015) from a tertiary care centre.

Material and Methods

This was a retrospective study and was carried out in the department of clinical Microbiology of the Hospital. The data on the antibiotic sensitive pattern of the *Staphylococcus aureus* isolated from the skin and soft tissue infections studied in the department of Microbiology from January 2009 to December 2015 on alternative years (that is 2009, 2011, 2013 and 2015) was collected from Hospital database after obtaining the necessary permission from the Chief of Medical Records Department.

The sensitive pattern for the following antibiotic was collected from the database: ampicillin (10µg) amoxycylav (20/10 µg), cefuroxime (30 µg), cefoxitin (30 µg), ceftriaxone (30 µg), cefotaxime (30 µg), cotrimoxazole (1.25/23.75 µg), gentamicin (10 µg), amikacin (30 µg), ciprofloxacin (5 µg), levofloxacin (5 µg), azithromycin (15 µg), clindamycin (2 µg), vancomycin (30 µg), linezolid (30 µg), teicoplanin (30 µg) according to CLSI guidelines[5]. The drug resistance pattern for each isolate was entered in the Microsoft Excel, coded and then subjected to frequency analysis.

Observations & Results

The incidence of resistance for a particular antibiotic and expressed in table 1. In the present study with regard to antibiotic ampicillin, it was observed that the percentage of resistant bacteria was almost in the same range (> 75%) throughout the study period indicating that the over prescription and erratic non adherence to the treatment regimen must have lead to wide spread resistance.

With regard to amoxycylav it was observed that with time there was a reduction in the percentage of resistant MRSA organisms. In the year 2009, resistance was 46.80% which decreased to 37.84% in 2015. Analysis of drug resistance pattern for cephalixin showed that the peak resistance was seen for the year 2011 (57.29%) while the least was for 2013 (11.32%).

The results with cefoxitin showed that with time there was a reduction in the percentage of resistant MRSA organisms. In the year 2009 and 2011 nearly 16% were resistant while it decreased to the least in 2013. For the antibiotic cotrimoxazole it was observed that there was a reduction in the percentage of resistant MRSA organisms. In the year 2009, resistance was 44.91% which decreased to 30.75% in 2015.

With regard to gentamicin it was observed that a peak resistance (37.57%) was observed in the year 2011 which

decreased to 34.92 (in 2013) and 26.38 in the year 2015. Analysis of drug resistance pattern for amikacin showed that with time drug resistance increased from 2.90% in the year 2009 to 9.17 in the year 2013 and marginally decreased to 2.08 in the year 2015.

The results with antibiotic ciprofloxacin, it was observed that the percentage of resistant bacteria increased with time from 35.90 in the year to 2009 to 62.16 in 2015. This observation assumes importance as it suggests a rapid erratic use of the drug, over prescription and non adherence is contributing to the wide spread resistance.

The drug resistance pattern for levofloxacin showed that the drug resistance was initially 19.62% for 2009 and reached a peak to 36.35% in 2013, which later decreased marginally to 32.43% in the year 2015. The results for the drug resistance pattern for the antibiotic erythromycin showed that there was a almost two fold increase in the drug resistance from 20.93 in the year 2009 to 43.62 in 2013, which was then remained constant at 42.6% in 2015. With respect to the antibiotic clindamycin the drug resistance increased from 2.61% in 2009 to a peak of 17.11% in 2015.

Table 1: Change in drug resistance pattern for MRSA in a 7 year time period (2009 to 2015)

| Antibiotics used | Time period | | | |
|------------------|-------------|-------|-------|-------|
| | 2009 | 2011 | 2013 | 2015 |
| Ampicillin | 82.70 | 91.01 | 77.83 | 83.39 |
| Amoxycylav | 46.80 | 41.30 | 35.28 | 37.84 |
| Cephalexin | 30.52 | 57.29 | 11.32 | 14.92 |
| Cefoxitin | 16.27 | 16.56 | 9.53 | 14.92 |
| Cotrimoxazole | 44.91 | 37.22 | 40.16 | 30.75 |
| Gentamicin | 24.27 | 37.57 | 34.92 | 26.38 |
| Amikacin | 2.90 | 1.050 | 9.17 | 7.078 |
| Ciprofloxacin | 35.90 | 44.34 | 59.35 | 62.16 |
| Levofloxacin | 19.62 | 24.27 | 36.35 | 32.43 |
| Erythromycin | 20.93 | 26.25 | 43.62 | 42.59 |
| Clindamycin | 2.61 | 3.26 | 16.80 | 17.11 |

Discussion

MRSA is a major nosocomial pathogen causing significant morbidity and mortality. The important sources for MRSA in hospitals are infected patients and transient hand carriage on the hands of health care workers is the predominant mode for patient-to-patient transmission. In this study, the prevalence and antibiotic susceptibility patterns of various MRSA isolates were obtained from 2009 to 2015.

In the recent past in healthcare facilities, *Staphylococcus* have been accepted to be major emerging pathogens causing nosocomial infections and to cause several diseases including skin and wound infections, bacteremia, and necrotizing pneumonia. The epidemiological characteristics of *S. aureus*, especially the MRSA, are changing rapidly. Methicillin, the first penicillinase-resistant penicillin, revolutionized the treatment of penicillin-resistant *S. aureus*. However within two years, methicillin-resistant strains began to emerge and in the subsequent years, MRS strains continued to cause nosocomial infections worldwide [12].

In the present study, it was observed that the drug resistance pattern varied for the clinically used antibiotics. The most disturbing trend was the development and increase in the resistance to amikacin, cefoxitin, levofloxacin, erythromycin and clindamycin. The present study demonstrated that the drug resistance pattern was varied for the clinically used antibiotics. These findings indicate that continuous monitoring of antibiotic sensitivity and rationalizing the use

of antibiotics remain an important and effective strategy to minimize the emergence of multiple resistance strains. The major limitations of this study are that it is a monocentric study. The need of the time is to including multiple institutes/hospitals and this would have benefited the study.

Acknowledgement

The authors are grateful to Indian Council of Medical Research (ICMR), New Delhi for awarding a student research fellow ship (STS 2016) to Mr. Shah Nawaz. The authors are also thankful to Prof Rekha Bloor, Head of Microbiology for her support.

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