

Original Research Article

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## Changing Trends in Resistance Pattern of Methicillin Resistant *Staphylococcus aureus* in Burn Patients

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### ABSTRACT

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Historically, *S. aureus* has been one of the most common pathogens which caused pyogenic local and systemic infections in both hospitals and community. Methicillin resistance in *Staphylococcus aureus* is associated with multidrug resistance, an aggressive course, increased mortality and morbidity in both community and health care facilities. This cross sectional study was carried out in a 70 burn patients from May 2016 to July 2018 at DR.S.C.G.M.C, Nanded India. Swabs were taken and cultured for bacterial isolation and identification following standard operative procedures. Antimicrobial susceptibility was performed by Kirby Bauer's disc diffusion method which used a 30µg Cefoxitin disc according to CLSI 2018 guidelines. MRSA isolates showed high resistance to ciprofloxacin (76.4%), gentamicin (64.7%) as compared to other drugs. High prevalence of Ciprofloxacin resistance was detected. Multi resistant MRSA with a 'D' test positive was 79%. All MRSA isolates were sensitive to Vancomycin, Linezolid. MRSA had displayed increase in resistance to most antibiotics with 'D' test positive in recent years. Taking into consideration the prevalence of multidrug-resistance in MRSA, resistance patterns should be evaluated periodically and antibiotic therapy should be guided by susceptibility testing.

### Introduction

Historically, *S. aureus* has been one of the most common pathogens which caused pyogenic local and systemic infections in both hospitals and community. By virtue of a battery of virulence factors, *S. aureus* has propensity to cause a wide spectrum of infections which involve several organ systems, some of which, especially meningitis, endocarditis and blood stream infections, are frequently fatal in nature <sup>(1)</sup>. Methicillin

Resistant *S. aureus* (MRSA), are strains of *S. aureus* which express an altered penicillin binding protein (PBP2a), thus conferring resistance to beta lactam antibiotics. MRSA strains had caused several documented outbreaks of hospital cross infections throughout the world in 1970s and since then, they have drawn special attention in hospital acquired infections <sup>(2)</sup>. Severe and drug resistant infections which were predominantly restricted to hospitals are now becoming rampant in community, as novel MRSA

strains, which have been described as community acquired MRSA (CA-MRSA)<sup>(3)</sup>. MRSA are notorious for their wide variations in antibiotic resistance patterns. They not only develop chromosomal resistance to penicillins and cephalosporins but also frequently show resistance to a wide range of antibiotics which are commonly used in hospitals<sup>(4)</sup>. Within a country, there may be local variations in predominant hospital and community strains of MRSA<sup>(5,6)</sup>. The resistance pattern of CA-MRSA is essentially different from that of hospital acquired MRSA (HA-MRSA). Unlike CA-MRSA, hospital strains display more drug resistance in an attempt to survive in hospital environment. The resistance patterns of prevalent MRSA strains in any setup are liable to continuous changes over a period of time, owing to changes in antibiotic prescription patterns, infection control measures and awareness among healthcare workers. As a result of increasing antibiotic pressure in hospitals, new strains with higher antibiotic resistance emerge and they replace the previous strains. While methicillin resistance in *S. aureus* is less in countries like Norway and Sweden (1%), Netherlands (2%) and Canada (5-10%), it is 25-50% in the United States, 54% in Portugal and 43%-58% in Italy<sup>(7)</sup>. High prevalence of MRSA is an emerging problem in India. Several authors have reported a substantial increase in MRSA prevalence in India. It has increased from 12% in 1992 to 40% in 2009<sup>(8, 9)</sup>. Increasing resistance of MRSA in recent years has had a significant impact on several aspects of patient care and infection control. Antibiotic policies need to be updated regularly, along with comprehensive monitoring of antibiotic prescribing and antibiotic consumption in healthcare settings. These facts clearly highlight the need of a characterization of MRSA strains at a regular basis at all levels. Therefore, this study was done to determine changing patterns of MRSA infection in our

hospital over past seven years, with a special focus on resistance pattern.

To study the changing trends in resistance patterns of MRSA isolates in burn patient at our hospital.

## Materials and Methods

Analysis of 70 MRSA isolates in burn patients from June 2016 to July 2018 were studied. All clinical samples were processed in the laboratory as per standard guidelines. *S. aureus* isolates were identified by standard laboratory procedures. Disc diffusion test which used a 30µg Cefoxitin disc were performed and also subjected to the D-test as per Clinical and Laboratory Standards Institute (CLSI 2016-2018) guidelines, to detect MRSA stains<sup>(10)</sup>. A panel of commonly used antibiotics (Himedia, Mumbai, India) which comprised of Ciprofloxacin (5µg), Gentamicin (10µg), Amikacin (30µg), Erythromycin (15µg), Vancomycin (30µg), Linezolid (30µg), Clindamycin (5µg), were tested by Kirby Bauer disc diffusion method for susceptibility patterns. And the results were compared to the study done from July 2014- June 2016.

## Results and Discussion

70 MRSA isolates from burn patients were taken. Among these, 40 (57.14%) were female patients and 30 (42.85%) were males. The resistance patterns of MRSA to standard drugs in recent year have been compared in figure 1.

Out of 70 cases, 37 patients had inducible clindamycin resistance. Furthermore, a multiple non beta lactam antibiotic resistance was seen more in MRSA isolates of July 2016- July 2018 as compared to July 2014- June 2016 isolates<sup>(17)</sup> (Table 1). An increase in inducible clindamycin resistance from 2014 (25.31%) to 2018 (81%) shown in figure 2.

All strains were sensitive to Linezolid and Vancomycin by disc diffusion.

MRSA is a major cause of nosocomial outbreaks and serious infections, which causes increased mortality and morbidity. Skin and soft tissue infections, wound infections, burns, ulcers, pressure sores, lower respiratory and urinary tract infections, septicaemia and infections associated with invasive devices are most frequently reported<sup>(10)</sup>.

Clindamycin, a Lincosamide, has long been an option for treating Staphylococcal skin, soft tissue and bone infections because of its proven efficacy, low cost, the availability of its oral and parenteral forms, tolerability, excellent tissue penetration, its good accumulation in abscesses and because no renal dosing adjustments are required. It also directly inhibits the Staphylococcal toxin production and is a useful alternative for patients who are allergic to penicillin<sup>(11)</sup>. Its good oral absorption makes it an important option in the therapy of the outpatients or as a follow up after an intravenous (IV) therapy (de-escalation). This permits an early

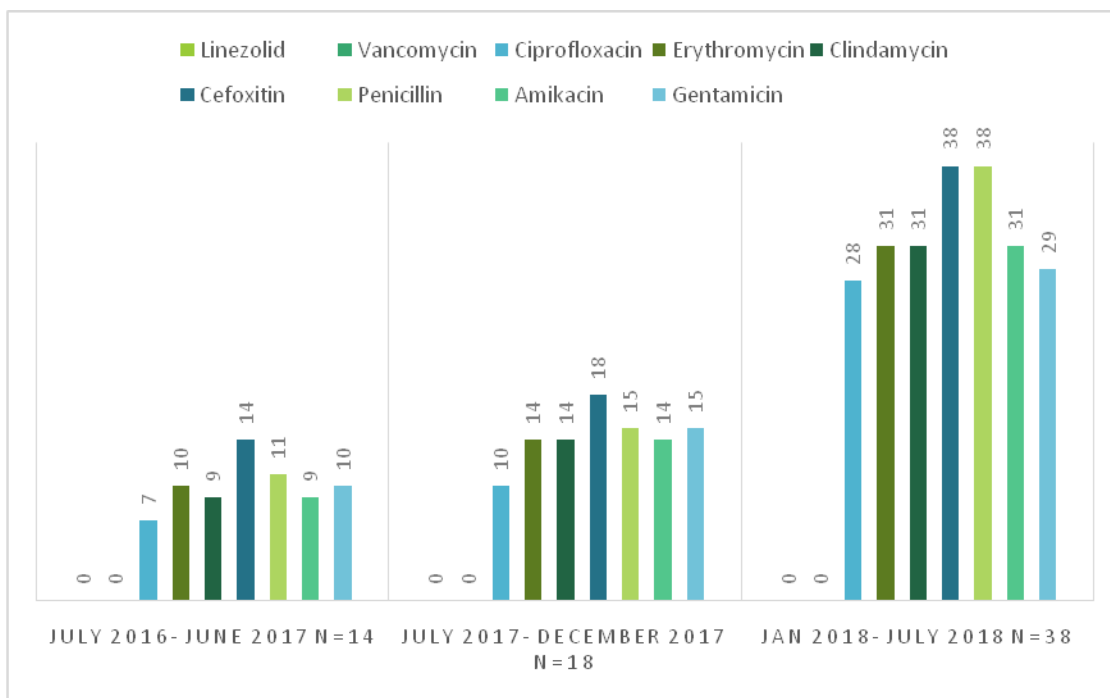
transition to the outpatient management of the susceptible infections without the complications of a continued IV access<sup>(12)</sup>. It is effective against both the methicillin resistant and the methicillin sensitive Staphylococcal infections<sup>(13)</sup>. The increased frequency of the Staphylococcal infections, along with the changing drug susceptibility patterns, have led to a renewed interest in the Clindamycin usage<sup>(14)</sup>, but the possibility of an inducible resistance to Clindamycin remains a major concern and this could limit the use of this drug. To report the Clindamycin susceptibility accurately, the *Staphylococci* which are isolated from the clinical specimens should first be subjected to the D-test, to exclude the isolates with an induced Clindamycin resistance (MLS<sub>Bi</sub>); as such isolates, when treated with Clindamycin, can undergo a rapid in vitro conversion to a constitutive resistance (MLS<sub>Bc</sub>) and this may result in the Clindamycin treatment failure.

In this study, females were predominated 40 (57.14%) over males 30 (42.85%). It is in accordance to other studies done by Pragathi *et al.*, and Dash *et al.*,<sup>(15,16)</sup>

**Table.1** Comparison of resistance pattern of MRSA isolates in past and recent years

ANTIBIOTICS	July 2014- May 2016 N= 79	July 2016- June 2017 N= 14	July 2017 – December 2017 N= 18	Jan 2018 – July 2018 N=38
<b>Vancomycin</b>	00	00	00	00
<b>Linezolid</b>	00	00	00	00
<b>Ciprofloxacin</b>	-	7 (50%)	10(55.55%)	28(73.68%)
<b>Erythromycin</b>	42 (53.17%)	10(71.42%)	14 (77.77%)	31 (81.57%)
<b>Clindamycin</b>	28 (35.45%)	9 (64.28%)	14 (77.77%)	31 (81.57%)
<b>Cefoxitin</b>	79 (100%)	14 (100%)	18 (100%)	38 (100%)
<b>Penicillin</b>	60 (75.94%)	11 (78.57%)	15 (83.33%)	38 (100%)
<b>Amikacin</b>	28 (35.45%)	9 (64.28%)	14 (77.77%)	31 (81.57%)
<b>Gentamicin</b>	30 (37.97%)	10 (71.42%)	15 (83.33%)	29 (76.31%)

**Fig.1** Resistance pattern of 70 MRSA isolates



**Fig.2** MRSA isolates shows inducible clindamycin resistance in past and present year



This study analysed antibiotic susceptibility pattern of 70 MRSA isolates and found three major changes in antibiotic resistance over

four years. Firstly, an increased resistance toward ciprofloxacin, Amikacin, Gentamicin. Secondly, all the isolates were sensitive to

Vancomycin and Linezolid. Thirdly an increase in inducible Clindamycin resistance from 2014 (25.31%) to 2018 (81%).

In conclusion, our study showed the changing patterns of antimicrobial resistance of MRSA strains in our hospital. MRSA had shown an increase in resistance to most of the antibiotics except Linezolid and Vancomycin, along with a substantial increase in multi-resistant MRSA strains over a period of four years. Resistance to Ciprofloxacin, Gentamicin and Amikacin was high in both recent and old MRSA isolates and therefore, these drugs are not suitable for empirical therapy of suspected Staphylococcal infections. Recent study showed MRSA had an increase of inducible clindamycin resistance from 25.31 % to 81% over four year. We conclude that *S. aureus* is a pervasive pathogen in our hospital and in community settings with constantly changing trends in virulence, resistance and epidemiology and thus, monitoring of clinical and microbiological parameters is necessary, for modifying our existing infection control measures and treatment options accordingly.

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