

Original Research Article

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## Prevalence and Antibiogram of Methicillin Resistant *Staphylococcus aureus* in a Tertiary Care Centre in Tumkur, India

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### ABSTRACT

Methicillin Resistant *Staphylococcus aureus* (MRSA) has emerged as a major community acquired and nosocomial pathogen. Antibiotic armamentarium available for the treatment of MRSA infections is limited. The increasing rate of drug resistance among the isolates demands the judicious use of the available antibiotics. Timely collection and analysis of the antibiotic susceptibility data facilitates rational implementation of empirical therapy. The present study was conducted to evaluate the prevalence and to assess the antibiotic susceptibility patterns of the MRSA isolates from our hospital. *Staphylococcus aureus* isolated from all clinical samples were included in the study and subjected to antibiotic susceptibility testing. Isolates of MRSA were identified and their susceptibility pattern was analysed. Of the 240 isolates of *Staphylococcus aureus* obtained from various samples 109 (45.42%) were found to be Methicillin resistant. 73.4% of the Methicillin resistant isolates were multi-drug resistant showing resistance to three or more antibiotics. The MRSA isolates showed 100% sensitivity to Vancomycin, Teicoplanin and Linezolid. In addition drugs like Amikacin, Nitrofurantoin, Netilmicin and Chloramphenicol were found to have good in-vitro activity against the isolates of MRSA. Antibiotic resistance among the MRSA isolates is increasing and treatment options available are few. Anti-MRSA drugs like Vancomycin, Teicoplanin, Linezolid, etc. should be used judiciously after appropriate antibiotic susceptibility testing. Regular monitoring of Antibiotic susceptibility pattern is essential to guide empirical therapy.

#### Keywords

*Staphylococcus aureus*, MRSA, Antimicrobial resistance, Multi-drug resistance.

#### Article Info

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### Introduction

*Staphylococcus aureus* is a versatile organism which on one hand is a normal human commensal and on the other is capable of causing a multitude of human infections ranging from skin afflictions to critical systemic infections. The increase in drug resistance among the isolates has contributed to its notoriety. Methicillin Resistant *Staphylococcus aureus* (MRSA) has emerged as a major hospital acquired and community

associated public health concern due to its evolving resistance pattern. Resistance to Methicillin is mediated by SCC mec (*Staphylococcal Cassette Chromosome mec*) which codes for an altered Penicillin Binding Protein (PBP 2a) with decreased affinity for the  $\beta$ -Lactam antibiotics (Kale *et al.*, 2016).

MRSA isolates were first reported in the year 1961, two years after Methicillin was

introduced for the treatment of Penicillin resistant *Staphylococcus aureus* (Kluytmans *et al.*, 2009; Nazari *et al.*, 2015). The 1990's saw a paradigm shift in the epidemiology of MRSA with the emergence of community associated (CA-MRSA) isolates (Watkins *et al.*, 2012). MRSA infections were no longer limited to the hospital milieu but also occurred in healthy individuals in the community with no predisposing factors for MRSA acquisition (Kluytmans *et al.*, 2009). Infections caused by Methicillin resistant isolates are associated with longer hospital stays, increased costs of health care and higher mortality in invasive infections (Watkins *et al.*, 2012).

The therapeutic armamentarium available against MRSA is limited. Periodic analysis of the susceptibility patterns of the isolates is essential to guide empirical therapy. Continued monitoring of the antibiogram of MRSA can minimize the inappropriate prescription of specific anti-MRSA drugs, when other antibiotics would be effective (Tiwari *et al.*, 2008). Periodic evaluation of the prevalence of resistant isolates and their susceptibility patterns is essential for every hospital to guide the formulation of appropriate antibiotic policy. It is essential for the identification of the problem areas and for the institution of appropriate preventive and corrective measures. The present study was conducted to assess the prevalence and to analyse the antibiotic susceptibility patterns of isolates of MRSA from our hospital.

### **Materials and Methods**

The study was conducted for a period of two years from January 2014 to December 2015 in the Microbiology Department of Shridevi Institute of Medical Sciences and Research Hospital, Tumkur. *Staphylococcus aureus* isolated from all clinical samples like pus, urine, sputum, blood and miscellaneous

samples like throat swabs, vaginal swabs, body fluids from both out-patients and in-patients submitted to the Microbiology laboratory during this period were included in the study. Processing of samples and the identification of the isolates were performed by conventional methods (Collee *et al.*, 1999).

Antimicrobial susceptibility testing was performed by Kirby-Bauer disc diffusion method and the susceptibility to antibiotics was assessed based on the Clinical Laboratory Standards Institute guidelines (CLSI, 2013).

The antibiotics tested include Penicillin-G (10units), Ampicillin (10µg), Amoxicillin-Clavulanic acid (20/10µg), Teicoplanin (30µg), Gentamicin (10µg), Amikacin (30µg), Netilmicin (30µg), Erythromycin (15µg), Tetracycline (30µg), Ciprofloxacin (5µg), Norfloxacin (10µg), Clindamycin (2µg), Cotrimoxazole (Trimethoprim 1.25µg/Sulfamethoxazole 23.75µg), Choramphenicol (30µg), and Linezolid (30µg). Vancomycin MIC was assessed using E-strip. For isolates obtained from urine Nitrofurantoin (300µg) disc was added. Isolates of *Staphylococcus aureus* showing a zone diameter of less than 22 mm with Cefoxitin (30µg) disc were classified as Methicillin Resistant *Staphylococcus aureus*. The isolates of Methicillin Resistant *Staphylococcus aureus* resistant to three or more antibiotics were classified as Multi-Drug Resistant (Tiwari *et al.*, 2008). All antibiotic discs were procured from Himedia Laboratories Pvt. Ltd. *Staphylococcus aureus* ATCC 25923 was used for quality control. Statistical significance was assessed by calculating p value using Fisher's exact test.

### **Results and Discussion**

A total of 240 isolates of *Staphylococcus aureus* were isolated from various clinical samples during the study period. Majority of

the isolates were obtained from pus samples. 109 (45.42%) isolates were identified as Methicillin Resistant (Table 1).

Majority of the Methicillin resistant isolates were obtained in the age group of 41 to 50 years followed by 21 to 30 years (Figure 1).

More than 50% of the Methicillin Resistant *Staphylococcus aureus* (MRSA) isolates were obtained from males, though the increased isolation of MRSA isolates from males was not found to be statistically significant (Table 2).

Majority (72.48%) of the MRSA isolates were obtained from in-patients. This finding was also not found to be statistically significant in comparison to the Methicillin sensitive isolates (Table 3).

Antimicrobial resistance patterns of the Methicillin sensitive and Methicillin resistant isolates were assessed. Methicillin resistant isolates demonstrated higher levels of resistance in comparison to the Methicillin sensitive isolates. 73.4% of the Methicillin Resistant isolates were multi-drug resistant showing resistance to three or more antibiotics.

All the isolates were sensitive to Vancomycin, Teicoplanin and Linezolid. In addition, the Methicillin resistant isolates demonstrated low level resistance to Amikacin (14.68%),

Nitrofurantoin (16.67%), Netilmicin (17.43%) and Chloramphenicol (19.27%). Ciprofloxacin and Cotrimoxazole were least effective with resistance levels of 73.39% and 69.72% respectively (Table 4 and Figure 2).

*Staphylococcus aureus* has continued to be an important bacterial pathogen of humans due to its ability to acquire novel strategies of drug resistance. Treatment options for drug resistant strains are limited, have more adverse effects and are more expensive (Kluytmans *et al.*, 2009). This study was conducted to assess the prevalence of MRSA and to elaborate its antibiotic susceptibility pattern in our hospital. Majority of the isolates of *S aureus* were obtained from pus samples. *Staphylococcus aureus* has been the commonest pathogen obtained from surgical site infections, purulent cellulitis and cutaneous abscesses (Tong *et al.*, 2015).

The prevalence of the MRSA isolates in the present study was found to be 45.42% which is alarmingly high. Studies have shown that the prevalence of MRSA in different parts of India is not uniform (Tiwari *et al.*, 2008). Variations have been seen between different regions and also between different hospitals in the same region (Joshi *et al.*, 2013) emphasising the importance of antibiotic prescribing practices on the development of drug resistance. Table 5 lists the prevalence of MRSA in various studies across India.

**Table.1** Distribution of *Staphylococcus aureus* isolates from various clinical samples

Sample	No. of <i>S. aureus</i>	No. of MRSA	% of MRSA from each sample
<b>Pus</b>	164	71	43.29
<b>Urine</b>	33	18	54.55
<b>Sputum</b>	7	2	28.57
<b>Blood</b>	24	13	54.17
<b>Miscellaneous</b>	12	5	41.67
<b>Total</b>	<b>240</b>	<b>109</b>	<b>45.42</b>

MRSA: Methicillin Resistant *Staphylococcus aureus*

**Table.2** Sex distribution of the isolates

	MSSA	MRSA	Total
<b>Male</b>	70 (53.44%)	60 (55.05%)	130 (54.17%)
<b>Female</b>	61 (46.56%)	49 (44.95%)	110 (45.83%)
<b>Total</b>	131	109	240

MSSA: Methicillin Sensitive *Staphylococcus aureus*, MRSA: Methicillin Resistant *Staphylococcus aureus*; Chi square = 0.0622, p value = 0.803087.

**Table.3** Distribution of isolates among in-patients and out-patients

	MSSA	MRSA	Total
<b>In-patients</b>	85 (64.89%)	79 (72.48%)	164 (68.33%)
<b>Out-patients</b>	46 (35.11%)	30 (27.52%)	76 (31.67%)
<b>Total</b>	131	109	240

MSSA: Methicillin Sensitive *Staphylococcus aureus*, MRSA: Methicillin Resistant *Staphylococcus aureus*; Chi square = 1.5846, p value = 0.208102.

**Table.4** Antimicrobial Resistance Pattern of the isolates

Antibiotic	MSSA (n = 131)	% of Resistance	MRSA (n = 109)	% of Resistance	p Value
<b>Penicillin</b>	117	89.31	109	100	0.0002
<b>Ampicillin</b>	88	67.18	109	100	<0.0001
<b>Amoxicillin-Clavulanic acid</b>	7	5.34	109	100	<0.0001
<b>Erythromycin</b>	40	30.53	74	67.89	<0.0001
<b>Clindamycin</b>	22	16.79	48	44.04	<0.0001
<b>Gentamicin</b>	8	6.11	75	68.81	<0.0001
<b>Netilmicin</b>	1	0.76	19	17.43	<0.0001
<b>Amikacin</b>	1	0.76	16	14.68	<0.0001
<b>Ciprofloxacin</b>	26	19.85	80	73.39	<0.0001
<b>Nitrofurantoin</b>	3/15	20	3/18	16.67	1.0000
<b>Tetracycline</b>	12	9.16	29	26.61	0.0005
<b>Chloramphenicol</b>	13	9.92	21	19.27	0.0426
<b>Cotrimoxazole</b>	55	41.98	76	69.72	0.0001
<b>Vancomycin</b>	0	0	0	0	---
<b>Teicoplanin</b>	0	0	0	0	---
<b>Linezolid</b>	0	0	0	0	---

**Table.5** Prevalence of MRSA isolates in various parts of India from clinical samples

Sl. No.	Author	Year	Region	No. of <i>S. aureus</i>	MRSA (%)
1	Vidhani <i>et al.</i> ,	2001	New Delhi	188	51.6
2	Anupurba <i>et al.</i> ,	2003	Uttar Pradesh	549	54.85
3	Rajaduraipandi <i>et al.</i> ,	2006	Tamil Nadu	803	31.1
4	Pai <i>et al.</i> ,	2010	Karnataka	237	29.1
5	Arora <i>et al.</i> ,	2010	Punjab	250	46
6	Surpur <i>et al.</i> ,	2013	Karnataka	244	54.91
7	Joshi <i>et al.</i> ,	2013	INSAR group	26,310	41
8	Rupali <i>et al.</i> ,	2014	Maharastra	192	58.33
9	Harshan <i>et al.</i> ,	2015	Kerala	205	29.7
10	Bouchiat <i>et al.</i> ,	2015	Karnataka	92	52.2
11	Armugam <i>et al.</i> ,	2016	Tamil Nadu	212	27.83
12	Bhattacharya <i>et al.</i> ,	2016	West Bengal	1049	25.45
13	Jindal <i>et al.</i> ,	2016	Punjab	248	64.9
14	Present study	2017	Karnataka	240	45.42

Fig.1 Age-wise distribution of isolates of *Staphylococcus aureus*

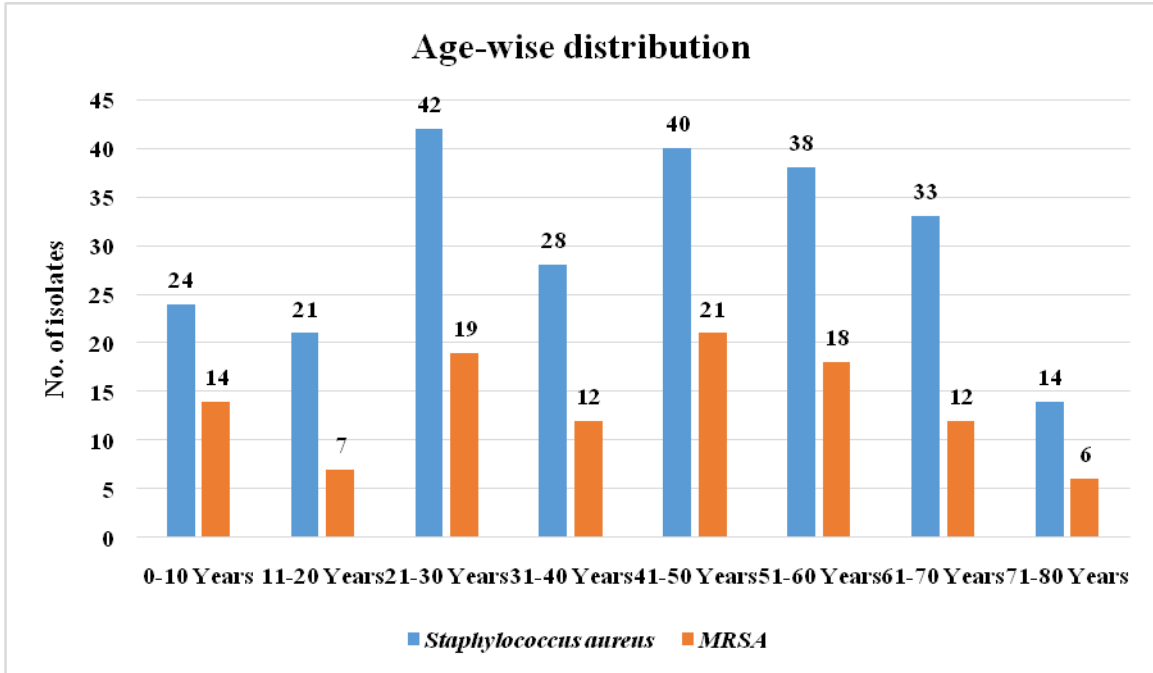
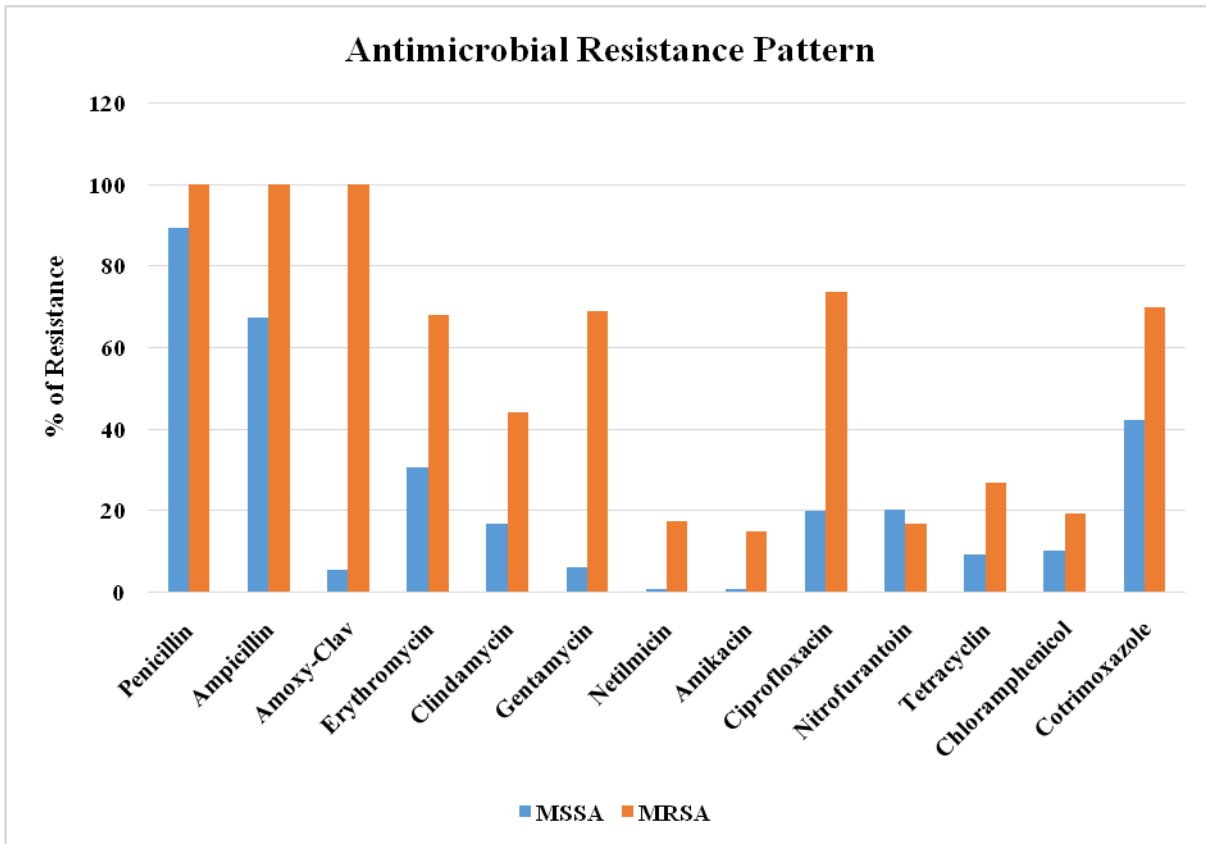


Fig.2 Antimicrobial resistance pattern of the isolates



Prevalence of MRSA has been found to be high with various studies demonstrating a prevalence of more than 50% of Methicillin resistant isolates in different geographical areas.

Glycopeptides like Vancomycin are one of the main antibiotics used for the treatment of critical infections caused by MRSA (Tiwari *et al.*, 2006). All isolates in the current study were sensitive to glycopeptides. Empirical use of these drugs without appropriate testing can lead to development of drug resistance. Vancomycin Intermediate *Staphylococcus aureus* (VISA) (Tong *et al.*, 2015; Menezes *et al.*, 2008; Bhattacharya *et al.*, 2013) and Vancomycin Resistant *Staphylococcus aureus* (VRSA) (Nazari *et al.*, 2015) have been reported from few studies in India. Development of Vancomycin resistance has further complicated the treatment of MRSA infections.

The oxazolidinone antibiotic Linezolid is another drug that has been found to be highly effective against MRSA. Global surveillance data has revealed <1% resistance to Linezolid among *S aureus* isolates (Gu *et al.*, 2013). Our study did not demonstrate any Linezolid resistant isolates. Linezolid however is expensive and associated with serious adverse effects including lactic acidosis, irreversible peripheral neuropathy, anaemia, thrombocytopenia and optic neuritis when prescribed for more than 28 days. Drugs available for treatment of MRSA are limited. Antibiotics like Vancomycin and Linezolid should be used judiciously to prevent development of resistance.

Aminoglycosides like Amikacin and Netilmicin were found to be effective against MRSA, exhibiting low levels of resistance in-vitro. Similar results were found by other studies (Harshan *et al.*, 2015; Arora *et al.*, 2010).

Nitrofurantoin is an oral antibiotic used for the treatment of urinary tract infections caused by MRSA (Gould *et al.*, 2009). Though only a few isolates from urine were studied, the isolates of MRSA showed good sensitivity to Nitrofurantoin.

Isolates of MRSA in the study have demonstrated high level of in-vitro susceptibility to Chloramphenicol. A study in Pakistan has shown good in-vitro activity of Chloramphenicol against MRSA isolates (Fayyaz *et al.*, 2013). Antibiotics like Chloramphenicol need to be explored as alternative treatment options for MRSA infections though potential adverse effects and variable activity is a concern.

Prevalence of MRSA infections in India is demonstrating an increasing trend. Therapeutic options available against these infections are limited. Indiscriminate use of these drugs leads to development of resistance and poses further challenge for the treatment of infections caused by resistant isolates.

There is a need to review other potential antibiotics like Chloramphenicol, Netilmicin, and Amikacin as alternate treatment options for MRSA infections after appropriate susceptibility testing. Anti-MRSA drugs like Glycopeptides and Linezolid can thus be reserved for the treatment of life-threatening infections caused by MRSA.

### **Conflict of interest**

The authors deny any conflicts of interest related to this study.

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