

PREEJA¹, SANATH KUMAR², VEENA A SHETTY³

(CC) BY-NC-ND

ABSTRACT

Microbiology Section

Introduction: Methicillin Sensitive *Staphylococcus aureus* (MSSA) is a significant human pathogen, involved in both hospital and community associated settings. MSSA, being more susceptible to antibiotics compared to Methicillin Resistant *Staphylococcus aureus* (MRSA), is found to acquire Multidrug Resistance (MDR) and with the presence of virulence factors can pose difficulty in patient treatment.

Aim: To study the prevalence and antibiotic resistance profile of MSSA from community and hospital associated infections.

Materials and Methods: The present cross-sectional study was conducted in tertiary care hospital in Mangalore, Karnataka, India from January 2015 to February 2017. Three hundred and five *Staphylococcus aureus* were isolated from various clinical specimens and tested for methicillin susceptibility using cefoxitin disc. Antibiotic resistance profiles against 23 antibiotics were determined by disc diffusion method. The

difference was compared for antibiotic sensitivity with respect to Community Associated Methicillin Sensitive *Staphylococcus aureus* (CA-MSSA) and Hospital Associated Methicillin Sensitive *Staphylococcus aureus* (HA-MSSA) and Chi-square test was used for statistical analysis.

Results: Of 305 MSSA isolated, 219 (71.8%) were CA-MSSA and 86 (28.2%) were HA-MSSA. *S. aureus* was isolated mostly from Skin and Soft Tissue Infections (SSTI, 61.3%). Resistance was observed against ciprofloxacin (64.6%), erythromycin (43.9%), ofloxacin (42.3%), clindamycin (20.7%), ampicillin (100%) and penicillin (90.5%). There was a significant difference (p<0.05) between the resistance of CA-MSSA and HA-MSSA against cefotaxime and co-trimoxazole.

Conclusion: The present study showed the increasing prevalence of MSSA in the community and hospital settings with the emergence of MDR which has to be dealt immediately with appropriate control measures.

Keywords: Antibiotic resistance, Community associated infections, Gram positive bacteria, Hospital associated infections, Methicillin resistance

INTRODUCTION

Staphylococcus aureus a highly pathogenic microorganism can remain as a commensal in human skin and nares. *Staphylococcus aureus* causes infections ranging from SSTIs to necrotising pneumonia. MRSA appeared in 1960s soon after the introduction of the antibiotic methicillin [1] and since then, MRSA became one of the most predominant nosocomial pathogen worldwide [2]. Though MRSA became prevalent in community and healthcare settings alike [3,4], the proportion of *Staphylococcus aureus* showing methicillin susceptibility was found to be higher [5,6].

MSSA found to have a higher prevalence in patients and carriers compared to the MRSA, although the prevalence rate varies worldwide [5-7]. A hospital based study from Pondicherry, reported MSSA prevalence rate of 78.12% and MRSA of 21.98% [7]. A cross-sectional study from Northeast Ethiopia reported prevalence rate of MSSA of 71.7% and MRSA of 28.3% [5]. In India, a study conducted by Indian Network for Surveillance of Antimicrobial Resistance (INSAR) group in 15 Indian tertiary care centers from January 2008 to December 2009 found MSSA prevalence rate of 59% and 41% of MRSA in inpatients and outpatients [8]. MSSA carriage in patients, healthcare workers and healthy individuals suggest their widespread distribution. A study from USA reported MSSA colonisation higher (35.7%) in surgeons than in high risk patient group [9].

MSSA can be classified as CA-MSSA isolated from patients without hospital associated risk factors, within 48 hrs of hospital admission and the remaining as HA-MSSA according to Centers for Disease Control

and Prevention (CDC) definition for CA-MRSA. Studies reported higher prevalence of CA-MSSA compared to HA-MSSA [10,11].

Generally, MSSA are found to be more susceptible to beta-lactam and non beta-lactam antibiotics compared to MRSA [8,12,13]. Higher antibiotic susceptibility pattern of MSSA helps in proper treatment and infection control. However, recent studies have reported emergence of higher antibiotic resistance in MSSA [6,14]. Increasing resistance against ciprofloxacin, erythromycin shown by MSSA have been reported [8,10,15,16]. It is anticipated that the increasing Multidrug Resistance (MDR) MRSA in community and hospital settings, MRSA might outnumber MSSA without appropriate control measures [12,17,18]. A study from Punjab reported higher prevalence of MRSA (64.9%) compared to MSSA (35%) [19]. Several studies reported, MSSA becoming more virulent with the presence of Panton-Valentine Leukocidin (PVL) gene and MDR which can be fatal [14]. The PVL positive MSSA isolates appeared as a reservoir for CA-MRSA [20].

Literature survey shows though data regarding comparative study of MSSA and MRSA were available, detailed study about MSSA including CA-MSSA and HA-MSSA from India was limited [10,15]. The aim of this study was to understand the prevalence and antibiotic resistance profile of MSSA from the community and hospital-associated infections for better antibiotic stewardship which can help to control the emergence of MDR in MSSA and prevent the replacement of MSSA by MRSA in hospitals and community. The results of this study revealed increasing prevalence of MSSA in community and hospital settings and emerging MDR in CA-MSSA similar to HA-MSSA.

MATERIALS AND METHODS

This cross sectional study was conducted in a tertiary care hospital, Mangalore (South India), from January 2015 to February 2017. Ethical approval for the study was obtained from Institutional Ethical Committee (Ref: NU/CEC/Ph.D-65/2012) and informed consent was obtained from the patients. Demographic details and all other relevant clinical details were also documented.

Patients without hospital associated risk factors such as the long term admission to a medical care facility, surgery or dialysis in the previous year, previous MRSA isolation or colonisation were considered as having community associated infections and remaining cases as hospital associated infections and comparative study of CA-MSSA and HA-MSSA were statistically computed. Duplicate isolates of *Staphylococcus aureus* from the same patient at a different site of infection was excluded during the study period.

From the available hospital records, the prevalence of *Staphylococcus aureus* infections in previous years was studied. In this study, *Staphylococcal* strains were collected from the tertiary care hospital laboratory during the study period and the prevalence of MSSA in community and hospital associated infections were analysed. *Staphylococcus aureus* was isolated from various clinical samples (pus, blood, cerebrospinal fluid, body fluids, sputum, throat swab, urine). *Staphylococcus aureus* was isolated and identified from clinical specimens by standard laboratory procedures [21]. *S. aureus* was phenotypically identified by cultural characteristics on blood agar and Mac Conkey's agar (Hi-Media) incubated at 37°C for 24-48 hours, Gram reaction, catalase test, coagulase test and mannitol fermentation [21]. *Staphylococcus aureus* ATCC (American Type Culture Collection) 25923 was used as the quality control strain.

Detection of methicillin resistance in *S. aureus* was done by disc diffusion test using cefoxitin disc (30 μ g) on Muller-Hinton agar (Hi-Media, Mumbai, India) [22]. A zone of inhibition \leq 21 mm was considered as methicillin resistant, and a zone of inhibition \geq 22 mm was considered as methicillin sensitive, according to Clinical and Laboratory Standards Institute (CLSI) guidelines [23]. For quality control *S. aureus* ATCC 29213 (MSSA) and ATCC 43300 (MRSA) were used.

Antibiotic resistance profiles of *S. aureus* isolates against commonly prescribed antibiotics were determined by the Kirby-Bauer disc diffusion method on Mueller-Hinton agar (Hi-Media, Mumbai, India) and the results were interpreted according to the CLSI guidelines [21]. The antibiotics used were amikacin (30 μ g), ampicillin (10 μ g), cephalexin (30 μ g), cefoxitin (30 μ g), cefotaxime (30 μ g), ciprofloxacin (5 μ g), doxycycline (30 μ g), erythromycin (15 μ g), gentamicin (10 μ g), levofloxacin (5 μ g), penicillin (10 U), rifampicin (30 μ g), tetracycline (30 μ g), tigecycline (30 μ g), teicoplanin (30 μ g) and vancomycin (30 μ g).

STATISTICAL ANALYSIS

Data analysis was done using Statistical Package for Social Sciences (SPSS) software version 20. The collected information were summarised by using frequency, percentage, mean and standard deviation. Chi-square test was used to compare the difference in antibiotic sensitivity with respect to CA-MSSA and HA-MSSA, a p-value <0.05 was considered as statistically significant.

RESULTS

A total of 305 *S. aureus* were isolated during the study period. *Staphylococcus aureus* were isolated from various clinical samples [Table/Fig-1]. Out of 305 *Staphylococcus aureus* isolated, 219 (71.8%) were CA-MSSA and 86 (28.2%) were HA-MSSA. Out of 305 MSSA cases, inpatient admissions (IP) were 64.9% and outpatient admissions (OP) were 35.1% [Table/Fig-2]. The median age of the patients was 40 years, minimum age was 1 year and the maximum

age was 85 years. Frequency of isolation of *Staphylococcus aureus* from cases of different age groups is shown in [Table/Fig-3]. There was a significant difference between the isolation of CA-MSSA and HA-MSSA with regard to age group and IP/OP admission (p<0.05). In this study, 107 (35.1%) were females and 198 (64.9%) were males. *Staphylococcus aureus* were isolated mostly from Skin and Soft Tissue Infections (SSTI), (61.3%) [Table/Fig-4]. In this study, the overall mortality rate observed was 14 (4.6%). There was no significant difference between CA-MSSA and HA-MSSA with regard to gender, isolation from clinical samples and mortality rate. Patients with HA-MSSA infection had longer duration of hospital stay compared to patients with CA-MSSA infection [Table/Fig-5]. The clinical details of CA-MSSA and HA-MSSA cases are given in [Table/Fig-6].

Sample	Frequency (n=305) (%)			
Blood	20 (6.6)			
Body fluid	1 (0.3)			
CSF	1 (0.3)			
Pus	279 (91.5)			
Sputum	1 (0.3)			
Throat swab	2 (0.7)			
Urine	1 (0.3)			
Table/Fig. 11. Isolation of Staphylococours aurous from clinical camples				

[Table/Fig-1]: Isolation of *Staphylococcus aureus* from clinical samples.

	MSSA (n=305)		Chi-	
IP/OP	CA-MSSA (n=219) (%)) HA-MSSA (n=86) (%) v		p- value*
IP	119 (54.3)	79 (91.9)	38.175	<0.001
OP	100 (45.7)	7 (8.1)		
[Table/Fig.2]. Innatient and outpatient admission				

*significant; IP: Inpatient admission; OP: Outpatient admission; CA-MSSA: Community associated

metnicillin sensitive stap staphylococcus aureus

Age	MSSA (n=305)		Chi-square	
(years)	CA-MSSA (219) (%)	HA-MSSA (86) (%)	value	p-value*
0-10	13 (5.9)	4 (4.7)	_	
11-20	26 (11.9)	10 (11.6)		
21-30	56 (25.6)	11 (12.8)		
31-40	33 (15.1)	6 (7)		
41-50	39 (17.8)	19 (22.1)	21.486	0.006
51-60	25 (11.4)	14 (16.3)	-	
61-70	18 (8.2)	15 (17.4)		
71-80	5 (2.3)	7 (8.1)		
81-90	4 (1.8)	0 (0)		
[Table/Fig-3]: Isolation of MSSA from patients of different age groups. *significant				

Antibiotic Resistance

Antibiotic resistance profiles of MSSA against a panel of 23 antibiotics were studied [Table/Fig-7]. All MSSA isolates were 100% sensitive to amikacin, oxacillin, cefoxitin, linezolid and vancomycin. MSSA showed 100% resistance to ampicillin. MSSA showed higher antibiotic resistance against ciprofloxacin (64.6%), erythromycin (43.9%) and ofloxacin (42.3%). Comparative antibiotic resistance profile of CA-MSSA and HA-MSSA is shown in [Table/Fig-8]. Both CA-MSSA and HA-MSSA showed increased susceptibility to netilmycin, tigecycline, doxycycline, tetracycline, chloramphenicol and teicoplanin. There was a significant difference between CA-MSSA and HA-MSSA resistance shown against cefotaxime and co-trimoxazole (p<0.05). Of 305 MSSA isolates, 184 (60.3%) were found to be multidrug resistant. There was a significant difference between CA-MSSA 124 (56.6%) and HA-MSSA 60 (69.8%) showing MDR (p<0.05).

Disease Frequency (n=305) (%				
Skin and soft tissue infections	187 (61.3)			
Respiratory tract infections	15 (4.9)			
Bone and joint infections	24 (7.9)			
Septicaemia	10 (3.3)			
Ear infection	11 (3.6)			
Eye infection	2 (0.7)			
Acute febrile illness	8 (2.7)			
Abdominal infection	3 (1)			
Gas gangrene	1 (0.3)			
Renal disease	4 (1.3)			
Liver disease	2 (0.7)			
Pancreatitis 1 (0.3)				
Neurological disease 9 (3)				
Cardiovascular disease	4 (1.3)			
Carcinoma	16 (5.2)			
Sinusitis	4 (1.3)			
Tuberculosis	3 (1)			
Urinary tract infection	1 (0.3)			
[Table/Fig-4]: Clinical conditions of patients admitted to hospital during the study period.				

MSSA (n=305) Duration of CA-MSSA HA-MSSA Chi-square hospital stay (n=219) (%) (n=86) (%) value p-value* 1-7 days 182 (83.1) 36 (41.9) 8-14 days 25 (11.4) 18 (20.9) 15-21 days 1 (0.5) 1 (1.2) 22-28 days 0 (0) 1 (1.2) 64.214 < 0.001 11 (5) 1 months 26 (30.2) 2 months 0 (0) 3 (3.4) >2 months 0 (0) 1 (1.2) [Table/Fig-5]: Duration of hospital stay of patients with CA-MSSA and HA-MSSA

[Table/Fig-5]: Duration of hospital stay of patients with CA-MSSA and HA-MSSA infections. *Significant

	MSSA (n=305)				
Clinical details	CA-MSSA (n=219) (%)	HA-MSSA (n=86) (%)	Chi-square value	p-value	
Pyrexia	59 (26.9)	23 (26.7)	0.001	0.972	
Diabetes	35 (16)	23 (26.7)	4.645	0.031*	
Hypertension	20 (9.1)	17 (19.8)	13.960	0.001*	
Chronic infection	15 (6.8)	20 (23.3)	16.362	<0.001*	
Previous medication	17 (7.8)	46 (53.5)	78.779	<0.001*	
Allergy	22 (10)	1 (1.2)	6.988	0.008*	
Smoking	5 (2.3)	1 (1.2)	0.402	0.526	
Alcohol	7 (3.2)	2 (2.3)	0.163	0.686	
Epilepsy	0 (0)	2 (2.3)	5.127	0.024*	
Asthma	0 (0)	1 (1.2)	2.555	0.110	
Tuberculosis (TB)	1 (0.5)	2 (2.3)	2.215	0.137	
Cancer	0 (0)	16 (18.6)	43.000	<0.001*	
Surgery	3 (1.4)	20 (23.3)	42.423	<0.001*	
Transplant	0 (0)	0 (0)	NA	NA	
Dialysis	0 (0)	6 (7)	15.586	<0.001*	
Blood transfusion	0 (0)	2 (2.3)	5.127	0.024*	
Mortality rate	11 (5)	3 (3.5)	1.273	0.529	
[Table/Fig-6]: Clinical details of patients with CA-MSSA and HA-MSSA infections. *Significant; NA: Not applicable					

Antibiotic	MSSA (n=305) Resistant (%)			
Amikacin	O (0)			
Ampicillin	305 (100)			
Cephalexin	29 (9.5)			
Cefoxitin	O (0)			
Cefotaxime	49 (16.1)			
Ciprofloxacin	197 (64.6)			
Clindamycin	63 (20.7)			
Co-trimoxazole	47 (15.4)			
Chloramphenicol	3 (1)			
Doxycycline	3 (1)			
Erythromycin	134 (43.9)			
Gentamicin	22 (7.2)			
Levofloxacin	31 (10.2)			
Linezolid	0 (0)			
Netilmycin	4 (1.3)			
Oxacillin	O (O)			
Ofloxacin	129 (42.3)			
Penicillin	276 (90.5)			
Rifampicin	21 (6.9)			
Tetracycline	8 (2.6)			
Tigecycline	3 (1)			
Teicoplanin	14 (4.6)			
Vancomycin	O (O)			
[Table/Fig-7]: Overall antibiotic resistance profile of MSSA isolated from community and hospital associated infections.				

		MSSA (n=305)			
		CA-MSSA	HA-MSSA		
Antibiotic class	Antibiotics	(n=219) (Resistant (%)	(n=86) (Resistant (%)	Chi- square value	p-value
	Ampicillin	219 (100)	86 (100)	NA	NA
Penicillins	Oxacillin	0 (0)	0 (0)	NA	NA
	Penicillin	194 (88.6)	82 (95.3)	3.284	0.070
	Cephalexin	21 (9.6)	8 (9.3)	0.006	0.939
Cephalosporins	Cefoxitin	0 (0)	0 (0)	NA	NA
	Cefotaxime	28 (12.8)	21 (24.4)	6.197	0.013*
	Amikacin	0 (0)	0 (0)	NA	NA
Aminoglycosides	Gentamicin	15 (6.8)	7 (8.1)	0.154	0.695
	Netilimycin	2 (0.9)	2 (2.3)	0.952	0.329
Fluroquinolones	Ciprofloxacin	139 (63.5)	58 (67.4)	0.426	0.514
	Clindamycin	45 (20.5)	18 (20.9)	0.006	0.941
Macrolide	Erythromycin	91 (41.6)	43 (50)	1.789	0.181
Sulphonamides	Co-trimoxazole	28 (12.8)	19 (22.1)	4.104	0.043*
Quinolone	Levofloxacin	20 (9.1)	11 (12.8)	1.744	0.418
Quinoione	Ofloxacin	92 (42)	37 (43)	0.026	0.872
Oxazolidinones	Linezolid	0 (0)	0 (0)	NA	NA
Rifamycin	Rifampicin	12 (5.5)	9 (10.5)	2.394	0.122
Glycylcycline	Tigecycline	1 (0.5)	2 (2.3)	2.215	0.137
Tatus a valia a	Doxycycline	1 (0.5)	2 (2.3)	2.215	0.137
Tetracycline	Tetracycline	6 (2.7)	2 (2.3)	0.041	0.839
Chloramphenicol	Chloramphenicol	2 (0.9)	1 (1.2)	0.039	0.842
Olycoportido	Teicoplanin	11 (5)	3 (3.5)	0.332	0.564
Glycopeptide	Vancomycin	0 (0)	0 (0)	NA	NA

[Table/Fig-8]: Antibiotic resistance profile of CA-MSSA and HA-MSSA. *Significant; NA: Not applicable

DISCUSSION

MSSA Prevalence

This study revealed a higher prevalence of MSSA in patients attending a tertiary care hospital with community or hospital associated infections caused by Staphylococcus aureus. Several previous studies corroborate this observation [5,6,24,25]. A total of 305 MSSA were isolated during the study period. In this study, there was a significant difference between CA-MSSA and HA-MSSA with regard to age group. Higher prevalence of CA-MSSA was seen among age group 21-30 years (25.6%) and HA-MSSA from age group 41-50 years (22.1%). Authors found HA-MSSA prevalence was increasing in the older age groups with hospital associated risk factors compared to CA-MSSA found mostly in the younger and middle aged groups. Shenoy MS et al., found isolation of CA-MRSA mainly from patients of age group 21-30 years [26]. In this study, MSSA were mostly isolated from males compared to females, but no significant difference was observed between CA-MSSA and HA-MSSA with regard to gender, mortality rate and isolation from clinical specimens.

Out of 305 MSSA isolates, 71.8% were CA-MSSA which shows a higher prevalence of CA-MSSA compared to HA-MSSA 28.2%. In a study from Sikkim reported a prevalence rate of 42% in CA-MSSA and 22.7% in HA-MSSA [27]. In a study to know the epidemiology of Staphylococcus aureus in Bangalore CA-MSSA was 32% and HA-MSSA was 12% [10]. In this study, CA-MSSA were almost equally isolated from outpatients (45.7%) and inpatients (54.3%), while (91.9%) of HA-MSSA were from inpatients. The isolation of MSSA from inpatients and outpatients showed that MSSA is prevalent in the hospital and community settings. A study from Uttar Pradesh reported Staphylococcus aureus nasal carriage rate of 46.7% in children [28]. Since in this study, MSSA were isolated from cases admitted to different departments, measures have to be implemented for better patient treatment and prevent spread of MSSA in hospital and community settings. The available literature review on the prevalence of MSSA isolated from different places in India was studied and shown in [Table/Fig-9] [6,7,10,17,18,24,25,27,29].

Author name, (Reference	Study		Prevalence of Staphylococcus aureus (%)	
number)	Place Year		MSSA	MRSA
Aggarwal S et al., [6]	Bhuvaneshwar	July 2007- November 2015	70.6	29.4
Bhutia KO et al., [27]	Sikkim	September 2009- March 2011	64.7	35.3
Venniyil PV et al., [7]	Pondicherry	November 2009- May 2011	78.12	21.98
Eshwara VK et al., [18]	Manipal	August 2010- July 2011	46	54
Senthilkumar K et al., [29]	Pondicherry	August 2011- July 2013	53	47
Bouchiat C et al., [10]	Bangalore	November 2011- February 2012	47.8	52.2
Chatterjee A et al., [17]	Manipal	November 2011 -December 2012	48	52
Ravishankar A et al., [24]	Delhi	February-August 2013	76	24
Mamtora D et al., [25]	Mumbai	January 2015- December 2017	67.3	29.7
Present study		January 2015- February 2017	CA-MSSA HA-MSSA	NA
	Mangaluru		71.8 28.2	
[Table/Fig-9]: Literature review on prevalence of MSSA and MRSA in India				

[Table/Fig-9]: Literature review on prevalence of MSSA and MRSA in India [6,7,10,17,18,24,25,27,29]. In present study, MSSA were isolated mainly from SSTI (61.3%). A relatively lower MSSA isolation rate of 53% has been reported from Pondicherry [29], while a study from Delhi reported a higher isolation rate of 76% [24]. A study from China reported 81.2% of MSSA from SSTI [30].

Studies have reported a higher prevalence rate of MSSA compared to MRSA in India and different countries but varies worldwide [5,7]. In a study to determine the antibiotic susceptibility, virulence profile and genomic diversity among MSSA and MRSA from different parts of India from 2007 to 2015 found 70.6% MSSA and 29.4% MRSA [6]. A study from a tertiary care center in Mangalore to detect MRSA carriage in Critical Care Departments reported prevalence rate of MSSA in 15% and MRSA in 2.5% of healthcare workers [31]. A study from Mumbai reported prevalence rate of MSSA 67.3% and MRSA 29.7% [25]. A study from Northern Taiwan reported one third of *Staphylococcus aureus* infections in paediatric patients were due to MSSA [11].

A higher prevalence of MRSA have also been reported from several studies which has to be considered as MRSA might outnumber MSSA from the hospital and community settings [12,19]. A study from South Western India reported 52% MRSA and 48% MSSA [17,13]. Robinson DA et al., reported that the descendants of early penicillin resistant clone of Staphylococcus aureus, the phage type 80/81 have acquired methicillin resistance and re-emerged as CA-MRSA [32]. Staphylococcus aureus phage type 80/81 which caused early pandemic belonged to clonal complex 30 (CC30) [33]. A study from Singapore reported majority of CA-MRSA (SCCmec IV c) isolates belonged to sequence type (ST 30) and were highly transmissible [34]. D'Souza N et al., from Mumbai reported isolation of eleven PVL positive. MSSA isolates and all were ST 30 (CC30) and also found the presence of SCCmec IVc [4]. Mera RM et al., reported annual MRSA prevalence increased from 32.7% in 1998 to 53.8% in 2007 [35]. There could be a horizontal transfer of methicillin resistance gene from MRSA to multiple ST 30 MSSA isolates and subsequent dissemination, which can lead to outbreak of MRSA infections. Studies from South India reported increasing prevalence of MRSA compared to MSSA [17,18].

Antibiotic Resistance

In this study, the overall antibiotic resistance profile showed MSSA were susceptible to several antibiotics. MSSA were all susceptible to amikacin, cefoxitin, linezolid, oxacillin and vancomycin. A study by INSAR group reported 100% sensitivity to vancomycin and linezolid [8]. In this study the overall resistance profile of clindamycin was found to be 20.7%. A study from Mumbai, found MSSA highly susceptible to several antibiotics compared to MRSA [25]. In this study MSSA showed 100% resistance to ampicillin and were more susceptible to chloramphenicol, doxycycline, netilmycin, tetracycline, tigecycline and teicoplanin. MDR-resistance to more than three antibiotics was found in MSSA, showing greater resistance to ciprofloxacin 64.6%, erythromycin 43.9% and ofloxacin 42.3%. Shahkarami F et al., reported resistance to tetracycline 51.5%, gentamicin 30.3% and lower resistance to ciprofloxacin 22.2% and erythromyvin 15.2% [13]. Bouchiat C et al., reported resistance to erythromycin as 54.3% and no significant difference between MSSA and MRSA [10].

Staphylococcus aureus resistance to fluoroquinolones has been found to be increasing [12]. MSSA showed a resistance of 54.5% to ciprofloxacin reported by Bouchiat C et al., from Bangalore [10]. In India, a study reported 46.6% of MSSA resistant to ciprofloxacin [8].

In this study, a significant difference was found between CA-MSSA and HA-MSSA regarding antibiotic resistance profile against cefotaxime and co-trimoxazole (p<0.05). From this study, no significant difference was found between CA-MSSA and HA-MSSA resistance against ciprofloxacin 63.5% and 67.4% and erythromycin 41.6% and 50%, respectively (p>0.05). A study from Bangalore found no significant difference between CA-MSSA and HA-MSSA regarding

antibiotic resistance against erythromycin 43.8% and 41.7% and against ciprofloxacin 56.3% and 50%, respectively [10]. Kini AR et al., reported CA-MSSA with 67% resistance to erythromycin and 48% resistance to ciprofloxacin [15]. A study from Andhra Pradesh reported CA-MSSA and HA-MSSA resistance against ciprofloxacin 57.1%, and 66.7% and against erythromycin 29.3% and 17.4%, respectively and no significant difference between CA-MSSA and HA-MSSA in antibiotic resistance [12]. In this study, it was found CA-MSSA and HA-MSSA susceptible to multiple classes of antibiotics, and CA-MSSA showed increased susceptibility to gentamicin, netilmycin, rifampicin, tigecycline levofloxacin, doxycycline and chloramphenicol compared to HA-MSSA. Emerging clindamycin resistance and increasing resistance against erythromycin is of great concern as macrolides have a significant role in the treatment of Staphylococcal infections.

In this study CA-MSSA and HA-MSSA showing MDR were found. MDR shown by HA-MSSA were found to be higher compared to CA-MSSA. Both CA-MSSA and HA-MSSA showed resistance to ciprofloxacin, erythromycin, ofloxacin, ampicillin, penicillin and the emergence of clindamycin resistance. Aggarwal S et al., reported out of 109 Staphylococcus aureus isolated from a variety of infections in India, 102 (93.6%) were MDR and from the total 70.6% were MSSA, 29.4% were MRSA respectively [6] A study from Punjab reported higher prevalence of MRSA compared to MSSA and MDR [19]. Tayebi Z et al., reported 69.4% of MSSA exhibited MDR [14]. Emergence of MDR in MSSA is a matter of great concern as MDR MSSA will spread in hospitals and to the community which can create difficulty in patient treatment. Studies reporting increasing prevalence of virulent MRSA in community and hospital settings [3], there is an increased chance to transfer mobile methicillin resistant gene from MRSA to MSSA and MRSA might replace MSSA from hospital and community settings and measures to be taken to prevent MSSA becoming MDR and becoming methicillin resistant which can cause treatment failure.

Limitation(s)

In the present study, antibiotic susceptibility testing for vancomycin by Minimum Inhibitory Concenteration (MIC) method was not carried out and authors did not analyse the severity of MSSA infections caused in each clinical condition.

CONCLUSION(S)

From this study, it was found that MSSA is increasingly prevalent in community and hospital settings with emergence of MDR. Immediate control measures have to be taken to prevent the spread of MDR MSSA in the hospital settings and to the community also to prevent the replacement of MSSA by more virulent MRSA. Strict aseptic techniques in hospitals, treatment of patients and carriers, screening of hospital staff, antibiotic stewardship and treatment plan has to be implemented immediately to prevent the spread of MSSA and emergence of MDR.

Acknowledgement

We acknowledge our gratitude to K.S. Hegde Medical Academy, Nitte (Deemed to be University), Mangalore for all the support in our research work.

REFERENCES

- Jevons MP. "Celbenin"-Resistant Staphylococci. Br Med J. 1961;1(5219):124-25.
 Turner NA, Sharma-Kuinkel BK, Maskarinec SA, Eichenberger EM, Shah PP, Carugati M, et al. Methicillin-resistant Staphylococcus aureus: An overview of
- basic and clinical research. Nat Rev Microbiol. 2019;17:203-18.
 [3] Nakaminami H, Takadama S, Ito A, Hasegawa M, Jono C, Noguchi M, et al. Characterization of SCCmec type IV methicillin-resistant *Staphylococcus aureus* clones increased in Japanese hospitals. J Med Microbiol. 2018;67(6):769-74.
- [4] D'Souza N, Rodrigues C, Mehta A. Molecular characterization of methicillinresistant *Staphylococcus aureus* with emergence of epidemic clones of sequence type (ST) 22 and ST 772 in Mumbai, India. J Clin Microbiol. 2010;48(5):1806-11.

- [5] Tsige Y, Tadesse S, G/Eyesus T, Tefera MM, Amsalu A, Menberu MA, et al. Prevalence of methicillin-resistant *Staphylococcus aureus* and associated risk factors among patients with wound infection at referral hospital, Northeast Ethiopia. *J Pathog.* 2020;2020:3168325.
- [6] Aggarwal S, Jena S, Panda S, Sharma S, Dhawan B, Nath G, et al. Antibiotic susceptibility, virulence pattern, and typing of *Staphylococcus aureus* strains isolated from variety of infections in India. Front Microbiol. 2019;10:2763.
- [7] Venniyil PV, Ganguly S, Kuruvila S, Devi S. A study of community-associated methicillin resistant *Staphylococcus aureus* in patients with pyoderma. Indian Dermatol Online J. 2016;7:159-63.
- [8] Indian Network for Surveillance of Antimicrobial Resistance (INSAR) group, India. Methicillin resistant *Staphylococcus aureus* (MRSA) in India: prevalence & susceptibility pattern. Indian J Med Res. 2013;137(2):363-69.
- [9] Schwarzkopf R, Takemoto RC, Immerman I, Slover JD, Bosco JA. Prevalence of Staphylococcus aureus colonisation in orthopaedic surgeons and their patients: A prospective cohort controlled study. J Bone Joint Surg Am. 2010;92(9):1815-19.
- [10] Bouchiat C, El-Zeenni N, Chakrakodi B, Nagaraj S, Arakere G, Etienne J. Epidemiology of *Staphylococcus aureus* in Bangalore, India: Emergence of the ST217 clone and high rate of resistance to erythromycin and ciprofloxacin in the community. New Microbes New Infect. 2015;7:15-20.
- [11] Chen YJ, Chen PA, Chen CJ, Huang YC. Molecular characteristics and clinical features of pediatric methicillin-susceptible *Staphylococcus aureus* infection in a medical center in northern Taiwan. BMC Infect Dis. 2019;19:402.
- [12] Alvarez-Uria G, Reddy R. Prevalence and antibiotic susceptibility of communityassociated methicillin-resistant *Staphylococcus aureus* in a rural area of India: Is MRSA replacing methicillin-susceptible *Staphylococcus aureus* in the community? ISRN Dermatol. 2012;2012:248951.
- [13] Shahkarami F, Rashki A, Rashki Ghalehnoo Z. Microbial susceptibility and plasmid profiles of methicillin-resistant *Staphylococcus aureus* and methicillinsusceptible *S. aureus*. Jundishapur. J Microbiol. 2014;7(7):e16984.
- [14] Tayebi Z, Goudarzi H, Dadashi M, Goudarzi M. Genotype distribution of methicillin-susceptible *Staphylococcus aureus* clinical isolates in Iran: High multiresistant clonal complex 8. BMC Res Notes. 2020;13:277.
- [15] Kini AR, Shetty V, Kumar AM, Shetty SM, Shetty A. Community-associated, methicillin-susceptible, and methicillin-resistant *Staphylococcus aureus* bone and joint infections in children: Experience from India. J Pediatr Orthop B. 2013;22(2):158-66.
- [16] Zabielinski M, McLeod MP, Aber C, Izakovic J, Schachner LA. Trends and antibiotic susceptibility patterns of methicillin-resistant and methicillin-sensitive *Staphylococcus aureus* in an outpatient dermatology facility. JAMA Dermatol. 2013;149(4):427-32.
- [17] Chatterjee A, Rai S, Guddattu V, Mukhopadhyay C, Saravu K. Is methicillinresistant *Staphylococcus aureus* infection associated with higher mortality and morbidity in hospitalized patients? A cohort study of 551 patients from South Western India. Risk Manag Healthc Policy. 2018;11:243-50.
- [18] Eshwara VK, Munim F, Tellapragada C, Kamath A, Varma M, Lewis LE, et al. Staphylococcus aureus bacteremia in an Indian tertiary care hospital: Observational study on clinical epidemiology, resistance characteristics, and carriage of the Panton-Valentine leukocidin gene. Int J Infect Dis. 2013;17(11):e1051-55.
- [19] Jindal N, Malhotra R, Grover P, Singh S, Bansal R, Kaur S. Methicillin resistant Staphylococcus aureus (MRSA) in Malwa region of Punjab (North-West India). Indian J Med Res. 2016;143(3):371-72.
- [20] Rasigade JP, Laurent F, Lina G, Meugnier H, Bes M, Vandenesch F, et al. Global distribution and evolution of Panton-Valentine leukocidin-positive methicillin-susceptible *Staphylococcus aureus*, 1981-2007. J Infect Dis. 2010;201(10):1589-97.
- [21] Baird D, Collee JG, Fraser AG, Marmion BP, Simmons A (Eds). Mackie and Mc Cartney Practical Medical Microbiology (14th ed). New York: Churchill-Livingstone; 1996;245-61.
- [22] Broekema NM, Van TT, Monson TA, Marshall SA, Warshauer DM. Comparison of cefoxitin and oxacillin disk diffusion methods for detection of *mecA*-mediated resistance in *Staphylococcus aureus* in a large-scale study. J Clin Microbiol. 2009;47(1):217-19.
- [23] CLSI. Performance Standards for Antimicrobial Susceptibility Testing; Approved Standard M100-S26. Wayne, PA, USA: Clinical and Laboratory Standards Institute; 2016.
- [24] Ravishankar A, Singh S, Rai S, Sharma N, Gupta S, Thawani R. Socio-economic profile of patients with community-acquired skin and soft tissue infections in Delhi. Pathog Glob Health. 2014;108(6):279-82.
- [25] Mamtora D, Saseedharan S, Bhalekar P, Katakdhond S. Microbiological profile and antibiotic susceptibility pattern of Gram-positive isolates at a tertiary care hospital. J Lab Physicians. 2019;11(2):144-48.
- [26] Shenoy MS, Bhat GK, Kishore A, Hassan MK. Significance of MRSA strains in community associated skin and soft tissue infections. Indian J Med Microbiol. 2010;28:152-54.
- [27] Bhutia KO, Singh T, Adhikari L, Biswas S. Molecular characterization of community-& hospital-acquired methicillin-resistant & methicillin-sensitive *Staphylococcus aureus* isolates in Sikkim. Indian J Med Res. 2015;142(3):330-35.
- [28] Singh AK, Agarwal L, Kumar A, Sengupta C, Singh RP. Prevalence of nasal colonisation of methicillin-resistant *Staphylococcus aureus* among schoolchildren of Barabanki district, Ultar Pradesh, India. J Family Med Prim Care. 2018;7(1):162-66.
- [29] Senthilkumar K, Biswal N, Sistla S. Risk factors associated with Methicillin-resistant Staphylococcus aureus infection in children. Indian Pediatr. 2015;52:31-33.
- [30] Gu FF, Hou Q, Yang HH, Zhu YQ, Guo XK, Ni YX, et al. Characterization of Staphylococcus aureus isolated from non-native patients with skin and soft tissue infections in Shanghai. PLoS ONE. 2015;10(4):e0123557.

- [31] Radhakrishna M, D'Souza M, Kotigadde S, Saralaya KV, Kotian MS. Prevalence of methicillin resistant *Staphylococcus aureus* carriage amongst health care workers of critical care units in Kasturba Medical College hospital, Mangalore, India. J Clin Diagn Res. 2013;7(12):2697-700.
- [32] Robinson DA, Kearns AM, Holmes A, Morrison D, Grundmann H, Edwards G, et al. Re-emergence of early pandemic *Staphylococcus aureus* as a communityacquired meticillin-resistant clone. Lancet. 2005;365(9466):1256-58.
- [33] Chambers HF, Deleo FR. Waves of resistance: Staphylococcus aureus in the antibiotic era. Nat Rev Microbiol. 2009;7(9):629-41.
- [34] Hsu LY, Koh YL, Chlebicka NL, Tan TY, Krishnan P, Tzer-Pin Lin R, et al. Establishment of ST30 as the predominant clonal type among communityassociated methicillin-resistant *Staphylococcus aureus* isolates in Singapore. J Clin Microbiol. 2006;44(3):1090-93.
- [35] Mera RM, Suaya JA, Amrine-Madsen H, Hogea CS, Miller LA, Lu EP, et al. Increasing role of *Staphylococcus aureus* and community-acquired methicillin-resistant *Staphylococcus aureus* infections in the United States: A 10-year trend of replacement and expansion. Microb Drug Resist. 2011;17(2):321-28.

PARTICULARS OF CONTRIBUTORS:

- 1. Research Scholar, Department of Microbiology, KS Hegde Medical Academy, Nitte (Deemed to be University), Mangaluru, Karnataka, India.
- 2. Senior Scientist (Microbiology), Department of QC Laboratory, ICAR Central Institute of Fisheries Education, Versova, Mumbai, Maharashtra, India.
- 3. Additional Professor, Department of Microbiology, KS Hegde Medical Academy, Nitte (Deemed to be University), Mangaluru, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR: Dr. Veena A Shetty,

Additional Professor, Department of Microbiology, KS Hegde Medical Academy, Nitte (Deemed to be University), Deralakatte, Mangalore-575018, Karnataka, India. E-mail: veenashetty@nitte.edu.in

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA
- PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Dec 23, 2020
- Manual Googling: Jan 28, 2021
- iThenticate Software: Feb 09, 2021 (16%)

Date of Submission: Dec 12, 2020 Date of Peer Review: Dec 23, 2020 Date of Acceptance: Jan 29, 2021 Date of Publishing: Mar 01, 2021

ETYMOLOGY: Author Origin