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Methicillin resistant *Staphylococcus aureus* (MRSA) in India: Prevalence & susceptibility pattern

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***Background & objectives*: Methicillin resistant *Staphylococcus aureus* (MRSA) is endemic in India and is a dangerous pathogen for hospital acquired infections. This study was conducted in 15 Indian tertiary care centres during a two year period from January 2008 to December 2009 to determine the prevalence of MRSA and susceptibility pattern of *S. aureus* isolates in India.**

***Methods*: All *S. aureus* isolates obtained during the study period in the participating centres were included in the study. Each centre compiled their data in a predefined template which included data of the antimicrobial susceptibility pattern, location of the patient and specimen type. The data in the submitted templates were collated and analysed.**

***Results*: A total of 26310 isolates were included in the study. The overall prevalence of methicillin resistance during the study period was 41 per cent. Isolation rates for MRSA from outpatients, ward inpatients and ICU were 28, 42 and 43 per cent, respectively in 2008 and 27, 49 and 47 per cent, respectively in 2009. The majority of *S. aureus* isolates was obtained from patients with skin and soft tissue infections followed by those suffering from blood stream infections and respiratory infections. Susceptibility to ciprofloxacin was low in both MSSA (53%) and MRSA (21%). MSSA isolates showed a higher susceptibility to gentamicin, co-trimoxazole, erythromycin and clindamycin as compared to MRSA isolates. No isolate was found resistant to vancomycin or linezolid.**

***Interpretation & conclusions*: The study showed a high level of MRSA in our country. There is a need to study epidemiology of such infections. Robust antimicrobial stewardship and strengthened infection control measures are required to prevent spread and reduce emergence of resistance.**

Key words Antimicrobial susceptibility - India - MRSA - prevalence - *Staphylococcus*

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Staphylococcus aureus continues to be a dangerous pathogen for both community-acquired as well as hospital-associated infections. *S. aureus* resistant to methicillin were reported soon after its introduction in October 1960[1]. Methicillin resistant *S. aureus* (MRSA) is now endemic in India. The incidence of MRSA varies from 25 per cent in western part of India[2] to 50 per cent in South India[3]. Community acquired MRSA (CA-MRSA) has been increasingly reported from India[4].

A network of microbiology laboratories (Indian Network for Surveillance of Antimicrobial Resistance - INSAR) at premier medical colleges and hospitals in India was formed with support from the World Health Organization (Figure). The network aims to monitor antimicrobial resistance and to review the magnitude of its problem in India. Initially, a few organisms of public health importance have been chosen for monitoring their prevalence and antimicrobial resistance patterns, with *S. aureus* being chosen among the Gram-positive organisms. All participating laboratories shared their antimicrobial susceptibility data and provided technical support to other members. The present study provides a national level initiative to understand emerging trends of antimicrobial resistance among clinical isolates of *S. aureus* and provides a platform to initiate epidemiological studies for staphylococcal infections.

Material & Methods

The present study was a two year (January 2008 to December 2009) retrospective study. Each centre provided their susceptibility data for *S. aureus* isolates for the study period in a defined template. The data were collated and analysed. The template included patient's location, source/specimen of the isolate and the antibiotic susceptibility profiles. The antibiotic susceptibility testing was performed at different study

Fig. Places marked with red dots are INSAR members whose data one oncluded in teh study. Places marked *are INSAR members whose data are not included in the study.

sites by the Kirby Bauer's' disc diffusion technique[5] and/or minimum inhibitory concentration (MIC) testing, using Clinical and Laboratory Standards Institute (CLSI) recommendations[5]. Cefoxitin (30 µg) and/or oxacillin (1 µg) were used for methicillin resistance.

The other antibiotics tested included penicillin (10 units), gentamicin (10 µg), co-trimoxazole (1.25/23.75 µg), ciprofloxacin (5 µg), erythromycin (15 µg), clindamycin (2 µg), vancomycin (30 µg) and linezolid (30 µg). Discs from Hi-media (Mumbai) and Oxoid (UK) were used by the participating laboratories. Inoculum was prepared by making a direct saline suspension of isolated colonies selected from an 18- to 24-h blood agar plate. Turbidity of the suspension was adjusted to achieve a turbidity equivalent to a 0.5 McFarland standard and five discs were applied on a 100mm Mueller Hinton agar plate as per CLSI guidelines. *S. aureus* ATCC 25923 was used as the quality control strain for disc diffusion.

Chi square test was used to compare antimicrobial susceptibility data.

Results

Of the 13975 isolates of *S. aureus* in 2008, 5864 (42%) were MRSA. In 2009, of the 12335 isolates, 5133 (40%) were MRSA. (Table I). Details of 5354 isolates in 2008 and 7088 isolates in 2009 were available (Table II). The majority of the isolates were obtained from inpatients - 3664 in 2008 and 4487 in 2009. The MRSA rates among outpatients, non-ICU inpatients and ICU patients were 28, 42 and 43 per cent, respectively in 2008 and 27, 49 and 47 per cent, respectively in 2009.

The details of the specimen were available for 12442 isolates. *S. aureus* was mainly isolated from

Table I: Distribution of *S. aureus* and MRSA among the study centres.

Centres	2008 Total S. aureus	MRSA 2008 (%)	2009 Total S. aureus	MRSA 2009 (%)	Total S. aureus	Total MRSA (%)
A	3109	1646 (53%)			3109	1646 (53%)
B	453	97 (21%)	625	167 (27%)	1078	264 (24%)
C	289	166 (57%)	306	90 (29%)	595	256 (43%)
D	266	157 (59%)	300	191 (64%)	566	348 (61%)
E	394	261 (66%)	430	95 (22%)	824	356 (43%)
F	3124	1046 (33%)	3375	1314 (39%)	6499	2360 (36%)
G	320	76 (24%)	254	55 (22%)	574	131 (23%)
H	164	70 (43%)	294	128 (44%)	458	198 (43%)
I	335	190 (57%)	387	220 (57%)	722	410 (57%)
J	650	192 (29%)	948	530 (56%)	1598	722 (45%)
K	889	340 (38%)	501	187 (37%)	1390	527 (38%)
L			760	260 (34%)	760	260 (34%)
M	994	599 (60%)	1093	662 (61%)	2087	1261 (60%)
N	903	227 (25%)	699	131 (19%)	1602	358 (22%)
O	1975	704 (36%)	2262	824 (36%)	4237	1528 (36%)
P	110	93 (84%)	101	50 (50%)	211	144 (68%)
Total	13975	5864 (42%)	12335	4904 (40%)	26310	10769 (41%)

A- All India Institute of Medical Sciences (AIIMS) – New Delhi, B- Apollo Health City (AHC) – Hyderabad , C- Indraprastha Apollo Hospital – New Delhi (IAH), D- BJ medical college (BJMC)-Pune, E- Choithram Hospital and Research Centre – Indore (CHRC), F- Christian Medical College (CMC) – Vellore (CMC), G- Chacha Nehru Bal Chikitsalaya (CNBC) – New Delhi, H- Fortis Hospital-Mohali (FHM) , I- Gujarat Cancer and Research Institute (GCRI) – Ahmedabad (GCRI), J- Govt Medical College (GMC) – Aurangabad (GMCA), K- Government Medical College & Hospital (GMC) – Chandigarh (GMCH), L- PD Hinduja National Hospital & MRC (PDNH)– Mumbai, M- Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) – Puducherry, N- Manipal Hospital – Bangalore (MHB), O- Postgraduate Institute of Medical Education & Research (PGIMER) – Chandigarh, P- Regional Institute of Medical Sciences (RIMS) – Imphal

Table II. Specimen-wise distribution of *S. aureus*

Specimen		2008			2009		
		Total	MRSA		Total	MRSA	
			n	(%)		n	(%)
Pus	Total	3450	1255	36	4326	1717	40
	OP	1024	268	26	1492	390	26
	Ward	2330	953	41	2704	1269	47
	ICU	96	34	35	130	58	45
Blood	Total	730	319	44	1013	483	48
	OP	45	14	31	94	23	24
	Ward	593	258	44	723	363	50
	ICU	92	47	51	196	97	49
Respiratory samples	Total	450	197	44	647	265	41
	Op	78	25	32	136	35	26
	Ward	265	129	49	360	155	43
	ICU	107	43	40	151	75	50
Urine	Total	110	45	41	130	67	52
	Op	43	12	28	69	29	42
	Ward	60	30	50	51	34	67
	ICU	7	3	43	10	4	40
Sterile body fluids	Total	61	21	34	138	74	54
	Op	1	0	0	12	6	50
	Ward	55	20	36	115	64	56
	ICU	5	1	20	11	4	36
Tissue	Total	71	24	34	145	56	39
	Op	8	6	75	34	17	50
	Ward	57	18	32	106	37	35
	ICU	6	0	0	5	2	40
Other specimens ear swabs, nasal swabs and skin swabs and fluids	Total	482	222	46	689	303	44
	Op	147	58	39	175	53	30
	Ward	304	142	47	428	200	47
	ICU	31	22	71	86	50	58
Total specimens	Total	5354	2083	38.9	7088	2695	38
	Op	1346	383	28.4	2012	553	27
	Ward	3664	1550	42.3	4487	2122	49
	ICU	344	150	43.6	589	290	47

OP- Outpatients.
ICU- Intesive Care Unit

Table III. Antibiotic susceptibility results of *Staphylococcus aureus* 2008-2009

Antibiotics	Strain (N)	Sensitive (%)	Resistant (%)	*P* value
Erythromycin	MRSA (6575)	1917 (29.2)	4658 (70.8)	0.000
	MSSA (9048)	6672 (73.7)	2376 (26.3)	
Clindamycin	MRSA (3903)	2083 (53.4)	1820 (46.6)	0.000
	MSSA (5480)	4674 (85.3)	806 (14.7)	
Gentamicin	MRSA (5464)	2278 (41.7)	3186 (58.3)	0.000
	MSSA (7433)	6139 (82.6)	1294 (17.4)	
Co-trimoxazole	MRSA (3199)	1421 (44.4)	1778 (55.6)	0.000
	MSSA (4425)	3226 (72.9)	1199 (27.1)	
Ciprofloxacin	MRSA (6241)	1290 (20.7)	4951 (79.3)	0.000
	MSSA (8245)	4404 (53.4)	3841 (46.6)	
Vancomycin	MSSA & MRSA (13482)	13842 (100)	0	
Linezolid	MSSA & MRSA (8004)	8004 (100)	0	
Penicillin	MSSA (6919)	5288 (76.4)	1631 (23.6)	
	MRSA (4581)	0	4581 (100)	

MRSA and MSSA - methicillin resistant and sensitive *S. aureus*
(*P<0.005 is significant)

skin and soft tissue infections (64% in 2008 and 61% in 2009) followed by blood and respiratory samples including bronchial washings, endotracheal secretions and sputum (Table II). Throat swab and genital specimens were received mainly from outpatients whereas *S. aureus* isolated from tissue, catheter tips and fluid from sterile body sites were predominantly from inpatients. Other specimens received included ear swabs, nasal swabs and skin swabs and fluids.

Antibiotic susceptibility testing data for erythromycin, clindamycin, co-trimoxazole, gentamicin, vancomycin and linezolid were compiled. There was no resistance documented against vancomycin and linezolid. Resistance to antibiotics amongst the MRSA isolates was more than that in methicillin sensitive *S. aureus* (MSSA) (P<0.001) (Table III). The susceptibility to other antibiotics from different centres was analysed. (Table IV). There was no uniform difference in the susceptibilities between centres of north, south and west India.

Discussion

Among the Gram-positive pathogens, *S. aureus* continues to cause skin and soft tissue infections (SSTI) in the community as well as invasive infections in the hospitalized patients. In a recent Europe-wide survey, the most common organisms in SSTIs were *S. aureus* (71% cases) with 22.5 per cent being MRSA[6]. The proportion of MRSA varied among countries ranging from 0.4 per cent in Sweden to 48.4 per cent in Belgium[6]. In a study in US[7] spanning over 10 years, there was an increase in the overall incidence of *S. aureus* during this period with an increase in community onset MRSA SSTI.

The overall MRSA prevalence in our study was 42 per cent in 2008 and 40 per cent in 2009. The prevalence of MRSA in a study from Chennai[3] was reported as 40-50 per cent. *S. aureus* constituted 17 per cent of catheter related blood stream infections (CRBSIs) in that centre. A high prevalence of MRSA (35% in ward and 43% in ICU) was observed from blood culture specimens in a

Table IV: Percentage Susceptibilities of *S. aureus* isolates from different INSAR centers (2008-09).

Centres	Ery	Cli	Gen	Sxt	Cip	Van	Lin
A	44	-	47	100	41	100	100
B	70	81	-	-	-	100	100
C	67	74	63	75	50	100	100
D	36		57	34	33	100	100
E	46	79	70	70	49	100	100
F	49	-	91	91	35	100	100
G	45	94	80	28	37	100	100
H	42	71	50	84	14	100	100
I	33	36	-	-	-	100	100
J	46	46	40	40	64	100	100
K	72	74	79	67	43	100	100
L	43	70	66	66	29	100	100
M	40	-	45	45	27	100	100
N	71	82	79	79	64	100	100
O	59	34	78	-	14	100	100
P	54	56	59	59	42	100	100
Total	**52**	**79**	**69**	**70**	**36**	**100**	**100**

A- All India Institute of Medical Sciences (AIIMS) – New Delhi, B- Apollo Health City (AHC) – Hyderabad , C- Indraprastha Apollo Hospital – New Delhi (IAH), D- BJ medical college (BJMC)-Pune, E- Choithram Hospital and Research Centre – Indore (CHRC), F- Christian Medical College (CMC) – Vellore (CMC), G- Chacha Nehru Bal Chikitsalaya (CNBC) – New Delhi, H- Fortis Hospital-Mohali (FHM) , I- Gujarat Cancer and Research Institute (GCRI) – Ahmedabad (GCRI), J- Govt Medical College (GMC) – Aurangabad (GMCA), K- Government Medical College & Hospital (GMC) – Chandigarh (GMCH), L- PD Hinduja National Hospital & MRC (PDNH)– Mumbai, M- Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) – Puducherry, N- Manipal Hospital – Bangalore (MHB), O- Postgraduate Institute of Medical Education & Research (PGIMER) – Chandigarh, P- Regional Institute of Medical Sciences (RIMS) – Imphal
Ery- Erythromycin, Cli- Clindamycin, Gen- Gentamicin, Sxt – Cotrimoxazole, Cip- Ciprofloxacin, Van- Vancomycin, Lin – Linezolid.

study in Delhi[8]. In the present study, MRSA isolation rates from ICU and wards were higher than that seen among outpatients. Patel et al[2] reported a change in the blood stream infections with *S. aureus* emerging as the predominant pathogen in recent years.

Around 60 per cent of the *S. aureus* isolates in our study were from SSTI. The prevalence of MRSA varies between regions and between hospitals in the same region as seen in a study from Delhi[9] where the MRSA prevalence in nosocomial SSTI varied from 7.5 to 41.3 per cent between three tertiary care teaching hospitals. In our study, the MRSA isolation varied between different hospitals. The participating centres included teaching hospitals, tertiary care private hospitals and a children's hospital. The patient profile varied between these centres and may account for the different MRSA isolation rates. Verghese *et al*[10] reported Gram-negatives being predominantly isolated from their samples. *S. aureus* accounted for less than 25 per cent of SSTI among their patients and the overall MRSA rate was 35 per cent[10].

CA-MRSA isolates are now being increasingly reported from India. D' Souza *et al*[4] studied 412 confirmed cases of MRSA and found that 54 per cent were true CA-MRSA possessing the *SCCmec IV* and *SCC mec V* genes. These were mainly isolated from SSTIs. CA-MRSA isolates also showed variable resistance to ciprofloxacin, erythromycin, clindamycin and tetracycline. Chatterjee *et al*[11] found the overall prevalence of *S. aureus* nasal colonization was 52.3 per cent and that of MRSA was 3.89 per cent in the community.

In a study from north India[12], the prevalence of MRSA was 46 per cent and MRSA isolates were found to be more resistant to other antibiotics than MSSA. Significant difference was observed in case of erythromycin, ciprofloxacin, gentamicin and amikacin.

Vancomycin is considered inferior to β-lactams for the treatment of MSSA bacteraemia and endocarditis[13]. Therefore, the first-generation cephalosporins are the drugs of choice for the treatment of MSSA infections in patients who are unable to tolerate antistaphylococcal penicillins. De-escalation of vancomycin to β-lactams should be encouraged in all cases of MSSA. With MRSA isolates being widespread, it is imperative that treating physicians de-escalate to β-lactams once the culture sensitivity results reveal a MSSA isolate. Preservation of glycopeptides and linezolid for use only in MRSA cases should be encouraged.

Our study had the following limitations. Firstly, the data obtained from all the centres were not uniform with respect to the antibiotics tested. Hence an accurate determination of multidrug resistance in all the MRSA

isolates could not be done. Secondly, molecular studies have not been done for these isolates to differentiate between CA-MRSA and healthcare associated MRSA (HA-MRSA).

In conclusion, this study demonstrates that MRSA is a problem in India. More number of MRSA isolates were multidrug resistant as compared with the MSSA isolates. Glycopeptides and linezolid continue to remain the mainstay for treatment for MRSA infections.

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