Original Article

Antimicrobial Susceptibility Profile of *Staphylococcus aureus* Isolates Obtained from Skin and Soft Tissue Infections : A Real-World Study Based on a Large Diagnostic Laboratory Data

Manmohan Singh[1], Gifty Immanuel[2], Aarathy Kannan[3]

Introduction : Skin and soft tissue infections (SSTIs) are infections of the epidermis, dermis, or subcutaneous tissues caused by the microbial invasion of the skin and underlying soft tissues. India reported an incidence rate of SSTIs to be 18.21/1000 person-years. The susceptibility of *Staphylococcus aureus* to prescribed antimicrobials varies widely across the geographic regions due to increasing resistance. This study aims to assess the susceptibility profile and trends by utilizing the diagnostic laboratory-based data from multiple centers across India.

Methods : It is an observational retrospective study conducted on secondary data retrieved from multiple diagnostic laboratories located across different Indian states. A total of 6142 specimens of *Staphylococcus aureus* from different skin and soft tissue samples, were included in the study. The included samples were from different specimen categories such as pus swab, breast abscesses, skin scrapping, bedsore swab, hand swab, nipple discharge and nail scrapping. Only the records of the patients, who attended diagnostic labs between Jan 2010-Dec 2019, were considered for the analysis.

Results : Overall, 29252 specimens (pus swab, breast abscess, skin scrapping, bedsore swab, hand swab nipple discharge and nail scrapping) of SSTIs were considered, out of which, 6142 were found to be positive for *Staphylococcus aureus* and were included in the final analysis. Susceptibility of *Staphylococcus aureus* was found to be highest for 1st generation cephalosporins (84.7% & 88% for cephalexin and cephazolin respectively), followed by 79.5% for second generation cephalosporin (cefuroxime) and 53.8% for third generation cephalosporin (cefixime). For other two commonly used antimicrobial agents, clindamycin & amoxicillin-clavulanic acid in SSTI susceptibility was found to be 78.5% and 66.1% respectively. *Staphylococcus aureus* was found to be highly resistant to amoxicillin (sensitivity 7.4%).

Conclusion : This study highlighted the increase in resistance to the newer generation antimicrobial agents and there are significant regional differences in sensitivity patterns of culture isolates.

[*J Indian Med Assoc* 2021; **119(3):** 21-6]

S kin and soft tissue infections (SSTIs) are defined as infections of the epidermis, dermis, or subcutaneous tissues caused by the microbial invasion of the skin and underlying soft tissues. These infections have highly variable presentations, severity, etiologies are frequently observed in clinical practice[1]. According to a study conducted on the general population in the USA, the estimated incidence rate of SSTIs was found to be 24.6 per 1000 person-years[2]. Another study reported an estimated prevalence of 7-10% of SSTIs amongst hospitalized patients[3]. Further, a study highlighted SSTIs as the third most diagnosed disease condition in emergency care settings after chest pain and asthma[4]. A study conducted on patients visiting the Emergency Department of Tamil Nadu, India reported an incidence rate of SSTIs to be 18.21/1000 person-years[5].

The infections contributing to the purulent type of SSTIs are carbuncles, furuncles and abscesses while non-purulent infections

Editor's Comment :
- Continuous surveillance of AMR remains the key step in detecting spatiotemporal deviation in resistance patterns.
- Abandoned antimicrobials can be resurrected and repositioned for the chemotherapy of skin infections with resistant organisms.
- Physicians' clinical decision trees and algorithms should be guided by real-time data studies.

include cellulitis, erysipelas and necrotizing fasciitis[1]. Further, SSTIs can be classified into other categories like the mild, moderate and severe type of infections[6]. Severe purulent infections show symptoms like tachycardia, rise of temperature (>38°C), tachypnea and abnormal count of White Blood Cell (WBC). Moderate non-purulent infections of mild type include erysipelas or cellulitis with systemic symptoms of infections[7].

The spectrum of SSTIs ranges from mild infections such as pyoderma to life-threatening infections. The possible reasons for this can range from the inappropriate medical management or the presence of other co-morbidities such as diabetes and immunocompromised conditions like HIV/AIDS[6]. *Staphylococcus aureus* is the causative organism of a large percentage of SSTIs (39%) and blood infections (22%)[8]. It is capable of evading antimicrobials and host defenses by multiplying and persisting in

[1]MD, Medical Director, Department of Medico Clinical, Technology Healthcare Big Data Analytics, Gurugram 122001 and Corresponding Author

[2]MD (Infectious Disease), Head, Department of Infectious Diseases, Church of South India Hospital, Bangalore 560051

[3]MD, Physician, Sundaram Arulrhaj Hospital, Tuticorin 628002

biofilms formed on surfaces of the prosthetic devices in the hosts[9].

SSTIs are common, and the emergence of resistant *Staphylococcus aureus* isolates limits the available treatment options[10,11]. Monitoring the spatiotemporal variations of antibiotic resistance is crucial component of any antimicrobial stewardship program[12].

MATERIAL AND METHODS

Study Objectives :

To understand the sensitivity profile of *Staphylococcus aureus* isolated from clinical specimens of skin and soft tissue infections against commonly used antimicrobial agents such as cephalexin, amoxicillin, amoxicillin-clavulanate, cefuroxime, clindamycin, cefazolin and cefixime by using laboratory-based culture and sensitivity data.

Research Design and Methods :

Study type :

This is an observational retrospective study conducted on secondary data retrieved from multiple diagnostic laboratories located across different Indian states.

Study platform :

Skin and soft tissue infection culture and sensitivity data retrieved from multiple diagnostic laboratories located across four different Indian regions; East (Assam, Bihar, Jharkhand, Manipur, Tripura, Orrisa, West Bengal, Andaman and Nicobar Island), West (Goa, Gujarat, Rajasthan, Madhya Pradesh, Maharashtra), North (Chandigarh, Delhi, Haryana, Himachal Pradesh, Jammu & Kashmir, Uttar Pradesh, Punjab, Uttarakhand) and South (Andhra Pradesh, Karnataka, Kerala, Tamil Nadu, Telangana) was retrieved and utilized in the study.

Sampling Method and Sample Size :

A total of 6142 specimens of *Staphylococcus aureus* from different skin and soft tissue samples, were included in the study. The included samples were from different specimen categories such as pus swab, breast abscesses, skin scrapping, bedsore swab, hand swab, nipple discharge and nail scrapping. Only the records of the patients, who attended diagnostic labs between Jan 2010-Dec 2019, were considered for the analysis. Samples with missing variables like age, sex were excluded from the analysis.

Data Analysis :

Data was analyzed using Microsoft Excel and R Studio Open 3.5.3. Detail of descriptive variables such as mean age, gender distribution etc. was provided in the study. The culture sensitivity indices were described in the form of proportions. Categorical variables such as gender and sensitivity were presented as percentage/proportions and compared using the Chi-square test/ Fischer exact test. Statistical significance was considered at $p < 0.05$. Percentage sensitivity was calculated by dividing total number of sensitive samples by total samples. Samples with intermediate sensitivity were also considered as resistant. Sensitivity patterns were analyzed across age, gender, states, regions and time (Year).

Ethical Issues :

Confidentiality of subjects was maintained by using anonymized and de-identified data only.

RESULTS

Descriptive Statistics :

A total of 29252 specimens (pus swab, breast abscess, skin scrapping, bedsore swab, hand swab nipple discharge and nail scrapping) suggestive of SSTIs were considered for this study (Fig1A). Out of total 29252 specimens, 6142 were found to be positive for *Staphylococcus aureus* and were included in the final analysis. Most of samples were from pus,6074 (98.89%), followed by breast abscess 54(0.87%) and rest 14(0.22%) from other categories such as skin scrapping, bedsore swab, hand swab, nipple discharge and nail scrapping (Fig 1B). A total of 44.7% samples were from females and 55.3% from males. Most of the samples, 2582(42%) were from young adults (>18-45years), followed by 1635(26.8%)from older adults (>45-60years), 1371(22.5%) from elderly (>60years) and 554(9%) from the pediatric population (0-18years) (Table 1).

The samples included in the study were obtained from different parts of India, but majority of the samples were from Maharashtra1757(28.6%) followed by Kerala1187(19.3%), Madhya Pradesh 836(13.6%), Uttar Pradesh 541(8.8%), Delhi 322(5.2%),Karnataka 288(4.7%), Chandigarh 228(3.7%), Tamil Nadu 201(3.3%), Punjab 177(2.9%), Assam 172(2.8%) and rest 15.2% from other states (Table 2). Table 2 highlights the state-wise positivity rate of culture for *Staphylococcus aureus*. The analysis demonstrated highest positivity rate of culture for *Staphylococcus aureus* in Chandigarh (228 positives out of 667 samples; 34.18%), followed by Maharashtra (1757 positives out of 5380 samples; 32.66%) and least positivity rate in Other States (207 positives out of 3918 samples; 5.28%).

Table 3 provides the gender-wise susceptibility pattern of *Staphylococcus aureus* to various antimicrobial agents.

On conducting analysis across the different age groups, the susceptibility pattern of *Staphylococcus aureus* to none of the

| Table 1 — *Descriptive Details of Overall Samples*			
Specimen	Pus	Breast abscess	Others	Total
Age and gender wise distribution of *Staphylococcus aureus* positive samples				
Male N (%)	3392(55.8%)	2(3.7%)	2(14.3%)	3396(55.3%)
Female N (%)	2682(44.2%)	52(96.3%)	12(85.7%)	2746(44.7%)
Total	6074(100%)	54(100%)	14(100%)	6142(100%)
Age-wise distribution of samples with positive culture				
0-18 Years	552(9.1%)	2(3.7%)	(0%)	554(9%)
>18-45 years	2528(41.6%)	44(81.5%)	10(71.4%)	2582(42%)
>45-60 Years	1628(26.8%)	7(13%)	(0%)	1635(26.6%)
>60 Years	1366(22.5%)	1(1.9%)	4(28.6%)	1371(22.3%)
Total	6074(100%)	54(100%)	14(100%)	6142(100%)
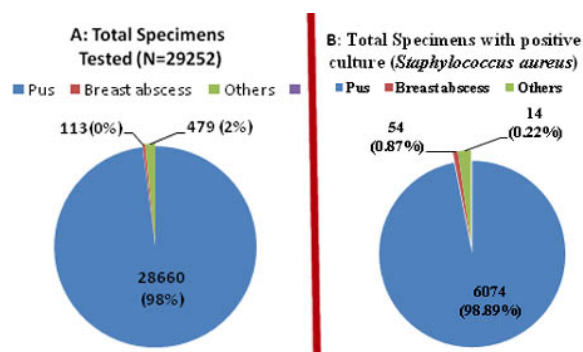
Fig 1 — Pictorial representation of the (A) Total specimens tested and (B) Total specimens with positive culture for Staphylococcus aureus

antimicrobial agent except for amoxicillin-clavulanic acid showed a statistically significant difference (P<0.05).

The analysis was performed to identify the comparative susceptibility pattern of *Staphylococcus aureus* across the different regions and states of India. The susceptibility varied significantly across the different regions for all the antimicrobial agents except for amoxicillin (P< 0.05) (Table 3). Table 4 presents the state-wise susceptibility pattern of Staphylococcus aureus to various antimicrobial agents. Maximum susceptibility (95.6%) of Staphylococcus aureus was found to be highest for cefazolin (1st generation cephalosporin) in Haryana, followed by Maharashtra (94.2%) and cephalexin (1st generation cephalosporin) in Kerala (91.8%). From the analysis it was found that *Staphylococcus aureus* was resistant to amoxicillin in West Bengal (sensitivity 4.7%), followed by Maharashtra (sensitivity 3.5%).West and South Zones have better susceptibility profile of *Staphylococcus aureus* for most of the antimicrobial agents.

Fig 2 provides the antimicrobial sensitivity status of *Staphylococcus aureus* to different antimicrobials across pus, breast abscess and other samples. For pus specimens which included majority of test samples,susceptibility of *Staphylococcus aureus* was found to be highest for 1st generation cephalosporins (84.7% & 88% for cephalexin and cephazolin respectively), followed by 79.5% for second generation cephalosporin (cefuroxime) and 53.8% for third generation cephalosporin (cefixime). Susceptibility for other two commonly used antimicrobial agents, clindamycin & amoxicillin-clavulanic acid in SSTI was found to be 78.5% and 66.1% respectively. *Staphylococcus aureus* was found to be highly resistant to amoxicillin (sensitivity 7.4%).

The year-wise susceptibility trend provided a clear picture of the dynamics for the past ten years (Fig 3).The antimicrobial susceptibility of *Staphylococcus aureus* to cephalexin in year 2010-2011 was 68.97%, 2012-2013; 95.59%, 2014-2015; 91.22% followed by 78.88% in 2016-2017 and then 82.16% in 2018-2019. Similarly, for cefazolin in year 2010-2011 was 79.59%, 2012-2013; 82.19%, 2014-2015; 87.93% followed by 88.49% in 2016-2017 and then 90.91% in 2018-2019 (Table 5).

DISCUSSION

The result from this study suggests that the first-generation

Table 2 — State-wise Distribution of Samples with Positive Culture and State-wise Positivity Rate of Culture Tested for Staphylococcus Aureus				
States	**Pus**	**Breast abscess**	**Others**	**Grand Total**
Maharashtra	1721(28.3%)	32(59.3%)	4(28.6%)	1757(28.6%)
Kerala	1185(19.5%)	2(3.7%)	(0%)	1187(19.3%)
Madhya Pradesh	822(13.5%)	7(13%)	7(50%)	836(13.6%)
Uttar Pradesh	540(8.9%)	(0%)	1(7.1%)	541(8.8%)
Delhi	322(5.3%)	(0%)	(0%)	322(5.2%)
Karnataka	287(4.7%)	0%	1(7.1%)	288(4.7%)
Chandigarh	224(3.7%)	3(5.6%)	1(7.1%)	228(3.7%)
Tamil Nadu	200(3.3%)	1(1.9%)	(0%)	201(3.3%)
Punjab	177(2.9%)	(0%)	(0%)	177(2.9%)
Assam	172(2.8%)	(0%)	(0%)	172(2.8%)
Haryana	107(1.8%)	8(14.8%)	(0%)	115(1.9%)
West Bengal	110(1.8%)	1(1.9%)	(0%)	111(1.8%)
Himachal Pradesh	56(0.9%)	(0%)	(0%)	56(0.9%)
Rajasthan	53(0.9%)	(0%)	(0%)	53(0.9%)
Jammu & Kashmir	33(0.5%)	(0%)	(0%)	33(0.5%)
Goa	15(0.2%)	(0%)	(0%)	15(0.2%)
Jharkhand	11(0.2%)	(0%)	(0%)	11(0.2%)
Manipur	11(0.2%)	(0%)	(0%)	11(0.2%)
Andhra Pradesh	8(0.1%)	(0%)	(0%)	8(0.1%)
Uttarakhand	8(0.1%)	(0%)	(0%)	8(0.1%)
Gujarat	4(0.1%)	(0%)	(0%)	4(0.1%)
Bihar	3(0%)	(0%)	(0%)	3(0%)
Telangana	2(0%)	(0%)	(0%)	2(0%)
Andaman & Nicobar	1(0%)	(0%)	(0%)	1(0%)
Orissa	1(0%)	(0%)	(0%)	1(0%)
Tripura	1(0%)	(0%)	(0%)	1(0%)
Grand Total	**6074 (100%)**	**54 (100%)**	**14 (100%)**	**6142 (100%)**

States	**Positivity Rate**	**Total Samples**
Chandigarh	228 (34.18%)	667
Maharashtra	1757 (32.66%)	5380
Karnataka	288 (32.54%)	885
Kerala	1187 (29.89%)	3971
Madhya Pradesh	836 (25.49%)	3280
Delhi	322 (22.79%)	1413
Tamil Nadu	201 (22.02%)	913
Assam	172 (14.65%)	1174
Uttar Pradesh	541 (14.32%)	3779
Punjab	177 (12.38%)	1430
Haryana	115 (6.06%)	1898
Others	207 (5.28%)	3918
West Bengal	111 (20.40%)	544
Grand Total	**6142 (21.00%)**	**29252**

Table 3 — *Comparative Susceptibility Patterns of Staphylococcus Aureus to Various Antimicrobial Agents among Male and Female and Different Regions*

Gender	Amoxicillin clavulanic acid	Amoxicillin	Cefazolin	Cefixime	Cefuroxime	Cephalexin	Clindamycin
Female	1481(67.5%)	79(10.1%)	924(87.3%)	299(52.8%)	793(80.2%)	481(83.6%)	1504(79.5%)
Male	1819(65.3%)	86(4.7%)	1076(88.2%)	449(53.7%)	1007(79%)	587(85%)	1917(77.6%)
Total	3300(66.2%)	165 (7.3%)	1600 (87.8%)	748(53.3%)	1800(79.6%)	1068(84.4%)	3421(78.4%)
P-value	0.18	0.18	0.56	0.82	0.55	0.52	0.20

Region	Amoxicillin clavulanic acid	Amoxicillin	Cefazolin	Cefixime	Cefuroxime	Cephalexin	Clindamycin
East	267(59.6%)	77(5.2%)	50(62%)	9(11.1%)	93(59.1%)	18(66.7%)	298(67.8%)
North	353(56.4%)	(0%)	176(63.6%)	142(47.9%)	142(62%)	197(79.2%)	1293(72.9%)
South	271(29.9%)	4(25%)	71(84.5%)	162(49.4%)	59(61%)	518(87.5%)	328(82.3%)
West	2361(72.7%)	83(8.4%)	1657(91.1%)	433(57.3%)	1505(83.2%)	335(83.6%)	1453(84%)
P-value	<0.05	0.29	<0.05	<0.05	<0.05	<0.05	<0.05

Table 4 — *State-wise susceptibility pattern of Staphylococcus aureus to various antimicrobial agents*

States	Amoxicillin clavulanic acid	Amoxycillin	Cefazolin	Cefixime	Cefuroxime	Cephalexin	Clindamycin
Assam	166(66.3%)	8(0%)	6(100%)	(0%)	7(85.7%)	(0%)	172(74.4%)
Chandigarh	144(78.5%)	(0%)	68(72.1%)	85(61.2%)	53(67.9%)	26(69.2%)	217(80.6%)
Delhi	172(39%)	(0%)	65(56.9%)	46(23.9%)	48(52.1%)	144(86.8%)	299(77.9%)
Haryana	48(62.5%)	(0%)	45(95.6%)	2(100%)	2(50%)	1(0%)	112(80.4%)
Karnataka	67(19.4%)	(0%)	4(25%)	78(71.8%)	13(84.6%)	77(67.5%)	168(82.1%)
Kerala	97(54.6%)	(0%)	5(100%)	13(23.1%)	4(75%)	390(91.8%)	1(100%)
Madhya Pradesh	795(49.6%)	(0%)	378(80.2%)	62(32.3%)	455(74.3%)	(0%)	363(87.3%)
Maharashtra	1539(84.2%)	57(3.5%)	1252(94.2%)	370(61.6%)	1023(86.7%)	335(83.6%)	1019(84.1%)
Others	45(82.2%)	35(20%)	35(100%)	8(12.5%)	43(88.4%)	8(37.5%)	196(60.2%)
Punjab	7(57.1%)	(0%)	(0%)	7(57.1%)	17(70.6%)	2(50%)	134(67.9%)
Tamil Nadu	101(10.9%)	10%)	58(86.2%)	70(30%)	39(48.7%)	49(85.7%)	149(81.2%)
Uttar Pradesh	29(48.3%)	(0%)	43(60.5%)	4(25%)	21(61.9%)	24(50%)	491(72.5%)
West Bengal	90(48.9%)	64(4.7%)	41(53.7%)	3(0%)	75(57.3%)	12(83.3%)	100(58%)

Table 5 — *Susceptibility Trend of Staphylococcus Aureus to Various Antimicrobials from Year 2010 to 2019*

Year	Amoxicillin clavulanic acid	Amoxi-cillin	Cefazolin (1st Generation cephalosporin)	Cephalexin (1st Generation cephalosporin)	Cefuroxime (2nd Generation cephalosporin)	Cefixime (3rd Generation cephalosporin)	Clindamycin
2010-2011	107(96.26%)	-	49(79.59%)	29(68.97%)	110 (91.82%)	88(85.23%)	113(92.92%)
2012-2013	307(96.09%)	-	292 (82.19%)	159 (95.60%)	209(92.34%)	74 (89.19%)	207(86.96%)
2014-2015	536(84.33%)	-	439 (87.93%)	262(91.22%)	133 (82.71%)	86(72.09%)	477(83.65%)
2016-2017	1050(55.05%)	-	747 (88.49%)	461 (78.31%)	555(70.81%)	307(37.79%)	959(80.08%)
2018-2019	1300(58.31%)	7.27% (165)	473(90.91%)	157 (82.17%)	793(80.08%)	193(41.45%)	1665(73.93%)

cephalosporins, cefazolin(87.8%) and cephalexin(84.4%) demonstrated the highest antimicrobial activity against *Staphylococcus aureus* followed by second generation cephalosporins, cefuroxime(79.6%) and clindamycin (78.4%).On the other hand, other antimicrobials such as amoxicillin-clavulanic acid (66.2%), cefixime (53.3%) showed moderate activity while sensitivity was very low for amoxicillin (7.3%).

Staphylococcus aureus associated SSTIs were more prevalent in males (55.3%) compared to females (44.7%). The male preponderance observed in our study is like the results reported

by multiple other studies[13,14]. The odds of being a carrier for *Staphylococcus aureus* were also high among males (odds ratio of 1.38 {1.31–1.46})[14,15]. There is no defined explanation for a higher risk and different immune response in males and in females[16,17].

The results in our study demonstrated susceptibility of *Staphylococcus aureus* to cephazolin was maximum (95.6%) in Haryana followed by Maharashtra (94.2%) and for clindamycin it was maximum (87.3%) in Madhya Pradesh, followed by Maharashtra (84.1%). A prospective study conducted by RS Phakade *et al*, in a tertiary care center in Mumbai, Maharashtra enrolled eight hundred and twenty patients with community-acquired (CA) SSTIs. Susceptibility patterns of *Staphylococcus aureus* to antimicrobials (cephazolin: 100%, clindamycin: 97%) tested were in congruence to our findings[18].

Majority of the antimicrobial agents showed better activity in South and Western Zone. Similarly, ICMR AMR Surveillance report 2017 concluded that the prevalence of antimicrobial resistance varies across different regional locations[19].

The ICMR guidelines reported 78.7% antimicrobial sensitivity toclindamycin, followed by cefoxitin (64.2%), oxacillin (51.6%), trimethoprim-sulfamethoxazole (61.2%),erythromycin (47.2%) and ciprofloxacin (27.6%), and recommended first-generation cephalosporins in *Staphylococcus aureus* associated SSTIs[20].

Clindamycin is prescribed alone or in combination with other drugs such as cefazoline and amoxicillin-clavulanate as empirical therapy, for the treatment of SSTIs[6,20]. But,an increase in the prevalence of resistance to clindamycin has been observed in recent times amongst *Staphylococcus aureus*[21,22]. A study from tertiary care centre in north-east India reported inducible resistance (10.70%) and constitutive resistance (16.88%) in *Staphylococcus aureus*isolates[22].

A hospital in Southern India assessed sensitivity percentage of*Staphylococcus aureus* isolates from OPD and IPD settings pertaining to both, community-acquired and hospital-acquired skin infections. The study documented high resistance for penicillins (85.4%) and amoxicillin-clavulanic acid (41%)[23]. Similarly, high resistance (97.7%) to penicillins was documented in hospital settings of Andhra Pradesh[24]. The results of this study are consistent with resistance observed for amoxicillin (92.6%) and amoxicillin-
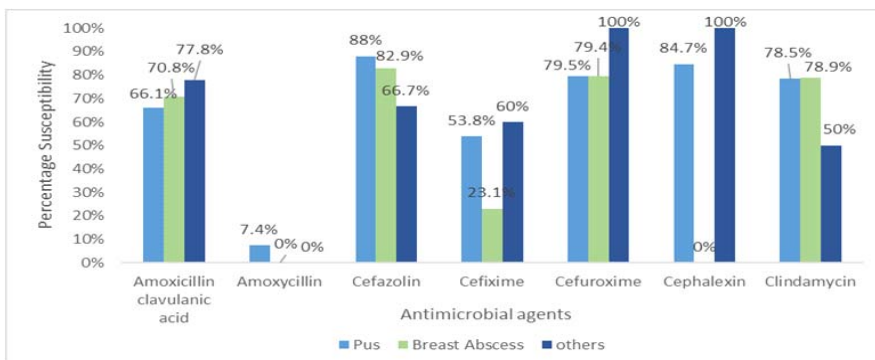

Fig 2 — Comparative susceptibility patterns of Staphylococcus aureus to various antimicrobial agents across different specimen
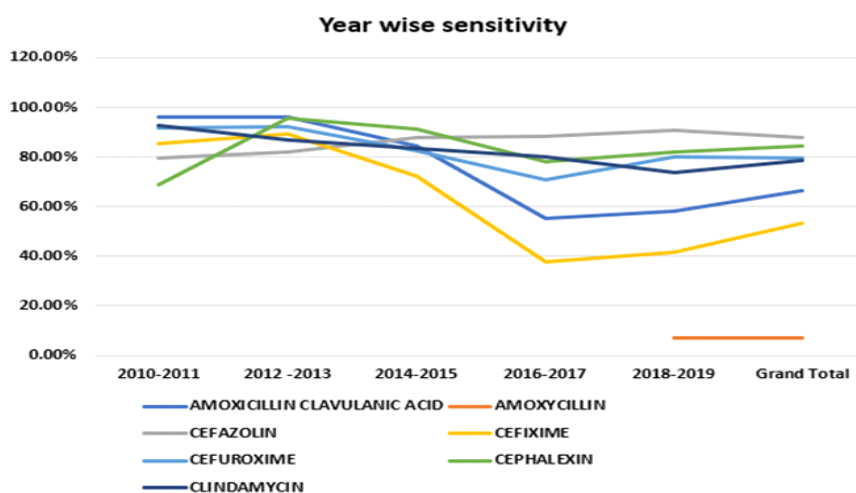

Fig 3 — Line diagram showing Susceptibility trend of Staphylococcus aureus to various antimicrobials from year 2010 to 2019

clavulanic acid (33.9%) in our study. An increase in resistance for clindamycin from 2.61% (2009) to 17.11% (2015)[25] was noted.

The results from present study support older or first-generation cephalosporins, cefazolin and cephalexin are emerging antimicrobials for treatment of SSTIs and these trends must be considered while developing empirical therapy.

Limitations :

The study was limited in a way as clinical information such as prior exposure to antimicrobials, prescriptions provided to patients after confirmation of infections, follow up data of patients and details of settings whether OPD, IPD or ICU were unavailable (as data has been retrieved from diagnostic laboratory).

CONCLUSION

Real-time surveillance is the key to understand spatiotemporal trends of antimicrobial resistance. There are several significant findings, which need to be considered during the management of *Staphylococcus aureus* associated skin and soft tissue infections at the clinic level.

(1) There is increasing resistance to the newer generation

antimicrobial agents but at the same time older generation drugs are improving and showing better activity.

(2) There is significant regional differences in sensitivity patterns of culture isolates and samples from Southern and Western India showed high sensitivity.

Source of Support : Nil
Conflicting Interest : None

REFERENCES

1 Chahine EB, Sucher AJ — Skin and soft tissue infections. *PSAP* 2015; **1:** 1-27.

2 Ellis Simonsen SM, Van Orman ER, Hatch BE, Jones SS, Gren LH, Hegmann KT, *et al* — Cellulitis incidence in a defined population. *Epidemiology and Infection* 2006; **134(2):** 293-9. doi: 10.1017/S095026880500484X.

3 Van Damme PA, Hartman EH — Rapidly progressive soft tissue infections. *The Lancet Infectious Diseases* 2006; **6(2):** 65. doi: 10.1016/s0733-8627(05)70175-9.

4 Roberts R — Management of Patients with Infectious Diseases in an Emergency Department Observation Unit. *Emergency Medicine Clinics of North America* 2001; **19(1):** 187-207.

5 Hewapathirana R, Wijayarathna G — Spatiotemporal antibiotic resistance pattern monitoring using geographical information system based hierarchical cluster analysis. *Studies in Health Technology and Informatics* 2010; **160(Pt 1):** 501-4.

6 Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, *et al* — Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clinical Infectious Diseases* 2014; **59(2):** e10-52.

7 Ramakrishnan K, Salinas RC, Higuita NI — Skin and soft tissue infections. *American Family Physician* 2015; **92(6):** 474-83.

8 Huang Y, Chen X, Xia Y — Selection, identification and application of a DNA aptamer against Staphylococcus aureus enterotoxin A. *Anal Method* 2014; **6:** 690-7.

9 Rajkovic A, Moualij BEI, Uyttendaele M, Brolet P, Zorzi W, Heinen E, *et al* — Immunoquantitative real-time PCR for Detection and Quantification of Staphylococcus aureus Enterotoxin B in Foods. *Appl Environ Microb* 2006; **72:** 6593-9. doi: 10.1128/AEM.03068-05

10 Eron LJ, Lipsky BA, Low DE, Nathwani D, Tice AD, Volturo GA — Managing skin and soft tissue infections: expert panel recommendations on key decision points. *Journal of Antimicrobial Chemotherapy* 2003; **52(suppl_1):** i3-17. doi: 10.1093/jac/dkg466.

11 Dryden MS— Complicated skin and soft tissue infection. *Journal of Antimicrobial Chemotherapy* 2010; **65(suppl_3):** iii35-44.

12 Surveillance— Who.int [Internet]. 2020 Apr 10 [cited 2020 Apr 10]; Available from: http://www.euro.who.int/en/health-topics/disease-prevention/antimicrobial-resistance/surveillance

13 Castleman MJ, Pokhrel S, Triplett KD, Kusewitt DF, Elmore BO, Joyner JA, *et al* — Innate Sex Bias of Staphylococcus aureus Skin Infection Is Driven by á-Hemolysin. *The Journal of Immunology* 2017; **200(2):** 657-68. doi: 10.4049/jimmunol.1700810.

14 den Heijer CD, van Bijnen EM, Paget WJ, Pringle M, Goossens H, Bruggeman CA, *et al* — Prevalence and resistance of commensal Staphylococcus aureus, including meticillin-resistant S aureus, in nine European countries: a cross-sectional study. *The Lancet Infectious Diseases* 2013; **13(5):** 409-15. doi: 10.1016/S1473-3099(13)70036-7.

15 McClelland EE, Smith JM — Gender Specific Differences in the Immune Response to Infection. *ArchivumImmunologiae et Therapiae Experimentalis* 2011; **59(3):** 203-13. doi: 10.1007/s00005-011-0124-3.

16 Laupland KB, Gregson DB, Church DL, Ross T, Pitout JDD— Incidence, risk factors and outcomes of Escherichia coli bloodstream infections in a large Canadian region. *Clinical Microbiology and Infection [Internet]* 2008; Nov 1 [cited 2020 Mar 23]; 14(11): 1041-7. Available from: https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(14)61815-2/fulltext

17 Treatment Guidelines for Antimicrobial Use in Common Syndromes 2019 New Delhi, India [Internet]. [cited 2020 Apr 6]. Available from: https://www.icmr.nic.in/sites/default/files/guidelines/Treatment_Guidelines_2019_Final.pdf

18 Phakade RS, Nataraj G, Kuyare SK, Khopkar US, Mehta PR — Is methicillin-resistant Staphylococcus aureus involved in community acquired skin and soft tissue infections?: Experience from a tertiary care centre in Mumbai. *Journal of Postgraduate Medicine* 2012; 58(1): 3.

19 Rajkumar S, Sistla S, Manoharan M, Sugumar M, Nagasundaram N, Parija SC, *et al* — Prevalence and genetic mechanisms of antimicrobial resistance in Staphylococcus species: A multicentre report of the indian council of medical research antimicrobial resistance surveillance network. *Indian J Med Microbiol* [serial online] 2017 [cited 2020 Apr 9];35:53-60. Available from: http://www.ijmm.org/text.asp?2017/35/1/53/202346-

20 Treatment Guidelines for Antimicrobial Use in Common Syndromes 2019 New Delhi, India [Internet]. [cited 2020 Apr 6]. Available from: https://www.icmr.nic.in/sites/default/files/guidelines/Treatment_Guidelines_2019_Final.pdf

21 Mokta KK — Inducible Clindamycin Resistance among Clinical Isolates of Staphylococcus aureus from Sub Himalayan Region of India. Journal of Clinical and Diagnostic Research, JCDR. 2015. DOI: 10.7860/jcdr/2015/13846.6382 PMID: 26435945 PMCID: PMC4576536

22 Banik A, Khyriem AB, Gurung J, Lyngdoh VW — Inducible and constitutive clindamycin resistance in Staphylococcus aureus in a northeastern Indian tertiary care hospital. *The Journal of Infection in Developing Countries* 2015; **9(07):** 725-31. doi: 10.3855/jidc.6336.

23 Furtado S, Bhat RM, Rekha B, Sukumar D, Kamath GH, Martis J, Nandakishore B — The clinical spectrum and antibiotic sensitivity patterns of staphylococcal pyodermas in the community and hospital. *Indian J Dermatol* 2014; **59:** 143-50. doi: 10.4103/0019-5154.127674.

24 Mishra D, Palo S — Antibiotic resistance pattern of bacterial isolates from skin and soft tissue infections. *International Journal of Research in Medical Sciences* 2016; **4(5):** 1458-62.

25 Ramakrishna Pai Jakribettu, Shah Nawaz, Ovine Loyster D'souza, Valerian Sudeep Pinto, Brincy Loyala D'souza, Laveena Agnis Tellis, *et al* — Study of antibiotic resistance pattern in Staphylococcus aureus in skin and soft tissue infections: A seven year analysis [Internet]. *IJAR* 2017; **3(9):** 302-4. [cited 2020 Apr 10].