ORIGINAL RESEARCH PAPER

Microbiology

EVALUATING THE CHANGING TRENDS IN EMERGENCE OF MULTIDRUG RESISTANCE AMONG GRAM POSITIVE ORGANISMS ISOLATED FROM SKIN AND SOFT TISSUE INFECTIONS FROM A TERTIARY CARE HOSPITAL, JHARKHAND

KEY WORDS:

Ramjanam Prasad — Postgraduate, Department of Microbiology, Rajendra Institute of Medical Sciences, Ranchi.

Sourav Kumar Tripathy* — Postgraduate, Department of Microbiology, Rajendra Institute of Medical Sciences, Ranchi.*Corresponding Author

Manoj Kumar — Professor, Department of Microbiology, Rajendra Institute of Medical Sciences, Ranchi.

Ashok Kumar Sharma — Associate Professor, Department of Microbiology, Rajendra Institute of Medical, Sciences, Ranchi.

ABSTRACT

Drug resistance among gram positive aerobic cocci poses a significant problem in management of patients with skin and soft tissue infections (SSTI's). S. aureus is the most common organism that causes mild skin and soft tissue infections to serious infections such as sepsis and toxic shock syndrome. Enterococcus and Streptococcus species have also emerged as a cause of skin and soft tissue infections and health care associated infections (HAI's). SSTI's is an inflammatory microbial invasion of epidermis, dermis and subcutaneous tissue. It is classified according to the layer of infection, severity of infection and microbiologic etiology. The practice guidelines of the Infectious Disease Society of America (IDSA) for the diagnosis and management of skin and soft tissue infection classifies SSTI's into five categories comprising superficial and complicated infections which include impetigo, erysipelas, cellulitis, necrotizing fasciitis, surgical site infection. Risk factors associated with development of SSTI's include poor hygiene, overcrowding, co-morbidities like diabetes, immunocompromised state, overuse of antibiotics, prolonged hospital stay, burn patients etc. Prompt recognition, timely surgical debridement or drainage with appropriate antibiotic therapy is the mainstay treatment for SSTI's. Empirical therapy includes penicillin, cephalosporins, clindamycin and cotrimoxazole. Multi-Drug resistance is of major concern commonly caused by MRSA (Methicillin resistant staphylococcus aureus) which includes CA-MRSA (Community acquired methicillin resistant Staphylococcus aureus), HA-MRSA (hospital acquired methicillin resistant Staphylococcus aureus), VRSA (vancomycin resistant staphylococcus aureus) & VRE (vancomycin resistant Enterococci). HA-MRSA is generally susceptible to clindamycin, vancomycin, Linezolid & trimethoprim-sulfamethoxazole. In contrast, CA-MRSA is usually sensitive to these former antibiotics as well as broader range of oral antimicrobial agents like clindamycin, linezolid, quinolones, daptomycin, tigecycline etc. These empirical therapeutic agents provide coverage for both S. aureus, Streptococcus species and Enterococcus species. Therefore, demographic knowledge of antimicrobial agents and their resistance pattern plays a significant role in management of SSTI's.

INTRODUCTION

SSTI's involve microbial invasion of the epidermis, dermis, superficial fascia, subcutaneous tissues, and muscle in an increasing form of severity.[1]

Skin and soft tissue infections (SSTIs) are a common type of infection that may contribute to prolonged hospital stay, increase the cost of medical care and play a important role in development of antimicrobial resistance. They are common cause of morbidity in both community and hospital settings.[2]

Common examples of SSTIs include cellulitis, abscesses, impetigo, folliculitis, furuncle, carbuncle, necrotizing fasciitis, diabetic foot infections and surgical site infections. Superficial infections can be treated by oral antibiotics and topical care. Complicated SSTI may prove fatal and require hospitalization, intravenous antibiotic and or surgery. SSTI is classified as complicated if the infection has spread to the deeper soft tissue, if surgical intervention is necessary or if the patient has comorbid conditions like Diabetes mellitus or human immune deficiency virus, hindering treatment response.[2,3]

The primary clinical presentation of SSTIs is inflammatory response with other signs and symptoms like pyrexia, bullae and lesions, which results in the production of pus.4,5 Most bacterial SSTIs are caused by gram-positive organisms like Staphylococcus aureus and Streptococcus predominantly.6 It is important to monitor the changing trends in bacterial infection and their antimicrobial susceptibility pattern to provide appropriate antimicrobial therapy for controlling infection, preventing morbidity and improving the quality of life. In this study, we intend to look to isolate, identify and detect the multidrug resistance pattern of gram positive organisms causing skin and soft tissue infections.

MATERIAL AND METHODS:

The current study is a descriptive study conducted from November 2020 to March 2022 in microbiology laboratory at RIMS (Rajendra Institute of Medical Sciences) Jharkhand. It included a total of 1207 culture positive samples. Patients of both sexes irrespective of age groups suffering from SSTIs attending or admitted in general surgery, orthopaedics, dermatology, gastroenterology, gynaecology and intensive care units at Rajendra Institute of Medical Sciences (RIMS), Ranchi were included in the study.

Inclusion criteria:

Clinical significant isolates of gram positive organism from pus, skin swab, skin tissues were received at our laboratory from the following SSTI's:-

- Impetigo
- Abscesses,
- Cellulitis
- Necrotizing skin and soft-tissue infections
- Surgical site infections
- Diabetic ulcers
- Burn wound

Exclusion criteria:

- Patients not willing to participate
- Patients who were given antibiotics before sample

collection
- Swab from chronic ulcers
- Samples not clinically significant
- Mixed growth samples which were not showing Gram positive cocci were excluded from the study.

The lesions were cleaned with sterile normal saline. Special care was taken while collecting pus or exudate samples to avoid contamination by normal flora of skin or mucus surface. The specimens were transported in sterile, leak-proof containers. The specimen were inoculated on nutrient agar, Mac-conkey agar and blood agar plates. Nutrient agar and Mac-conkey agar plates were incubated aerobically and blood agar plates were incubated in the presence of 5% CO2 at 37°C overnight. The isolates were identified by gram staining, colony morphology and standard biochemical tests: catalase, slide and tube coagulase, oxidase, bile esculin hydrolysis and bacitracin sensitivity test. Antibiotic susceptibility testing was performed as per CLSI guideline 2020/2021. Resistance to mupirocin was also detected by disk diffusion method using 5µg and 200µg disk to differentiate between low-level and high-level mupirocin resistance.

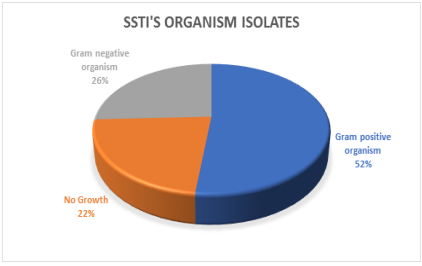
Detection of inducible clindamycin resistance in Staphylococcus aureus was done using 15µg erythromycin and 2 µg clindamycin disk and were spaced 15 mm apart and flattening of zone of inhibition adjacent to erythromycin disk was noted.

Screening for vancomycin resistant Staphylococcus aureus (VRSA) and vancomycin resistant Enterococcus (VRE) species was performed on brain heart infusion agar containing a final vancomycin concentration 6 µg/ml according to CLSI standards and inoculum of 1 to 10 µL of 0.5 Mac Farland suspension was spotted on to the surface of agar and incubated at 35±2°C.

RESULTS

Total 1557 pus samples were obtained during our study period. Number of positive bacterial isolates obtained were 1207. Out of these 1207 isolates, Gram positive cocci 807 (66.85%) & gram negative bacilli 400 (33.14%) were identified. Among total samples Staphylococcus aureus accounted for 645 (41.42%) followed by Streptococcus species 113 (7.25%) & Enterococcus 49 (3.14%). Staphylococcus aureus was the most predominant organism found among all the samples.

IMAGE 1: Distribution of organisms isolated from all samples of SSTI's.



2. AGE AND SEX DEMOGRAPHIC DISTRIBUTION TABLE

Most of the patients suffering from SSTI's 194 (24.03%) were in 50-59 years age group followed by 185 (22.92%) isolates from 40-49 years age group. The lowest number of isolates 37 (4.58%) was obtained from below 20 years of age group patients.

Majority of patients with Gram positive organisms which were isolated constituted male population 68.52% and the remaining 31.50 % were female population.

Table 1: Age and sex distribution of Gram Positive Organisms

Age	Male	Female	Total (%)
<20	24	13	37 (4.58%)
20-29	33	28	61 (7.55%)
30-39	70	35	105 (13.01%)
40-49	142	43	185 (22.92%)
50-59	131	63	194 (24.03%)
60-69	78	29	107 (13.25%)
>=70	75	43	118 (14.62%)

3. DISTRIBUTION OF CASES IN STUDY

Most isolates were found from abscess (35.93%) followed by wounds (20.81%) and diabetic ulcers(18.95%). Staphylococcus aureus is the predominant organism among all the complicated SSTI's.

Table 2: Distribution pattern of Gram positive organisms with respect to types of skin and soft tissue infections (SSTI's)

Site of infection	Total (%)	S. aureus (%)	S. pyogenes (%)	Enterococcus (%)
Abscess	290 (35.93%)	232 (80%)	40 (13.79%)	18 (6.20%)
Wound	168 (20.81%)	132 (78.57%)	26 (15.47%)	10 (5.95%)
Diabetic ulcers	153 (18.95%)	121 (79.08%)	21 (13.72%)	11 (7.18%)
Cellulitis	89 (11.02%)	72 (80.89%)	12 (13.48%)	5 (5.61%)
SSI (surgical site infections)	57 (7.06%)	46 (80.70%)	8 (14.03%)	3 (5.26%)
Burn	32 (3.96%)	26 (81.25%)	5 (15.62%)	1 (3.12%)
Impetigo	12 (1.48%)	12 (100%)	0	0
Necrotizing Skin Infection	6 (0.74%)	4 (66.66%)	1 (16.66%)	1 (16.66%)

4. ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF GRAM POSITIVE COCCI

S. aureus is mostly sensitive 100% to Doxycycline and Mupirocin and showed most resistant to Ciprofloxacin 91.16%.

Among the 25 Enterococcus isolates 100% were sensitive to linezolid, 97.95 % to teicoplanin followed by high level gentamycin 91.83%. Enterococcus species were mostly resistant to erythromycin 85.71%.

Among 113 Streptococcal isolates 100% were sensitive to piperacillin-tazobactam, Amoxycillin and teicoplanin with resistance to erythromycin 48.67%.

Table 3: Antimicrobial Sensitivity pattern of Gram Positive Isolates

Staphylococcus aureus		
Antibiotics	Sensitive (%)	Resistant (%)
Gentamicin (10 µg)	538 (83.41)	107 (16.58)
Ciprofloxacin (5µg)	57 (8.83)	588 (91.16)
Erythromycin (15 µg)	441(68.37)	204(31.62)
Co-trimoxazole (1.25/23.75µg)	290(45.1)	355(55.03)
Cefoxitin (30µg)	404(62.63)	241(37.36)
Doxycycline (30µg)	645(100)	0
Clindamycin (2µg)	539(83.6)	106(16.43)
Linezolid (30µg)	636(98.7)	9(1.39)
Mupirocin (5µg/120µg)	645(100)	0

Enterococcus species		
Antibiotics	Sensitive (%)	Resistant (%)
Ampicillin (10µg)	44(89.79)	5(10.20)
High Level Gentamycin (120µg)	45(91.83)	4(8.16)
Erythromycin (15µg)	7(14.28)	42(85.71)
Doxycycline (30µg)	20(40.81)	29(59.18)
Linezolid (30µg)	49(100)	0
Teicoplanin (30µg)	48(97.95)	1(2.04)
Vancomycin (30µg)	49 (100)	0
Streptococcus species		
Antibiotics	Sensitive (%)	Resistant (%)
Amoxycillin (25µg)	113(100)	0
Clindamycin (2µg)	88(77.87)	25(22.12)
Erythromycin (15µg)	58(51.32)	55(48.67)
Piperacillin-Tazobactam (100/10µg)	113(100)	0
Ciprofloxacin (5µg)	80(70.79)	33(29.20)
Teicoplanin (30µg)	113(100)	0

TABLE 4: Prevalence of inducible clindamycin resistance in Staphylococcus aureus (D-Test)

Total no of S. aureus isolates	Positive	Negative
645	53 (8.21%)	592 (91.78%)

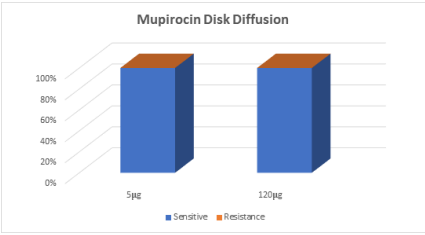
Table shows 53(8.21%) isolates of S. aureus showed positive D-test

TABLE 5: Vancomycin resistance by 6 µg agar screen method

Organism	Growth on vancomycin agar
Staphylococcus aureus	No growth
Enterococcus	No growth

Table shows that Staphylococcus aureus and Enterococcus species obtained from samples of SSTI's were highly susceptible to Vancomycin.

IMAGE 2: Shows that Staphylococcus aureus including the MRSA strains were 100% sensitive to both the concentration of mupirocin disk.



DISCUSSION

Bacterial skin and soft tissue infections are common clinical manifestation seen in most health care settings. They can range from superficial infections to complications like systemic blood stream infections[62]. *Staphylococcus aureus* is considered as relatively the most common organism to cause mild to moderate SSTIs. It poses serious challenges because of the plethora of infections they cause & increasing trends of antimicrobial resistance. The spread of multi-drug resistance clones in hospital is of major concern. They are typically associated with risk factors like debilitating conditions & use of broad-spectrum antibiotics.

The present study is conducted on total of 1557 samples from skin and soft tissue infections collected from patients admitted to Rajendra Institute of Medical Sciences (RIMS), Jharkhand from November 2020 to March 2022. 1207 (75%) samples were positive for aerobic bacterial growth. Gram positive cocci were isolated in 66.65% of culture positive cases. Out of 807 gram positive isolates collected from skin and soft tissue infections, 645(79.92%) samples yielded *S. aureus* organisms followed by 113(14%) samples of *Streptococcus* sp. and 49(6.07%) *Enterococcus* sp. A similar study from Ethiopia reported an isolation rate of 52% of bacterial pathogens of which *S. aureus* was the most predominant organism 65% of SSTI's.[8]

Studies have also observed a significant difference between different age groups in the prevalence of *S. aureus* causing SSTI's. In the present study, there is an increased prevalence of SSTI's among male patients (68.52%) than female patients(31.48%). Maximum number of cases were found in the age group of 50-59 years followed by 40-49 years. These findings were consistent by *Singh B et al*. showed 41-60(41%) years age group followed by 21-40(29%) was most commonly affected[9]. There was statistical significance seen between SSTI's & age group in our study population.

In our study, Abscess 290(35.93%) constituted the maximum percentage of SSTI's followed by wound 163(20.81%), diabetic ulcers 153(18.95%), cellulitis 89(11.02%), surgical site infections 57(7.06%) and burn patients 32(3.96%). Whereas least samples were obtained from impetigo 12(1.48%) and necrotizing skin infections 6(0.74%). A study conducted at Amritsar by *Singh B et al*. showed abscess formation (45%) was the most common clinical presentation of SSTI's. Others contributed Fournier's gangrene (15%), nonhealing ulcers and cellulitis (11%), infected diabetic foot (5%), infected sebaceous cyst (5%) and surgical site infection (4%) respectively[9].

Antimicrobial susceptibility testing panel for 645 isolates of *S. aureus* were performed in our study. Present study showed *S. aureus* 100% sensitivity to Mupirocin and Doxycycline followed by linezolid 98.7%, clindamycin 83.60% & cefoxitin 62.63%. High percentage of resistance to ciprofloxacin 91.16%, cotrimoxazole 55.03% was noted. *A study from Punjab by Trojan R et al. found S. aureus was 100% sensitive to linezolid, vancomycin, cloxacillin and clindamycin 73% sensitive followed by resistance to ciprofloxacin 73% and co-trimoxazole 66%*[10]. We found similar susceptibility and resistance pattern for our *Staphylococcal* isolates.

Hence, treatment options were limited to clindamycin, vancomycin, linezolid, daptomycin, tigecycline and cloxacillin. Among SSTI's, clindamycin is one of the drug of choice used for treatment of both MRSA and MSSA. Good oral absorption of clindamycin makes an alternate option for outpatients & also as follow-up treatment after IV therapy, esp considering de-escalation of therapy. As a result judicious use of the above antibiotics is recommended.

MRSA is a global phenomenon. In 1960, first outbreak of MRSA occurred in European hospitals. Since, then strain of MRSA & MR-CONS(Methicillin resistant coagulase negative *Staphylococcus* species) has established worldwide. Prevalence of MRSA is a cause of concern. MRSA strains are strains of *Staphylococcus aureus* that is resistant to penicillin group of antibiotics & cephalosporins. Resistance to methicillin is mediated via the mec operon, part of the staphylococcal cassette chromosomes mec (SCC*mec*). Resistance is conferred by *mec a* gene, which encodes for an altered penicillin-binding protein (PBP2a or PBP2) that has a lower affinity for binding beta lactams (penicillin, cephalosporins & carbapenems). This allows for resistance to all beta lactam antibiotics & obviates their clinical use during MRSA infections[11].

In our study, 37.36% of *S. aureus* isolates were resistant to methicillin which shows prevalence of MRSA at our settings at par with the average resistance levels found elsewhere. A study done by *Joshi et al.* in INSAR (Indian Network for

Surveillance of Antimicrobial Resistance) surveillance showed similar prevalence of MRSA isolates (41%) with our study[12]. A study by the Antimicrobial Research And Surveillance Initiative of Indian Council of Medical Research (ICMR-AMRSN) conducted the prevalence of MRSA in four premier institutes in India found out a similar prevalence of MRSA 37.3%[13]. Thus, for MRSA infections selecting appropriate antibiotics against resistant strains is significant. Treatment options for MRSA are limited to only few antibiotics like mupirocin, vancomycin, linezolid and tigecycline. As a result, judicious use of the above antibiotics is recommended.

There have been reports of Vancomycin resistance and vancomycin intermediate MRSA from India[14,15]. A meta-analysis study in Asia by *Wu Q et al.* found 3.5-fold increase in VRSA strains (5%) from 2006 to 2020[16]. However, in agar screen method performed in our study showed no vancomycin resistance on isolates of *S. aureus* and *Enterococcus* which implicates vancomycin still remains a drug of choice for MRSA strains causing SSTI's.

Incidence of inducible clindamycin resistance in present study was 8.21% which was less in comparison to global studies[17,18,19]. $iMLS_B$ (Inducible macrolide-lincosamide streptogramin B) resistance mechanism can't be recognized by using any standard susceptibility test so, the prevalence varies according to geographic distribution. Therefore, D-test becomes an essential part of routine antimicrobial susceptibility test for all isolates of *S. aureus*[20]. Our study found a high percentage of erythromycin resistant *S. aureus* 31.62%. These observations suggest, if D-test wouldn't have been performed then 8.21% *S. aureus* isolates which were erythromycin resistant would have been misidentified as clindamycin sensitive, which may have resulted in therapeutic failure.

Mupirocin is one of the topical antibiotic effective against *Staphylococcus aureus* and *Streptococcus pyogenes*[21]. Mupirocin resistance was tested by Kirby-Baur disc diffusion method using 5 µg and 200 µg disk. Present study, 645 isolates of *S. aureus* were 100% sensitive to mupirocin whereas, a study done at Tamil Nadu showed high level mupirocin resistance by 2% and low level resistance by 1.3%[22]. So, it concludes mupirocin has good efficacy and can be used in treating SSTI's, controlling spread of MRSA during outbreaks, preventing colonization in high-risk population and healthcare workers in intensive care units, dialysis units, orthopaedics and cardiothoracic surgery wards[23,24].

In our study *Streptococcus* species 113 (14%) were 100% sensitive to amoxycillin, piperacillin-tazobactam, teicoplanin with resistance to erythromycin 48.67%. A study done by *Makhtar C et al.* showed similar susceptibility pattern of antibiotics[25]. SSTI's caused by *Streptococcus* species may lead to large areas of necrotizing fascitis or also could be the source of bacteriemia in elderly or young patients. Present study showed 100% sensitive to penicillin group of drugs whereas, penicillin resistance has not been documented against this organism to date[26]. We found resistance to erythromycin 48.67 % and clindamycin 22.12% which are usually used as second line of treatment in penicillin allergic patients. These values were much higher when compared with other studies which were 8% resistant to erythromycin and 6% resistant to clindamycin[27]. Penicillin group of drugs still remains the antibiotic of choice for SSTI's. Combination of penicillin and aminoglycoside is often used in management ofserious infection. Macrolide such as erythromycin, azithromycin or clarithromycin are the drug of preference. In necrotizing fasciitis/ cellulitis and Streptococcal Toxic Shock Syndrome, combination of penicillin G and clindamycin can be used.

Susceptibility pattern of *Enterococcus* species in our study showed high susceptibility to vancomycin 100%, linezolid 100%, teicoplanin 97.95%, high level gentamycin 91.83% and ampicillin 89.79%. High resistance to erythromycin 85.71% followed by doxycycline 59.18% was noted. A study done by *Tsering Yangzom et al.* on *Enterococcal* isolates showed high resistance to ampicillin 53.8%, HLG 34.1% with less resistance to vancomycin 14.3%, teicoplanin 9.9%, and linezolid 0.5%[28]. Another study by *Zalelam Tena Ferede et al.* at Ethiopia showed resistance to doxycycline 73.3%, ampicillin 80% which contrarily in our study showed 80% sensitive to ampicillin. However, similar resistance was observed to common antibiotics[29]. About 85.71% of the isolates were resistant to macrolide (erythromycin) hence , proving it as an inadequate drug for treatment. Macrolides act by inhibiting protein synthesis by binding to 50s ribosome & resistance is by ribosomal methylase, encoded by erm B gene or by efflux mediated by *mef* gene[30,31]. High rates of macrolide and doxycycline resistance in our study highlights the dilemma in therapy of serious enterococcal infections like SSTI's, endocarditis, bacteraemia, etc for which synergistic treatment with cell wall synthesis inhibitor & high level aminoglycosides was recommended. In our study , there was low level of resistance to HLG (8%). Low uptake of aminoglycosides is said to be responsible for low level resistance in Enterococcus species. High level resistance is mediated by plasmid coded enzymes which modify aminoglycosides by adenylation , acetylation, or phosphorylation. Ribosomal resistance has been observed with streptomycin[32,33]. All the *Enterococcal* isolates in this study were sensitive to linezolid, a bacterio-static drug especially of good efficacy in skin & soft tissue infections. It acts by inhibiting protein synthesis, through binding with 23s fraction of 50 s ribosome & resistance if seen is associated with a g257 6t mutation in 23SrRNA[31,34]. Resistance to linezolid is rare. *Salem et al.* reported only 0.5 % resistance to linezolid[35]. The first case of linezolid resistance in UK was reported by *Auckland et al*[36]. Even nosocomial outbreaks due to linezolid resistance *Enterococci* have been also reported[37].

We also emphasized on vancomycin susceptibility in our study. VRE has alarmed global infectious disease community because there are fewer options for management of SSTI's. Vancomycin resistance is mediated by VAN A, VAN B , VAN C (most common) genes which encode a ligase responsible for synthesis of D alanyl – D LACTATE (high level resistance (van a & b) Or d-alanyl d-serine (low level resistance, van c) The altered terminals D ALA, D LAC & D ALA, DSER results in low affinity binding of vancomycin, there by resulting in resistance to antibiotic. van a gene is associated with inducible high level resistance to vancomycin & teicoplanin. Van b gene is associated with variable (moderate to high) levels of inducible resistance to vancomycin only, teicoplanin remaining susceptible. Van c resistance is non inducible low level resistance to vancomycin and teicoplanin susceptible[38,39].

Thus, it concludes that vancomycin, linezolid and teicoplanin remains the mainstay drugs for management of Enterococcus causing SSTI's. There results from our study and previous studies indicated that SSTI's is a major worldwide health problem. *Staphylococcus aureus Streptococcus* species and *Enterococcus* species are the major gram positive causative agent for SSTI's. In this era of emergence of MRSA and VRE, it is important to use antibiotics judiciously so, periodic testing for resistance pattern to antibiotics becomes mandatory. Prevention of MRSA is of utmost importance in healthcare settings. Simple infection practices like hand washing, barrier nursing and the de-colonisation provides a long way for controlling the transmission of MRSA infections.

CONCLUSION

The study emphasized the prevalence of gram positive cocci in skin and soft tissue infection and the most common clinical conditions implicated for the occurrence of SSTI's. The isolates were screened for the susceptibility pattern to know

the prevalence of MRSA in *S. aureus*, Vancomycin resistance for determining VRSA and VRE and antibiotic susceptibility pattern in *Enterococcus* and *Streptococcus* species, so that an appropriate antimicrobial therapy can be initiated. Since, vancomycin resistance was not reported in our study, it is advisable to use vancomycin as a reserve drug, which should be used only when other antibiotics fail.

REFERENCES

1. Leong HN, Kurup A, Tan MY, Kwa ALH, Liau KH, Wilcox MH. Management of complicated skin and soft tissue infections with a special focus on the role of newer antibiotics. Infect Drug Resist 2018:11:1959-74.
2. Mohanty S, Kapil A, Dhawan B, Das BK. Bacterilogical and antimicrobial susceptibility profile of soft tissue infections from northern India. Indian J Med Sci 2004;58:10-15.
3. Weigelt J, Itani K, Stevens D, Lau W, Dryden M, Knirsch C. Linezolid versus vancomycin in treatment of complicated skin and soft tissue infections. Antimicrob Agents Chemother 2005; 49: 2260- 66.
4. Ki V, Rotstein C. Bacterial skin and soft tissue infections in adults: A review of their epidemiology, pathogenesis, diagnosis, treatment and site of care. Can J Infect Dis Med Microbiol 2008;19:173-84.
5. Afroz Z, Metri BC, Jyothi P. Bacteriological profile and antimicrobial susceptibility pattern of skin and soft tissue infections among gram negative bacilli in a tertiary care hospital of South. Indian J Pharmaceut Sci Res 2015; 7: 397-400.
6. Stevens DL, Bisno AL, Chambers HF, Everett ED, Dellinger P, Goldstein EJC, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft-Tissue Infections. Clin Infect Dis2005;41:1373–406.
7. Ramana K V, Venkata Bharat Kumar Pinnelli, Bhanu Prakash et al. Complicated Skin and Skin Structure Infections (cSSSI's): A Comprehensive Review, American Journal of Medical and Biological Research, 2013, Vol. 1, No. 4, 159-164.
8. Mulu A, Moges F, Tessema B and Kassu A. pattern and multidrug resistance of bacterial pathogens isolated from wound infection at University of Gondar Teaching Hospital, North West Ethiopia. Ethiop Med J 2006; 44(2): 125-131
9. Singh B, Singh S, Khichy S, Ghatge A. Clinical Presentation of Soft-tissue Infections and its Management: A Study of 100 Cases. Niger J Surg. 2017 Jul-Dec;23(2):86-91. doi: 10.4103/njs.NJS_26_16. PMID: 29089730; PMCID: PMC5649435.
10. Trojan R, Razdan L, Singh N. Antibiotic Susceptibility Patterns of Bacterial Isolates from Pus Samples in a Tertiary Care Hospital of Punjab, India. Int J Microbiol. 2016;2016:9302692. doi: 10.1155/2016/9302692. Epub 2016 Oct 30. PMID: 27872643; PMCID: PMC5107258.
11. Barrett FF, McGhee RF, Finland M: Methicillin-resistant Staphylococcus aureus at Boston city Hospital, New England Journal of Medicine 1968; 279:448
12. Joshi S, Ray P, Manchanda V, Bajaj J, Chitnis D, Gautam V, Goswami P, et al. Methicillin resistant Staphylococcus aureus (MRSA) in India: prevalence and susceptibility pattern. Indian J Med Res. 2013; 137:363.
13. 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. 2017;35:53-60.
14. Saha B, Singh AK, Ghosh A, Bal M. Identification and characterization of a vancomycin-resistant Staphylococcus aureus isolated from Kolkata (South Asia). J Med Microbiol. 2008 Jan;57(Pt 1):72-79.
15. Emergence of vancomycin-intermediate Staphylococcus species in southern India, Correspondance. J Med Microbiology 2008; 57: 911-2.
16. Wu Q., Sabokroo, N., Wang, Y. et al. Systematic review and meta-analysis of the epidemiology of vancomycin resistance Staphylococcus aureus isolates. Antimicrob Resist Infect Control 10, 101 (2021).
17. Lertcanawanichakul M, Cchawawisit, Choopan A et al. Incidence of constitutive and Inducible Clindamycin Resistant in clinical isolates of Methicillin resistant Staphylococcus aureus. Walailak J.Sci and Tech 2007; 4:155-163
18. O'Sullivan MVN, Cai Y, Kong F et al. Influence of disk separation distance on accuracy of the disk approximation test for detection of inducible clindamycin resistance in Staphylococcus spp. J Clin Microbiology 2006;44(11):4072-76.
19. Stefani S and Varaldo PE. Epidemiology of Methicillin-resistant Staphylococci in Europe. Euro socclin microbiology and infectious diseases 2003; 9(12): 1179-86.
20. Gupta V, Datta P, Rani H, Chander J. Inducible clindamycin resistance in Staphylococcus aureus: A study from North India. J Postgrad Med. 2009;55: 176–9.
21. Darsi CK. MUBI rose in resistance in clinical isolates of medicine resistant Staphylococcus aureus from a tertiary care rural hospital. Int J Med Microbiology 2008; 57: 72-9.
22. S J, M M, A S SB, Mathew R, M K et al. Prevalence of High and Low Level Mupirocin resistance among Staphylococcal Isolates from Skin Infection in a Tertiary Care Hospital. J Clin Diagn Res. 2013 Feb;7(2):238-42. doi: 10.7860/JCDR/2013/4694.2736. Epub 2013 Feb1.
23. Braois A, Fluminhan Junior, Pizzolitto A. C. Multiplex PCR use for Staphylococcus aureus identification and oxacillin and neutralising resistance evaluation. Rev Ciênc Farm BásicaApl, 2009; 30(3); 303-307
24. Jean B. Patel, Rachel J. Gorwitz and John A Jernigan. Mupirocin Resistance, Clinical Infectitious Disease 2009; 49: 935-41.
25. Makhtar C, Assane D. Antibiotic susceptibility of Streptococcus pyogenes isolated from respiratory tract infection in Dakar, Senegal, PubMed, October 2013; Microbiology Insights 6(6): 71-5.
26. Gueye Ndiaye A, Sarr ND C, Thiam K and Boye CS. In Vitro Activity of Antimicrobial Agents Against Streptococcus pyogenes Isolates from Patients with Acute Tonsillopharyngitis in Dakar, Senegal, Microbiology Insights 2009:2 25-29.
27. Bingen E, P. Trieu-Cuot, A. Bouvet et al. Epidemiology of Invasive Streptococcus pyogenes Infections in France in 2007 J. Clin. Microbiol. 2011, 49(12):4094.
28. Yangzom T, Kumar Singh TS. Study of vancomycin and high-level aminoglycoside-resistant Enterococcus species and evaluation of a rapid spot test for enterococci from Central Referral Hospital, Sikkim, India. J Lab Physicians. 2019 Jul-Sep;11(3):192-199. doi: 10.4103/JLP.JLP_5_19. PMID: 31579233; PMCID: PMC6771325.
29. Ferede Z. T., Tullu K. D., Derese S. G., & Yeshanew A. G. (2018). Prevalence and antimicrobial susceptibility pattern of Enterococcus species isolated from different clinical samples at Black Lion Specialized Teaching Hospital, Addis Ababa, Ethiopia. BMC research notes, 11(1), 793.
30. Eliopolos GM. Antimicrobial resistance in the Enterococcus. In, Wax RG, Lewis K, Abigail A, Tabes H. Bacterial resistance to Antimicrobials, Second edition. CRC press; 2007:255-89.
31. Tripathi KD. Antimicrobial drugs. In, Essentials of Medical Pharmacology. 7th edition. New Delhi, Jaypee publishers; 2013. p 704-52.
32. Marothi YA, Agnihotri H, Dubey D.Enterococcal resistance- An overview. Indian J Med Microbiol 2005; 23(4): 214-9
33. Murray BE. The Life and Times of the Enterococcus. Clin Microbiol Rev. Jan 1990; 3(1): 46-65.
34. Schnitzler P, Schulz K, Lampson C, Geiss M, Geiss HK. Molecular analysis of linezolid resistance in clinical Enterococcus faecium isolates by PCR and pyrosequencing. Eur J Clin Microbiol Infect Dis 2011; 30: 121-25
35. Salem MM, Moussa IM, Muharram MM, Alanazy FK, Hefri HM. Prevalence and antimicrobial resistance pattern of multidrug resistant enterococci isolated from clinical specimens. Indian J Med Microbiol 2012; 30(1): 44-51
36. Auckland C, Teare L, Cooke F, Kaufmann ME, Warner M, Jones G et al. Linezolid resistant enterococci: report of the first isolates in the United Kingdom. J Antimicrob. Chemother. Nov 2002; 50 (5): 743-46
37. Kainer MA, Devasia RA, Jones TF, Simmons BP, Melton K, Chow S et al. Response to Emerging infection Leading to Outbreak of Linezolid Resistant Enterococci. Emerg. Infect. Dis. July 2007; 13(7): 1024-30
38. Xiaogang Xu, Dongfang Lin, Guoquan Yan, Xinyu Ye, Shi Wu, Yan guo et al. Van M, a New Glycopeptide resistance Gene cluster found in Enterococcus faecium. Antimicrob. Agents Chemother Nov 2010; 54(11): 4643-47
39. Lebreton F, Depardieu F, Bourdon N, Fines G, Berger P, Camiade S et al. D Ala-D Ser Van N type Transferable Vancomycin Resistance in Enterococcus faecium. Antimicrob. Agents Chemother. Oct 2011; 55 (10): 4606-12.