

ORIGINAL PAPER

**RETROSPECTIVE ANALYSIS OF ANTIMICROBIAL SUSCEPTIBILITIES OF  
GRAM-POSITIVE COCCI IN SKIN AND SOFT TISSUE INFECTIONS IN ONE  
TERTIARY CARE HOSPITAL IN SOUTHERN INDIA**

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Tables: 2

Figures: 4

References: 24

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### Summary

**Background.** Skin and soft tissue infections (SSTIs) are the most prevalent infection types worldwide, particularly in India. Regular assessment of microbial profiling data and antibiograms (cumulative susceptibility report) aids healthcare professionals in making informed decisions about optimal empiric antimicrobial therapy.

**Material and methods.** A retrospective investigation was conducted in a 300-bed tertiary care hospital (Institute of Cardio Vascular Diseases), focusing on the prevalence of SSTIs within the hospital wards.

**Results.** Out of the 816 positive samples, 44.1% comprised Gram-positive organisms (360 samples), 52.5% were Gram-negative (428 samples), and 3.4% were fungal (28 samples). In the specific investigation focusing on the Gram-positive organisms (360 samples), Coagulase-Negative *Staphylococci* (CoNS) accounted for 45.6% (164 samples), *Enterococcus* species for 18.6% (67 samples), *Staphylococcus aureus* (*S. aureus*) for 18.1% (65 samples), and other Gram-positive bacteria for 17.8% (64 samples). Our research reports reveal that Gram-Positive Cocci show high sensitivity patterns to Vancomycin, Teicoplanin, and Linezolid. Conversely, notable resistance was observed with Penicillin, Ciprofloxacin, and Levofloxacin.

**Conclusions.** CoNS has a higher incidence of infection among Gram-positive organisms, suggesting the potential inclusion of additional antibiotic classes in susceptibility studies.

Based on our study's results, discontinuing the use of antibiotics that show resistance may be considered.

**Keywords:** coagulase-negative *staphylococci*, skin and soft tissue infection, antibiogram, Vancomycin, resistance

## Introduction

Creating most tissues in the body, the largest organ of the body, skin is a tough, flexible, structural barrier that has an underlying soft tissue made up of fat layers, fascia, and muscle [1]. Skin exposure in cases like surgical or traumatic wounds and ulcers can result in the colonization of diverse bacteria and a change in the microbiota's composition, which can then cause the microbes to invade the epidermis and ultimately the bloodstream, causing skin and soft tissue infections (SSTIs) [1,2].

SSTIs are omnipresent and universal infections experienced by everyone in their lifetime, from mild to severe [3]. They have divergent clinical presentation and degree of severity. Based on their diversity and severity, they are generally divided into two classifications namely: purulent infections and nonpurulent infections. Furthermore, subcategorized into mild, moderate, and, severe [4]. SSTIs caused by bacteria are one the frequent presentations in emergency room patients. Oral agents can be used for treatments like  $\beta$ -lactamase stable penicillins, macrolides, and cephalosporins. However, patients with comorbidities such as ischemic ulceration, diabetes mellitus, chronic lymphoedema, or bacteremia are categorized as complicated and necessitate immense recovery [5]. The exclusive bacterial cause of SSTIs is Gram-positive bacteria (GPB), comprising *S. aureus*, group A and B streptococci, *Streptococcus viridans*, and *Enterococcus faecalis* [6].

SSTIs are a frequent source of morbidity in both the general population and hospitals. Oral antibiotics and topical treatment are often used in the outpatient setting to treat superficial SSTIs [7]. The most serious SSTIs are complicated SSTIs (cSSTIs), which affect deeper soft tissues and can result in serious complications such as infected cellulitis, infected burns, large abscesses, ulcer, or wound site infections, surgical site infections, skin and diabetic foot ulcers. Regulating the incidence and prevalence of SSTIs has been challenging due to the diverse presentation of the infections and the likelihood of repeated episodes. Complicating variables, like comorbidities or concomitant infections may be present in hospitalized patients with SSTIs as SSTIs solely may not direct to hospital or ICU admission [8].

Antibiograms (cumulative susceptibility reports) not only assist doctors and pharmacists in deciding on the most effective empiric antimicrobial therapy while awaiting culture and susceptibility results, but they also have an impact on the large healthcare ecosystem, providing information that can direct programs for infection prevention aimed at preventing the spread of antibiotic-resistant infections in hospitals [9,10]. The combined susceptibility data from an area can be transferred to external monitoring systems and utilized to comprehend the epidemiological spread of resistant organisms in particular circumstances, when it may be beneficial to public health to disseminate resistance data more widely [10].

### **Aim of the work**

The research paper presents a retrospective study conducted in a tertiary hospital, focusing on the prevalence of SSTIs within the hospital wards. The study aims at analyzing the patterns of SSTI occurrence by Gram-positive Cocci (GPC) and mitigating the susceptibility of the infections to various antibiotics. The study will lay out insights into the frequency and distribution of SSTIs in the hospital setting by examining the resistance and susceptibility data.

## **Material and methods**

### *Study design, period, and setting*

A comprehensive retrospective study was carried out within the Department of Microbiology at the Madras Medical Mission (MMM) Hospital, located in Chennai, India. Spanning a period of January 2022 to December 2022, the study has a sufficient time frame for analysis. In the period, all positive tissue samples (samples that contained bacterial infection) found in the bacteriology section were documented in the Electronic Health Record (EHR) portal or a Patient Portal of the MMM. The data is collected for each patient of the year 2022 and converted into an Excel sheet for systematic analysis.

### *Specimen collection and processing*

Specimens were collected as swabs of the wound, infected tissue, pus discharge, or the liquid drained from the infection site and sent to the microbiology department for testing where standard procedures are performed and final results are co-related and evaluated. In the case of tissue samples, the processing is done by fragmenting through a tissue grinder with the help of nutrient broth and then plated for further analysis. Smear examination and each sample were plated on blood agar, chocolate agar, MacConkey agar, Sabouraud's dextrose agar, Brain heart infusion broth (BHIB), and Thio glycolate broth based on the sample collected and incubated at 37° C for 24 hours in an aerobic incubator or CO<sub>2</sub> incubator based on the suspected organism. Manual and automated systems like the Vitek II Compact system further examine isolates.

### *Antimicrobial susceptibility testing*

Susceptibility testing of isolated organisms is done using various antibiotics by manual Kirby-Bauer disk diffusion and automated systems, such as the Vitek II Compact system. Identified isolates were checked for susceptibility to Penicillin, Oxacillin, Ampicillin, Gentamicin, Tetracycline, Erythromycin, Azithromycin, Clindamycin, Ciprofloxacin, Levofloxacin, Ofloxacin, Cotrimoxazole, Chloramphenicol, Vancomycin, Teicoplanin, and Linezolid based on the isolated organism. The antibiotics used are based on the available and frequently used antibiotics in the clinical geography and by physicians. The testing was evaluated using the Clinical and Laboratory Standards Institute (CLSI M100, 32nd edition) guidelines [11].

### *Quality control*

Each set of samples on a day has a quality control plate for early detection of contamination before the reporting of the organism. Furthermore, ventilation and water quality control are also done to ensure that there is no experimental error. American Type Culture Collection (ATCC) standard reference strains were used to cross-check the performance of the culture media.

### *Data analysis*

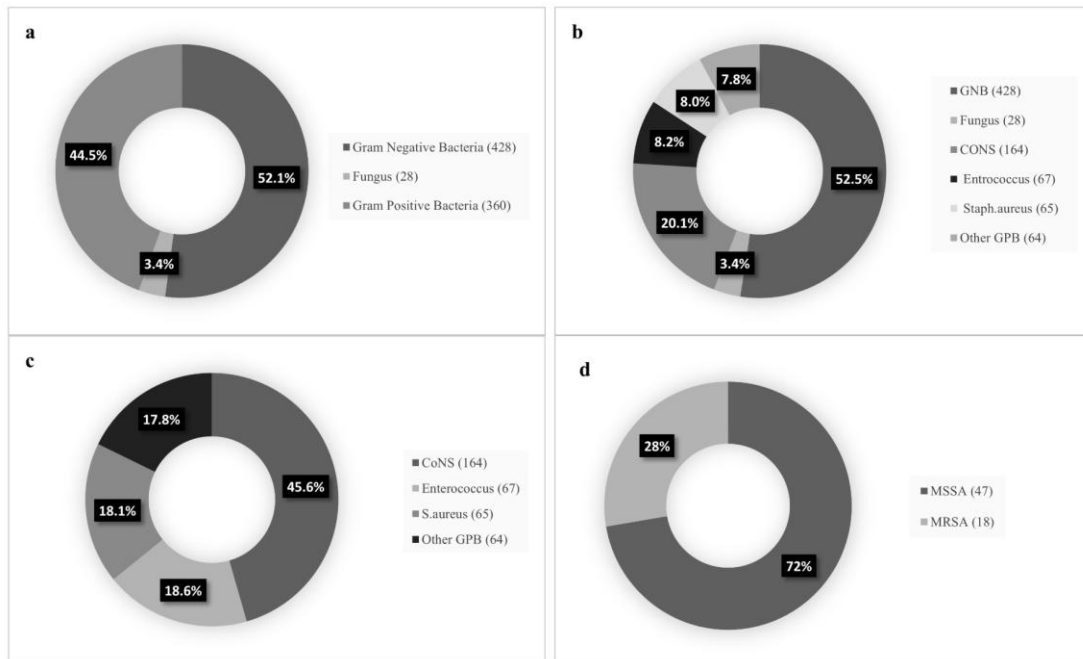
In the study, only antimicrobial profile data for the year 2022 was collected from the hospital and converted into an Excel sheet for systematic analysis. The study variables were positive samples, whereas gender, age, and antibiotic use were independent variables. The

susceptibility pattern between the bacterial species was analyzed using the chi-square test. The threshold was set as  $\alpha=0.05$ , with a  $p$ -value less than 0.05 considered statistically significant. The null hypothesis ( $H_0$ ) is that there is no significant difference in the antibiotic resistance pattern among the bacteria (*S. aureus*, Coagulase-Negative *Staphylococci* (CoNS), and *Enterococcus* species). The alternative hypothesis ( $H_1$ ) is that the antibiotic has a resistance pattern among the bacteria.

$P$ -values ( $<0.05$ ) suggest that the efficacy of certain antibiotics varies significantly among the bacterial species.  $P$ -values ( $>0.05$ ) indicate no significant difference in resistance patterns, suggesting consistent effectiveness across groups.

## Results

During 2022, a total of 881 skin and soft tissue samples from suspected patients with SSTIs were isolated and identified of which 816 samples were positive. They were tissue samples, pus samples, eye/ear swabs, and throat swabs. The samples were analyzed for identification of bacteria and their antimicrobial susceptibility testing. The patients were from the age group 1 year to 91 years. Typically, 59.8% of the patients were male and 41.6% were female. Of the 816 positive samples, there were GPB (360 samples, 44.1%), Gram-negative bacteria (GNB) (428 samples, 52.5%), and fungal (28 samples, 3.4%) (Figure 1a, b). For the study, focusing on the GPB (360 samples), CoNS (164 samples, 45.6%), *Enterococcus* (67 samples, 18.6%), *S. aureus* (65 samples, 18.1%), and other GPB (64 samples, 17.8%) were identified (Figure 1c). Focusing on the multi-drug resistance seen in *S. aureus*, Methicillin-Sensitive *Staphylococcus aureus* (MSSA) (47 samples, 72.3%) and MRSA (18 samples, 27.7%) were identified (Figure 1d).

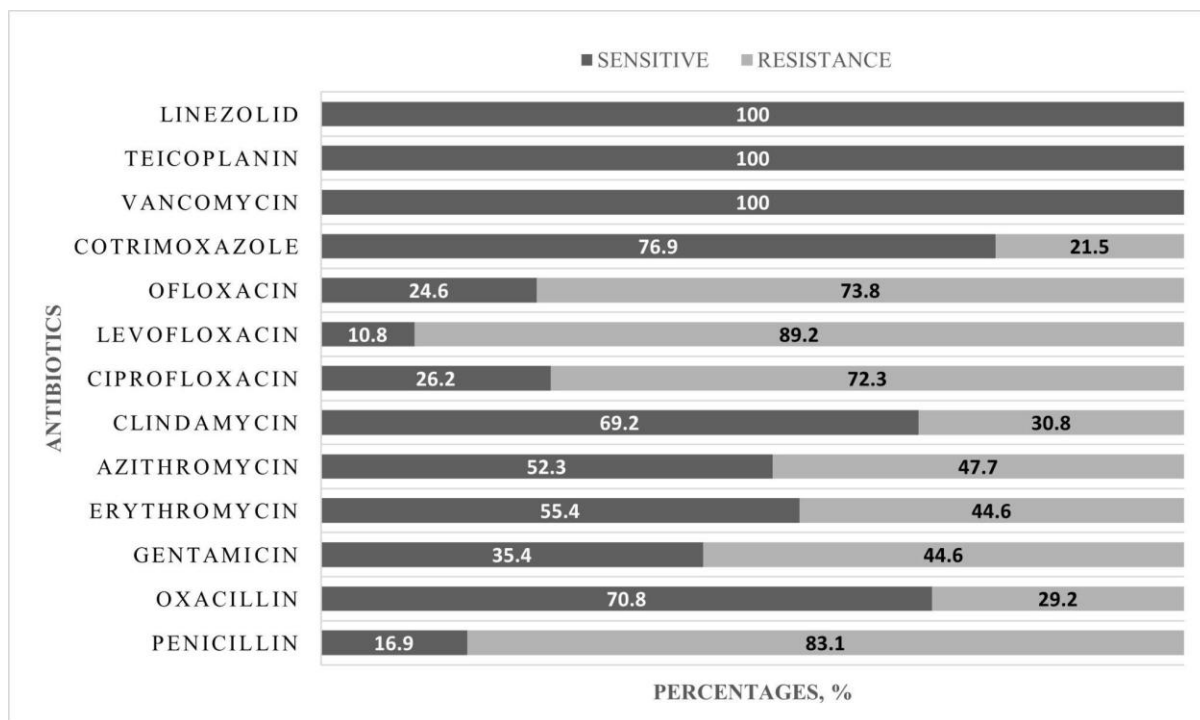


**Figure 1.** Prevalence of various microorganisms causing skin and soft tissue infections in the samples studied

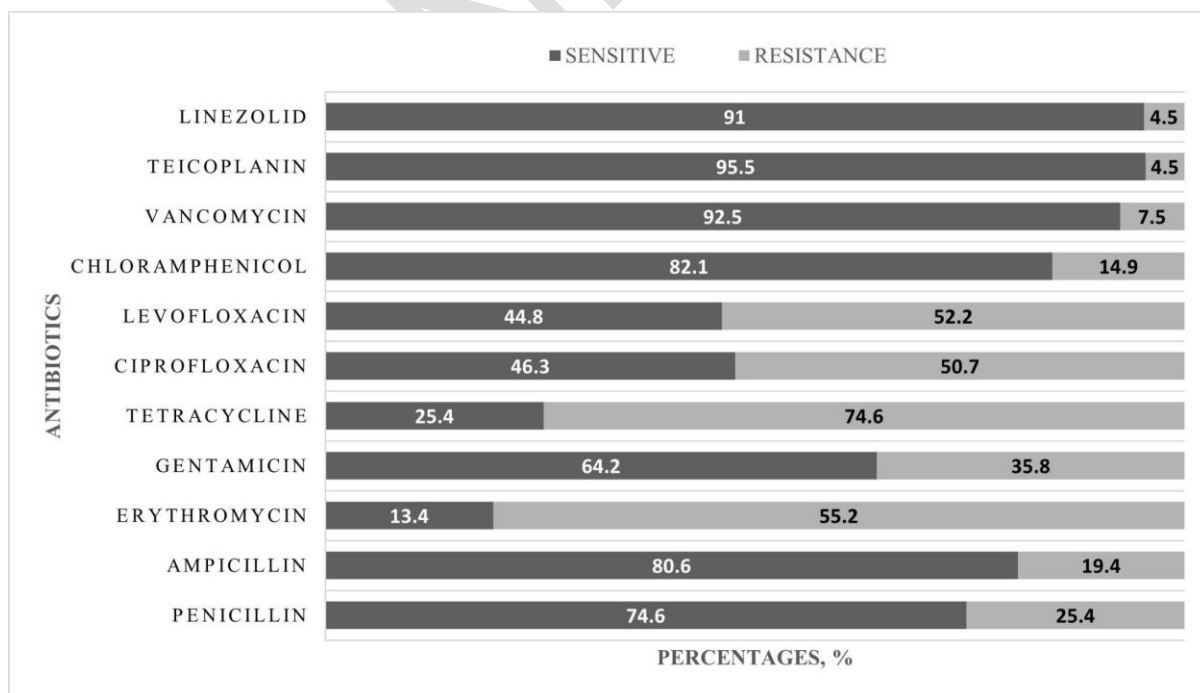
Notes: GNB – Gram-Negative Bacteria, GPB – Gram-Positive Bacteria.

With regards to the susceptibility pattern, the overall sensitive and resistant percentage (%) of *S. aureus* in SSTIs is shown in Figure 2. Vancomycin, Teicoplanin, and Linezolid show high sensitivity (n=65, 100% each) in comparison with all the other antibiotics, and Levofloxacin, following Penicillin shows high resistance (n=65, 89.2% and 83.1%), as compared to all other antibiotics. In Figure 3, the susceptibility pattern of *Enterococcus* species in SSTIs is shown where Teicoplanin has a higher sensitivity of 95.5 % (n=67) following Vancomycin (92.5%) and Linezolid (91%). Tetracyclin has higher resistance of 74.6% (n=67) in comparison too all the other antibiotics. The susceptibility pattern of CoNS is shown in Figure 4 where Vancomycin and Linezolid (n=164) have high sensitivity and resistance

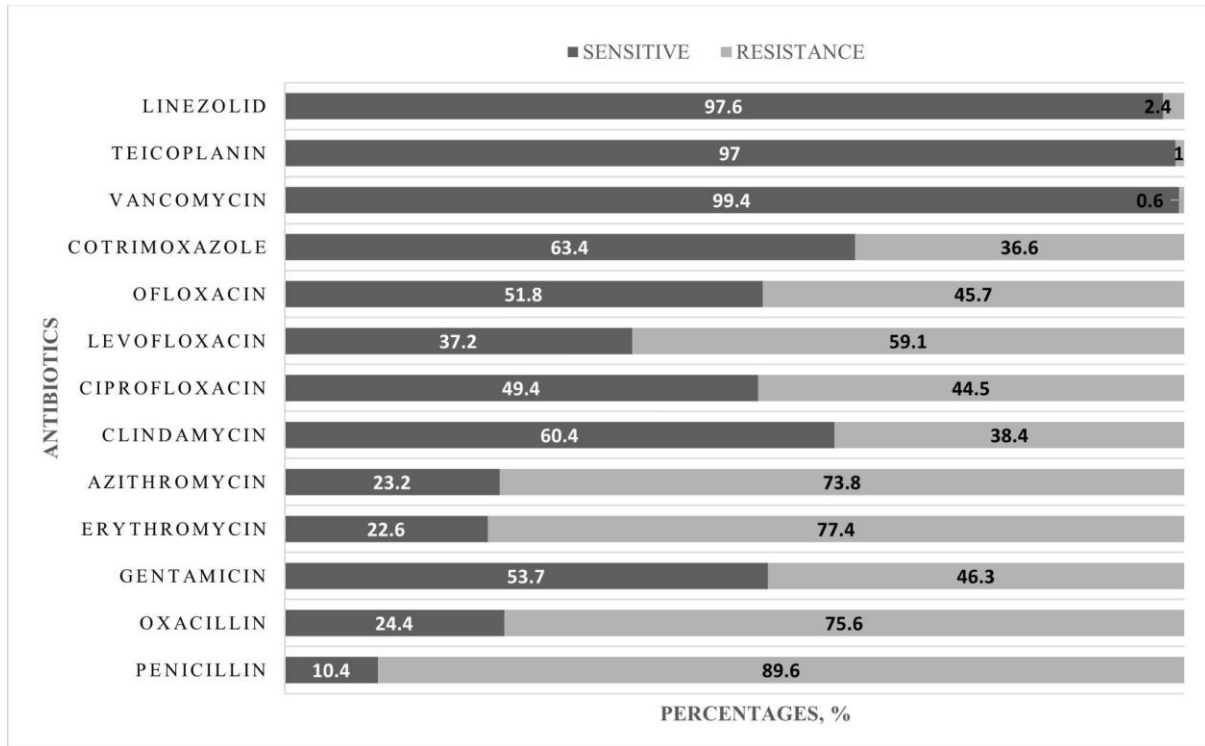
percentages of 60.4% and 89.4 %, as compared to other antibiotics analyzed. Penicillin with a higher resistance of 89.6% is observed.



**Figure 2.** Antibiotic sensitivity and resistance of *S. aureus* in SSTI samples



**Figure 3.** Antibiotic sensitivity and resistance of *Enterococcus* spp. in SSTI samples



**Figure 4.** Antibiotic sensitivity and resistance of CoNS in SSTI samples

The *p*-value in Table 1 highlights the statistical significance of the difference in antibiotic susceptibility among the three bacterial groups. Antibiotics with a *p*-value less than 0.05 signify variability across the groups like penicillin ( $p < 0.0000001$ ), Oxacillin ( $p < 0.0000001$ ), Ciprofloxacin ( $p = 0.0005$ ) and Levofloxacin ( $p < 0.000001$ ) showing resistance variation which is linked to bacterial species. Conversely, *p*-values greater than 0.05 indicate no significant differences in susceptibility patterns. Clindamycin ( $p = 0.233$ ) and Linezolid ( $p = 0.093$ ) demonstrate uniform efficacy among the bacterial groups. Notably, antibiotics such as Vancomycin, Teicoplanin, and Linezolid have high susceptibility (close to 100%) in all bacterial groups suggesting their broad-spectrum efficacy.

**Table 1.** Comparative antibiogram (cumulative susceptibility report) of bacterial strains isolated in skin and soft tissue infections

Antibiotics	<i>Staphylococcus aureus</i> (n=65) %	CoNS (n=164) %	<i>Enterococcus</i> species (n=67) %	p-value
Penicillin	16.9	10.4	74.6	<0.0000001
Oxacillin	70.8	24.2	NA	<0.0000001
Ampicillin	NA	NA	80.6	NA
Gentamicin	35.4	53.7	64.2	0.000203201
Tetracycline	NA	NA	25.4	NA
Erythromycin	56.9	22.6	13.4	<0.0000001
Azithromycin	52.3	23.2	NA	0.00004
Clindamycin	69.2	60.4	NA	0.233
Ciprofloxacin	26.2	49.4	46.3	0.0005
Levofloxacin	10.8	37.2	44.8	0.0000001
Ofloxacin	24.6	51.8	NA	0.00005
Cotrimoxazole	76.9	63.4	NA	0.022
Chloramphenicol	NA	NA	82.1	NA
Vancomycin	100	99.4	92.5	0.001
Teicoplanin	100	97	95.5	0.046
Linezolid	100	97.6	91	0.093

Notes: NA – not applicable; S – sensitive, green; R – resistant, red.

**Table 2.** Antibiogram of GPC in SSTIs

Bacterial isolate	n	PEN	OX	AM	GM	GM500	TE	EM	AZI	CM	CIP	LVX	OFX	TMP	CHL	VA	TEC	Lzd
<i>Staphylococcus aureus</i>	65	R	S	NA	NA	R	S	S	NA	S	R	R	R	NA	S	S	S	S
CoNS	164	R	R	NA	NA	S	R	R	NA	S	R	R	S	NA	S	S	S	S
<i>Enterococcus</i> spp.	67	S	NA	S	S	NA	R	NA	R	NA	R	R	NA	S	NA	S	S	S

Notes: n – number of isolates, PEN – Penicillin, OX – Oxacillin, AM – Ampicillin, GM – Gentamicin, GM500 – High Level Gentamicin, TE – Tetracycline, EM – Erythromycin, AZI – Azithromycin, CM – Clindamycin, CIP – Ciprofloxacin, LVX – Levofloxacin, OFX – Ofloxacin, TMP – Cotrimoxazole, CHL – Chloramphenicol, VA – Vancomycin, TEC – Teicoplanin and Lzd – Linezolid, S = sensitive, green; R = resistant, red; NA – not applicable.

## Discussion

SSTIs through bacteria is one of the most recurrent presentations seen in emergency room clinics and represents an important area of infection diseases that covers a large spectrum of pathologies and changing severity and complexity. Most SSTIs like folliculitis, cellulitis, furunculosis, and trauma-related wound infections are treated through topical or oral antibiotics like  $\beta$ -lactamase stable penicillins or macrolides, cephalosporins [5]. However, over the decade various resistant strains have been presented and the statistics are getting higher. Therefore, to understand the occurrence of SSTIs due to GPC and their antimicrobial profile we analyzed the data of the patients from January 2022 to December 2022 from the MMM hospital and drew an antibiogram (cumulative susceptibility report) that represents the pattern of resistance created by various organisms to antibiotics.

From the data, it is understood that from 881 suspected samples of SSTIs, 816 (92.6%) samples are positive (presence of bacterial infection). The high rate of positive samples is due to the specialty of the hospital. The hospital is an International Healthcare Provider providing healthcare services in the areas of Adult/Pediatric Cardiac care. So most of the patients have cardiovascular disease (CVD) and have been operated on for open heart surgery which infers that they have surgical wounds which take weeks to heal. So there is a high chance of surgical site infection in the patient population which supports the high number of positive samples.

Furthermore, most of the clinical history of the patients mention that they have an abscess, acute coronary syndrome, anterior wall myocardial infarction, coronary artery disease (CAD), acute decompensated heart failure, triple vessel disease (TVD), acute coronary syndrome, and non-ST-elevation myocardial infarction (NSTEMI) which correlates with the above discussion on high patients with positive samples. Through analyzing the site of the sample collection of patients, it was also identified that most of them had chest wounds or pus oozing out of the chest wound.

In the positive samples, GNB isolates are comparatively higher with 428 samples. This is because most of the GNB are resistant to most antibiotics and have outer membranes containing lipopolysaccharide (LPS), a potential toxin that triggers an immune response causing complications in the infected like inflammation. However, GPC also has a significant contribution to the SSTIs infection. And the emerging multi-drug resistant strain has made the treatments even more difficult. Moreover, patients with co-morbidities like ischemic ulceration, diabetes mellitus and chronic lymphoedema are more complicated to treat [5]. Even though it is known that most GPC infections can be treated with beta-lactam antibiotics, through that study it has been observed that both *S. aureus* and CoNS have shown more resistance of 83.1% and 89.6% to Penicillin and it states that there is emerging resistance to the antibiotic. For the reason, the paper focuses on the GPC of the SSTIs as *S. aureus* is a prime organism found in SSTIs.

Moreover, a significant patient population has a clinical history of sepsis. It might be that when SSTIs are left treated, it can result in the movement of pathogens from skin tissues to lymph nodes and blood leading to bloodstream infection that ultimately leads to sepsis. Numerous epidemiological studies have revealed that SSTIs are accountable for 4.3%–10.5% of septic episodes among hospitalized or severely sick patients [12]. SSTIs have been stated to affect at least 3% of all surgical procedures and can lead to issues like tissue damage, delayed

wound healing, incisional hernias, and sometimes even bloodstream infections [13].

As our study focuses on GPC, from 360 samples, 164 samples were CoNS, 67 samples were *Enterococcus* species, 65 samples were *S. aureus* and 64 samples were other GPB. The *Enterococcus* species includes *Enterococcus gallinarum*, *Enterococcus faecalis*, *Enterococcus gallinarum* (Vancomycin-resistant *Enterococcus*), *Enterococcus avium*, *Enterococcus faecium*, *Enterococcus faecium* (Vancomycin-resistant *Enterococcus*), *Enterococcus hirae* and *Enterococcus raffinosus*. The other GPB include *Streptococcus constellatus* subsp. *pharyngis*, *Streptococcus pyogenes*, and *Streptococcus sanguinis*. The organisms were not considered in the antibiogram as they have less than 30 isolates which cannot be used to find the susceptibility pattern as per CLSI M39-A3 [14]. Further, most of the isolates were commensal. The CoNs include *Staphylococcus lugdunensis*, *Staphylococcus warneri*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Staphylococcus hominis*, *Staphylococcus caprae*, *Staphylococcus pseudintermedius*, *Staphylococcus cohnii* subsp. *urealyticus*, *Staphylococcus saprophyticus*, *Staphylococcus stutzeri*, *Staphylococcus carnosus* and *Staphylococcus xylosum*.

From the 360 GPC samples, 65 samples were *S. aureus*, in which multi-drug resistance was observed, MSSA (47 samples, 72.3%) and MRSA (18 samples, 27.7%). Through a study of three tertiary-care hospitals in Greece, it was found that *S. aureus* accounts for 46.6% of the cases and the majority of the strain is MSSA at 78.2% [15]. Another prevalence study conducted by the European Centre for Disease Prevention and Control (ECDC) in 2011-2012 also states that most of the SSTI infections were caused by *S. aureus* [16]. *S. aureus* has been the leading bacterial death in 135 countries and millions of deaths and even it can be treated by oral therapy, however, antimicrobial-resistant strains like MRSA alone have been responsible for more than 100,000 deaths worldwide in 2019 [17]. Additionally, they were resistant to Clindamycin and Gentamicin which resembles the study conducted in a tertiary care hospital in Germany [18].

Focusing on the susceptibility pattern, *S. aureus* and CoNS are mostly resistant to penicillin probably due to the development of resistance against  $\beta$ -lactam antibiotics [19]. Introduced in the 1940s for *S. aureus*, Penicillin has been under strong selection pressure brought about by widespread usage, which has regularly led to the survival and spread of resistant bacteria, serving as a superb illustration of Darwinian evolution [20]. In a study in Odisha, 97.4% of the MRSA strains have shown resistance against penicillin which correlates with our study. However contradictorily, 23.6% of the MSSA strains will only be resistant to penicillin which can be due to geographical changes and strains that are spread in the healthcare sectors [18]. Another reason can be due to the community, as community-associated MRSA and MSSA have been identified in various presentations. Due to the misuse or abuse of antibiotics, higher resistant strains may be created in the community [21].

Ciprofloxacin and levofloxacin have shown more resistance to CoNS, *Enterococcus* species, and Coagulase-Negative Staphylococci from our study which correlates with most of the studies done in south India, USA and Europe [5,22]. Vancomycin, Teicoplanin, and Linezolid show 100% susceptibility for *S. aureus*, however, significant resistant strains have been identified in the CoNS and *Enterococcus* species which has already been discussed before, *Enterococcus gallinarum* (Vancomycin-resistant *Enterococcus*) and *Enterococcus faecium* (Vancomycin-resistant *Enterococcus*). *Enterococcus* can be found all over the body, especially the intestines, vagina, and urethra [23]. Another feature to note is that most of the patients had a clinical history of abnormal renal function, chronic kidney disease (CKD), abdominal wound discharge, and abnormal renal function. In the case of CKD, weakening of the immune response is created due to the inflammation, a suitable environment for *Enterococcus* infection. Even though they are not the primary infection for SSTIs, they can create a microbiota environment for SSTIs as they only infect already injured tissues [24]. The previous statement can be justified as most patients had abdominal wound discharge and function due to the change

in the microbiota environment. Another notable point is that most of the patients had diabetes mellitus and diabetic foot ulcers. The conditions suppress the healing process contributing to prone infection which is seen in the study.

One of the limitations of the study is that a significant amount of clinical history or the site of the sample was not collected due to patient confidentiality. The details were not given if they were not needed for the microbial study. Another significant limitation is the limited isolates for some of the organisms. Through CLSI guidelines it is noted that at least 30 isolates should be indeed for an efficient result and any isolates below that should be neglected as they can lead to errors. Therefore we neglected some isolates, they had 17-19 isolates [14]. On the other hand, we used both the VITEK 2 Compact Instrument and manual method to confirm the isolates which gives double assurance on the result of the biochemical and antimicrobial study.

## **Conclusions**

Understanding the causative agents of SSTIs and their antibiogram not only gives options for doctors and pharmacists to decide on the most effective empiric antimicrobial therapy when the culture and susceptibility results are pending but also to direct infection prevention programs that aim at preventing the spread of antibiotic-resistant infections in hospitals. Therefore, primary, secondary, and tertiary healthcare facilities must regulate accurate data analysis and antibiotic stewardship. From our study done in the MMM hospital, Vancomycin, Teicoplanin, and Linezolid were found to be the most sensitive to GPC. However, Penicillin, Ciprofloxacin, and Levofloxacin have been recorded to have high resistance to GPC. More classes of antibiotics may be practiced in the susceptibility study and the resistant antibiotics may be discontinued.

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This study did not require ethical approval as it involved only the analysis of existing data and did not include human or animal subjects.

Artificial intelligence (AI) was not used in the creation of the manuscript.

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