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Comparative Analysis of Antibiotic Susceptibility Pattern Shown by Staphylococcus Aureus Isolated from Pus Sample

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Abstract

Background: Antibiotic resistance poses a significant global health challenge, particularly concerning *Staphylococcus aureus*, a prominent pathogen notorious for its ability to develop resistance. This study aims to analyze the antibiotic susceptibility patterns of *S. aureus* isolated from pus samples over four years using the Vitek method.

Materials & Methods: A retrospective study was conducted at Padmashree Diagnostic, Bengaluru, analyzing data from January 2020 to December 2023. Pus samples from both genders, collected aseptically, were analyzed. The Vitek-2 system was employed for bacterial identification and antibiotic susceptibility testing. The data were statistically analyzed using SPSS version 22.0, with p-values < 0.05 considered significant.

Results & Discussion: The analysis of 116 isolates revealed high resistance rates to Ciprofloxacin (81%) and Levofloxacin (83.6%) across the years, with resistance peaking in 2021. Erythromycin resistance declined from 52% to 34.7%, while Gentamicin showed fluctuations in resistance rates. Notably, Tigecycline resistance emerged in 2023, showing a significant increase ($p = 0.007$). Trends suggest dynamic shifts in antibiotic susceptibility, highlighting the need for continued surveillance.

Conclusion: The study emphasizes the variability in resistance patterns of *S. aureus* over four years, with significant trends observed in Tigecycline and Trimethoprim/Sulfamethoxazole resistance. Continuous monitoring and targeted antibiotic stewardship are crucial in combating rising antibiotic resistance.

Keywords: Staphylococcus aureus, Antibiotic resistance, Vitek method, Ciprofloxacin, Tigecycline

1. INTRODUCTION

Pyogenic infections result in pus formation and are distinguished by numerous localized inflammations, typically caused by the growth of microorganisms. *Staphylococcus aureus* is the most frequent causal agent, accounting for 20–40% of all cases. *Pseudomonas aeruginosa* infections make up about 5–15% of cases. Pyogenic infections are commonly associated with *Escherichia coli, Klebsiella species, Proteus species*, and *Enterococci species*. [1,2]

Staphylococcus aureus causes skin, bone, and soft tissue infections, urinary tract infections, pneumonia, healthcare-associated bacteremia in community and hospital settings, and other invasive infections [3]. The most frequently encountered organism in hospitals and community-acquired infection, especially in elderly individuals is *Staphylococcus aureus* [4]; rates of *Staphylococcus aureus* infection have

increased during the past 2 decades [5].

Bacteremia due to *S. aureus* has been reported to be associated with mortality rates of 15%- 60% [6]. Infections with antibiotic-resistant organisms are thought to result in higher morbidity and mortality rates than similar infections with antibiotic-susceptible strains [7]. Penicillin G (benzylpenicillin), was first introduced in the early 1940s and provided a temporary solution to staphylococcal infections. However, prolonged use of this agent led to the selection of resistant bacteria that generated penicillinase (β-lactamase) [8].

Among the staphylococcus species, *Staphylococcus aureus* is the most virulent species of the genus causing both nosocomial and community-acquired infections worldwide [9,10]. The organism is the most common bacterial agent recovered from bloodstream infections, skin and soft tissue infections, pneumonia, and hospital-acquired post-operative wound infections [11]. Treatment of *S. aureus* infections has become increasingly challenging due to observed changes in the antibiotic susceptibility profile of the bacteria globally [12-14].

Pyogenic bacteria can produce pyodermas, which are skin diseases that can eventually lead to suppuration. *Staphylococcus aureus* and *Streptococcus pyogenes* are the most implicated in these purulent infections [15]. A common bacterium with an amazing capacity to endure harsh conditions is *Staphylococcus aureus*, which is typically detected in infections that develop into purparations. For those living with HIV/AIDS (PLWHA), these staphylococcal infections impair their immune system. It is therefore a significant nuisance for many patients.[16]

Asymptomatic carriers of this bacterium may also be Humans, especially on their nasal mucosa. Colonized individuals may spread *S. aureus* to other people, which could be especially dangerous if the carriers are healthcare workers [17]. Moreover, the treatment of infections caused by this bacterium is often complicated by increasing numbers of strains resistant to methicillin (MRSA) and other anti-staphylococcal drugs [18- 20]. Thus, novel ways of therapy are needed as an alternative to conventional antibiotic treatment [21-24].

Staphylococci's multidrug resistance is becoming a bigger issue in clinical settings, particularly with methicillin-resistant *S. aureus* (MRSA) strains. These strains are resistant to most of the antimicrobial agents, and isolates with reduced susceptibility and resistance to vancomycin, which is the last drug for the treatment of MRSA infections [25]. These strains of the multidrug-resistant bacteria may cause serious infections with a high death rate. In vitro, susceptibilities of MRSA strains, especially those from community-acquired infections, to clindamycin, macrolides, quinolones, tetracyclines, and trimethoprim-sulfamethoxazole have frequently been reported [26,27]. MRSA strains, which were previously mostly found in hospitals and long-term care facilities, are starting to appear in other parts of the community. The evolution of MRSA's epidemiology is very comparable to the decades-long rise of penicillinase-mediated resistance in *S. aureus*. [28,29]

When it was discovered that *Staphylococcus aureus* rapidly acquired resistance and was able to generate numerous strains resistant to antibiotics, the issue with the bacteria grew even more complex. In hospitals this is very common where drug-resistant "hospital strains' have caused *S. aureus* infection outbreaks resulting in deaths in surgical units and newborn nurseries [30]. These are the high-mortality and morbidity strains that are resistant to beta-lactam antibiotics, including MRSA. Antibiotic resistance results in longer hospital stays and higher treatment expenses. Besides these, it also results in potentially fatal infections

including chronic osteomyelitis and pyomyositis. The majority of MRSA strains worldwide have become resistant to multiple antibiotics including beta-lactams; aminoglycosides, macrolides, lincosamides, and more recently floroquinolines [31,32].

Antibiotic resistance poses a significant global health challenge, threatening the effectiveness of existing antimicrobial treatments and complicating the management of infectious diseases [33]. *Staphylococcus aureus*, a prominent human pathogen, is notorious for its ability to develop resistance to multiple antibiotics, further exacerbating treatment difficulties [34]. Understanding the evolving patterns of antibiotic susceptibility in *S. aureus* is imperative for informing clinical practice and guiding effective antimicrobial stewardship programs [35]. Microbial infections with antimicrobial-resistant strains increased the risk of mortality and increased costs related to treatment compared to infections caused by susceptible strains.[36]

Staphylococcus aureus continues to be a dangerous pathogen for community-acquired and hospital-associated infections. *Staphylococcus aureus* resistant to methicillin was reported soon after its preface in October 1960. Methicillin-resistant *S. aureus* (MRSA) is now endemic in India. [37,38]

According to several research studies, the prevalence rates of Vancomycin-resistant *S. aureus* ranged from as low as 1.3% to as high as 20%. [39]

Nosocomial infections are frequently caused by multidrug-resistant strains, especially Multidrug-Resistant *Staphylococcus aureus* (MRSA) strains, which are linked to higher morbidity and mortality rates. Resistance to commonly used antimicrobial drugs is often encountered with *Staphylococcus aureus*. There are several mechanisms of resistance, including inactivating antibiotics by enzymes, decreasing or inhibiting the antibiotic's affinity resulting from alteration of the target, efflux pumps, and trapping of the antibiotic. [40,41]

Further research on molecular studies is needed to evaluate the resistance genes and monitor the epidemiology of multiple drug-resistant *S. aureus* and MRSA.[40]

This study presents a comparative analysis of four years of data on the antibiotic susceptibility patterns exhibited by *S. aureus* isolated from pus samples, employing the Vitek method. The investigation aims to assess the changing profile of antibiotic susceptibility in *S. aureus* over the specified period, offering valuable insights into the dynamics of antimicrobial resistance.

The research draws upon a robust methodology, encompassing a retrospective analysis of data collected from Padmashree Diagnostic, Vijay Nagar, focusing on pus samples obtained aseptically from both genders within the Bengaluru population. Samples collected post-antibiotic administration were excluded to ensure the integrity of the analysis. The findings of this study will contribute to a better understanding of the local resistance patterns and support the development of targeted strategies to combat antibiotic resistance in *S. aureus*, ultimately improving patient outcomes and public health.

2. Aim of the Study

To assess the changing profile of antibiotic susceptibility shown by Staphylococcus aureus over four years from January 2020 to December 2023 Vitek method.

3. Review of Literature

3.1 . STAPHYLOCOCCUS

Staphylococcus was first observed in pus by von Recklinghausen (1871) and was first cultured in liquid

medium by Louis Pasteur (1880). It was named *Staphylococcus* (in Greek, Staphyle means 'bunch of grapes' and kokkos means berry) by Sir Alexander Ogston (1880). Rosenbach (1884) named two species of staphylococci based on the pigmentation of colonies S. aures (golden yellow colonies) and S. albus (white colonies). Later Passet (1885) named a third species as S. citreus (lemon yellow colonies).

Staphylococcus aureus is a catalase-positive, coagulase-positive, facultative anaerobe, non-motile, non-sporing, and occasionally capsulated. They are spherical cocci, about 1 µm in diameter, arranged in grape-like clusters. This arrangement is due to cell division in *S. aureus* occurs in multiple planes with daughter cells remaining close Together. It produces golden yellow pigmentation on nutrient agar and β hemolytic colonies on blood agar.

3.1.1 EPIDEMIOLOGY

S. aureus is the most virulent species among staphylococci; produces infections that range from localized pyogenic infections to life-threatening systemic infections in man. Its importance as a human pathogen is greatly enhanced especially in a hospital environment because of its ability to develop drug resistance.

Staphylococcus aureus is a part of normal human flora. About 25-50% of the healthy population are carriers of *S. aureus,* colonizing the organism persistently or transiently.

- Most common site(s) of colonization are anterior nares followed by skin (abraded), vagina, axilla, perineum, and oropharynx. These colonization sites serve as a reservoir for future infections.
- The rate of colonization is higher among insulin-dependent diabetics, HIV-infected patients, patients undergoing hemodialysis, and individuals with skin damage.
- Overall, *S. aureus* is a leading cause of nosocomial infections. In hospitals, the healthcare professionals are the potential carriers of *S. aureus*. Hospital strains are often multidrug-resistant, spread to patients either from hospital staff/ other patients/ environment or also from the patient's own endogenous flora.
- *S. aureus* is the most common cause of surgical site wound infections and a leading cause of primary bacteremia.
- In the community, *S. aureus* remains an important cause of skin and soft tissue infections, respiratory infections, and infective endocarditis.

3.1.2 MORPHOLOGY

- Gram-positive cocci arranged in grape-like clusters
- About 1 µm in diameter
- non-motile
- non-sporing
- occasionally capsulated

3.1.3 VIRULENCE FACTORS

Cell wall-associated factors

- Peptidoglycan
- Teichoic acid
- Cell surface adhesins- e.g. clumping factor
- Protein A

Toxins

- Membrane active toxin
- Hemolysins- α, β, γ, δ
- Leukocidin (or Panton valentine toxin)

- Epidennolytic toxin (exfoliative toxin)
- Enterotoxins
- Toxic shock syndrome toxin

3.2.4. PATHOGENESIS

Pathogenesis of *S. aureus* involves the following steps:

Colonization: *S. aureus* colonizes on various body surfaces, such as anterior nares, axilla, and perineal skin.

Introduction into the tissue: Organisms are introduced into the tissues as a result of minor abrasions or instrumentation. Then they adhere to the tissue surfaces; which is mediated by various adhesins, e.g. clumping factor.

Invasion: *S. aureus* can invade the tissues by elaborating enzymes, such as serine proteases, hyaluronidases., thermonucleases and lipases.

Evasion of host defense mechanisms: *S. aureus* exhibits various immune evasion mechanisms, such as:

1. Anti-phagocytic activity mediated by microcapsule and protein A.
2. Inhibition of leucocyte migration (by chemo1axis inhibitory protein of staphylococci).
3. Intracellular survival inside the endothelial cells (by formation of small colony variants).

Metastalic spread: Finally, *S. aureus* spreads 10 various distant sites by hematogenous spread.

3.2.5. CLINICAL MANIFESTATIONS

Staphylococcus aureus is a pluripotent pathogen, that causes various diseases through both toxin-mediated and non-toxin-mediated mechanisms.

It is responsible for both nosocomial and community-based infections that range from relatively minor skin and soft tissue infections to life-threatening systemic infections.[42]

Skin and soft tissue infections

S. aureus is one of the most common causes of various skin and soft tissue infections such as:

- Folliculitis (infection of hair follicles)
- Furuncle (boil)
- Carbuncle
- Impetigo
- Surgical site wound infections
- Cellulitis (inflammation of skin and subcutaneous tissue)
- Botryomycosis

Predisposing factors to *S. aureus* cutaneous infections are chronic skin conditions (e.g. eczema}, skin damage (trauma injections), or poor personal hygiene.

Musculoskeletal Infections

S. aureus is the most common cause of various conditions such as:

- Septic arthritis (most commonly involved joints are knees, shoulders, hips. and phalanges)
- Osteomyelitis (most commonly affected site in children is long bones and in adults is vertebrae)
- Pyomyositis (skeletal muscle infection)
- Abscess

Respiratory tract Infections

- Ventilator-associated pneumonia in adults
- Septic pulmonary emboli
- Post viral pneumonia (e.g. influenza)

- Empyema and Pneumothorax
- Pneumatocele- (shaggy, thin-walled cavities in lungs) in neonates: *S. aureus* is the most common cause.

Bacteremia and its complications

- Sepsis, septic shock
- Central line-associated bloodstream infection
- Metastatic foci of infection involving kidney, joints, bone, and lung
- Infective endocarditis

UTI (Urinary tract infection)

- Staphylococcal UTI and pyelonephritis usually occur secondary to bacteremia.
- Rarely UTI is seen following instrumentation and insertion of catheters or implants.

Toxin-mediated illnesses

- Toxic shock syndrome
- Food poisoning
- Staphylococcal scalded-skin syndrome

According to a study by Michel Kengne, of all the strains that were identified, 80% (201/205) and 20% (49/205) were methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-sensitive *Staphylococcus aureus* (MSSA). The MRSA strains exhibited a high level of resistance to the following drugs: erythromycin (55.7%), doxycycline (68.0%), kanamycin (69.7%), vancomycin (79.7%), lincomycin (70.3%), tobramycin (72.5%), and cefoxitin (100%). On the other hand, rifampicin showed a high susceptibility of 82.6%. Constitutive MLSB (17.4%) and KTG (42.3%) were the most often observed phenotypes. [3]

A study conducted by Tebelay Dilnessa1 and Adane Bitew reports that Of 1360 clinical specimens analyzed *S. aureus* was recovered from (194, 14.3 %) When it came to clinical specimens, pus had the greatest isolation rate of *S. aureus* (118, 55.4 %). From the CSF and urethral discharge, no *S. aureus* was recovered. Of the 194 isolates of *S. aureus*, 34 (17.5 %) were identified as MRSA, and the remaining 160 (82.5 %) as MSSA. Ninety-eight (50.5%) *S. aureus* isolates were found to be multidrug resistant.

The isolates with the highest penicillin resistance (187, 96.4%) and the lowest resistance to clindamycin (23, 11.9%) and vancomycin (10, 5.1%) were identified. Penicillin G, erythromycin, trimethoprim-sulfamethoxazole, and vancomycin (10, 29.4%) were the antibiotics against which MRSA strains were 100% resistant. Out of 194 *S. aureus* isolates (153, 79.0 %) were beta-lactamase producers.[9]

According to a study by Michel Kengne at the Yaoundé Central Hospital in Cameroon, ninety-eight (48) strains of *Staphylococcus aureus* were discovered. Many strains, including vancomycin (100.0%), pristinamycin (100.0%), chloramphenicol (100.0%), oxacillin (97.9%), cefoxitin (97.9%), gentamicin (87.5%), and tobramycin (83.3%), had a high rate of antibiotic sensitivity. Nonetheless, 89.6% of the strains exhibited significant resistance to penicillin G, and 64.6% to cotrimoxazole. Methicillin-resistant strains of *Staphylococcus aureus* (MRSA) constituted just 2.0% of the total. Similar to the induced phenotypic E staining (iMLSB) in macrolides-resistant organisms, the kanamycin tobramycin-gentamycin phenotype (KTG) was more prevalent in strains resistant to aminoglycosides.[16]

Out of 105 strains of *S. aureus* isolated from pus, urine, tracheal secretions, and blood, nearly half (46; 43.8%) were methicillin-sensitive *Staphylococcus aureus* (MSSA), and 59 (56.2%) were methicillin-resistant *Staphylococcus aureus* (MRSA), according to a study by Haji Mohammad Naimi. All strains were susceptible to vancomycin. In total, 100 (95.2%) strains were susceptible to rifampicin, 96 (91.4%)

susceptible to clindamycin, 94 (89.5%) susceptible to imipenem, 83 (79.0%) susceptible to gentamicin, 81(77.1%) susceptible to doxycycline, 77 (77.1%) susceptible to amoxicillin + clavulanic acid, 78 (74.3%) susceptible to cefazolin, 71 (67.6%) susceptible to tobramycin, 68 (64.8%) susceptible to chloramphenicol, 60 (57.1%) were susceptible to trimethoprim-sulfamethoxazole, 47 (44.8%) susceptible to ciprofloxacin, 38 (36.2%) susceptible to azithromycin and erythromycin, 37 (35.2%) susceptible to ceftriaxone and 11 (10.5%) were susceptible to cefixime. Almost all (104; 99.05%) were resistant to penicillin G and only 1 (0.95%) was intermediate to penicillin G. Interestingly, 74.6% of MRSA strains were azithromycin resistant with 8.5% of them clindamycin resistant. Ninety-six (91.4%) of the isolates were multi-drug resistant.[29]

A study conducted by Barbara Kot in the year 2019 reports that a large number of MRSA isolates showed resistance to ciprofloxacin (83%), levofloxacin (83.9%), erythromycin (77.7%), and clindamycin (72.3%). MRSA isolates were less likely to be resistant to tetracycline (10.7%), gentamicin, and trimethoprim with sulfamethoxazole (8.0%). No MRSA isolates were resistant to teicoplanin and linezolid. Among MRSA isolates, 92.9% were multidrug-resistant (MDR). Resistance to clindamycin, levofloxacin, ciprofloxacin, and erythromycin was the most common resistance pattern among MDR MRSA isolates. Most isolates were resistant to four groups of antimicrobials (53.8%). The number of drugs to which MRSA isolates were resistant in 2017 was significantly higher than that in the year 2016 ($p = 0.002$). [36]

A study conducted by Sangeeta Joshi, in India reports a total of 26,310 isolates were included in the study. During the study period, the overall prevalence of methicillin resistance was 41%. Isolation rates for MRSA from outpatients, ward inpatients, and ICU were 28, 42, and 43% in 2008 and 27, 49, and 47%, respectively. Most S. aureus isolates were obtained from patients with soft tissue and skin infections followed by those suffering from respiratory and bloodstream infections. Susceptibility to ciprofloxacin was low in both MRSA (21%) and MSSA (53%). As compared to MRSA isolates MSSA isolates showed a higher susceptibility to gentamicin, erythromycin, and clindamycin. No isolate was found resistant to vancomycin or linezolid. [37]

BMC Research Note published an article in the year 2018 "Antimicrobial susceptibility pattern of *Staphylococcus aureus* isolates from clinical specimens at KNH(Kenyatta National Hospital)". This study reports that a total of 944 *S. aureus* isolates were analyzed. *S. aureus* was highly sensitive to tigecycline (98.2), nitrofurantoin (97.6%), linezolid (97.3%), teicoplanin (97.1%), and vancomycin (95.1%). High resistance was recorded against trimethoprim/sulfamethoxazole (56.9%), and tetracycline (33.2%). MRSA prevalence among the patients at Kenyatta National Hospital was 27.8%. The highest proportion (80%) of MRSA was in a burn unit. MSSA and MRSA both were highly susceptible to tigecycline, linezolid, nitrofurantoin, and vancomycin and showed high resistance to commonly used antibiotics such as erythromycin, levofloxacin, gentamycin, and tetracycline. A large number of isolates were from pus specimens (68%). [40]

ANTIBIOTIC RESISTANCE

ANTIBIOTICS THAT TARGET THE CELL ENVELOPE

B-Lactam antibiotics

Staphylococcus aureus strains resistant to penicillin first appeared shortly after the antibiotic's introduction in the early 1940s. The drug's antibacterial activity was lost by hydrolyzing the crucial β-lactam bond,

which was expressed by the β-lactamase. Bulkier moieties were substituted into penicillin's native amino adipoyl chain to produce semisynthetic versions that weren't substrates for β-lactamase. The first was methicillin, although it had the drawback of being labile to acid. The acid-stable isoxazoyl penicillin oxacillin took its place. Methicillin-resistant *S. aureus* (MRSA) was identified soon after the antibiotic was introduced, and despite the fact that the term "methicillin" is no longer in use, MRSA has persisted.

Mechanism of action of and resistance to penicillin

The bifunctional transglycosylase-transpeptidase PBP2 is the main target of β-lactam antibiotics in *S. aureus*. The disaccharide pentapeptide peptidoglycan building block is transferred from membrane-bound lipid II to expanding polysaccharide chains by the enzyme's transglycosylase domain. On the other hand, the transpeptidase (TP) domain cross-links the fourth D-alanine of a neighboring chain's glycine cross-bridge.

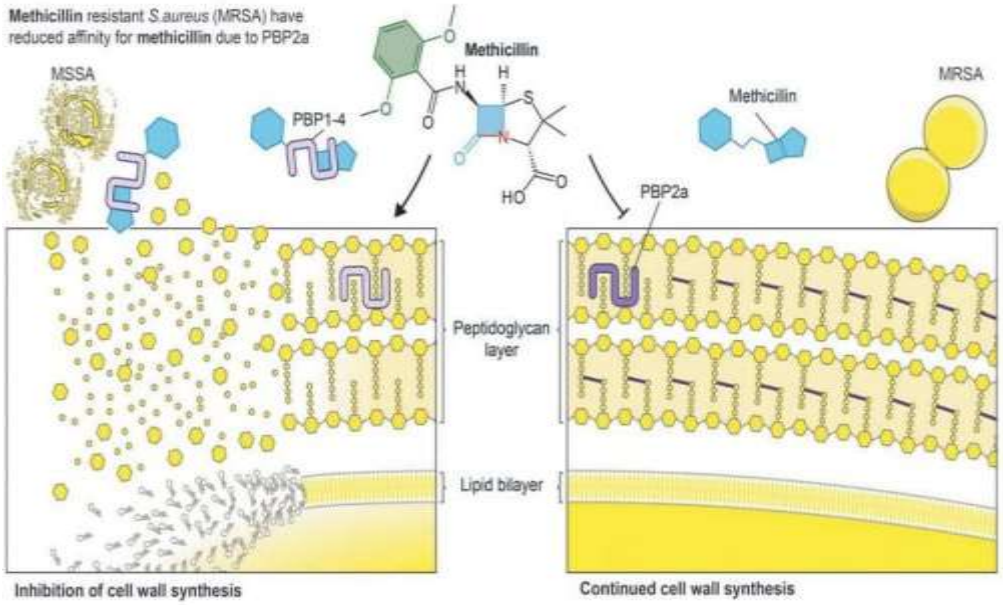

Fig :- *S. aureus* PBP2a confers methicillin resistance by lowering its affinity for the antibiotic. PBP1-4 found in MSSA (left side) are easily bound by methicillin, which prevents the formation of cell walls and peptidoglycan. In contrast, PBP2a can take part in the production of cell walls because of its decreased affinity for methicillin. PBP2a, penicillin-binding protein 2a; PBP1-4, penicillin-binding protein 1-4; MSSA, methicillin-susceptible *S. aureus*.[43]

Mechanism of resistance to methicillin and oxacillin

The basis of resistance to methicillin and oxacillin is the acquisition of a gene that encodes a homologue of the PBP2 called PBP2a or PBP2' which is not susceptible to drug action. This is because the active site serine of the TP of PBP2a is located in a deep Pocket which is not accessible to β-lactams. The enzyme can therefore take over PG biosynthesis if the PBP2 TP is inactivated. Because the PBP2a moiety is inactive, the PBP2 transglycosylase activity is necessary for the formation of peptidoglycans.

Expression of methicillin resistance

The mecA gene, which codes for PBP2a, is part of a family of unique but similar staphylococcal chromosomal cassette (SCC) components. But recently, MecC, a unique PBP2a with just 63% residue identity to MecA, was found. Some MRSA strains have spread over the world, whereas others are endemic

to specific geographic areas. Hospitals were the exclusive home of MRSA (hospital-associated MRSA). These strains typically possess large SCC mec components, exhibit resistance to numerous antibiotics, and have a greater level of pathogenicity against β-lactams. These strains commonly result in systemic and wound infections because of bacteremia.

Vancomycin and other glycopeptides

A common glycopeptide antibiotic used to treat hospital patients' severe infections brought on by MRSA strains is vancomycin. It attaches itself to the lipid II dipeptide D-Ala4-D-Ala5, which inhibits peptidoglycan remodeling and stops PBP2 and PBP2a from catalyzing transglycosylation and transpeptidation.

VISA

Vancomycin treatment failure is frequently caused by strains that arise from protracted therapy and acquire several chromosomal gene alterations that impact homeostasis and cell wall biosynthesis.

Vancomycin-intermediate Staphylococcus aureus (VISA) variations have a minimum inhibitory concentration (MIC) of 4–8 μg ml−1, whereas vancomycin-susceptible S. aureus (VSSA) variants have a MIC of ≤2 μg ml−1.

Resistance to tetracyclines: efflux

TetA(K) and TetA(L), two related Tet efflux pumps in staphylococci with 14 transmembrane helices, have been described. TetK is incorporated into the chromosomal SCCmecIII cassette of MRSA bacteria and is encoded by the tiny multicopy plasmid pT181. Both of them have 14 transmembrane domains, making them members of the major facilitator superfamily (MFS) transporters; most MFS transporters, such as the classic TetA protein of Gram-negative bacteria, have 12. In opposition to a concentration gradient, the Tet efflux proteins exchange a proton for a tetracycline molecule. Bacteria harboring TetK or TetL bestow little to no resistance because the hefty alterations on the tigecycline's ring D prevent the molecule from accessing the drug binding site in the efflux protein.

Resistance to linezolid by Cfr rRNA methyltransferase

Numerous different bacteria have mutations in their 23S rRNA genes that change the nucleotides at or around the linezolid binding site. In staphylococci, the mutation G2576U is significant. *S. aureus, S. epidermidis,* and *S. hemolytic* have all been linked to it. The number of mutant rRNA operons and the MIC to linezolid show a strong association. Clinical isolates of S. aureus have also been observed to carry the U2500A and G2447U mutations [44].

3.3.8. Antimicrobial Susceptibility Test

As *S. aureus* develops resistance to antibiotics readily, drugs should be prescribed according to the antimicrobial susceptibility test done on Mueller Hinton agar.

S. aureus shows resistance to β lactam antibiotics in various ways:

- Production of β Lactamase Enzyme
- By Alternation of Penicillin Binding Protein (PBP)

Antimicrobial resistance in *Staphylococcus aureus (S. aureus)* isolates, particularly those obtained from pus samples, presents a significant challenge in clinical settings worldwide. In the Indian context, numerous studies have shed light on the prevalence, patterns, and mechanisms of antimicrobial resistance in *S. aureus* isolated from pus specimens.

Studies conducted in India have consistently highlighted the alarming rates of resistance among *S. aureus* isolates obtained from pus samples. Research by Rajaduraipandi et al. revealed high levels of resistance to commonly prescribed antibiotics such as penicillin, erythromycin, and tetracycline among *S. aureus*

strains isolated from skin and soft tissue infections. [46] Similarly, Mohanthy S, et al. documented the prevalence of multidrug-resistant *S. aureus* strains in pus samples collected from patients in Indian hospitals, emphasizing the urgent need for effective antimicrobial stewardship programs. [47]

Furthermore, investigations into the genetic determinants of antimicrobial resistance in *S. aureus* have provided valuable insights into the molecular mechanisms driving resistance. Studies by Nagasundharam et al. [48] and Singh et al. [49] explored the genetic profiles of methicillin-resistant *S. aureus* (MRSA) isolates obtained from pus specimens, revealing the presence of various resistance genes, including mecA and erm genes, responsible for resistance to beta-lactams and macrolides, respectively.

In addition to genetic factors, environmental and clinical factors also contribute to the emergence and dissemination of antimicrobial resistance in *S. aureus* isolates from pus samples. Mishra et al. [50] highlighted the role of hospital environments in the transmission of resistant strains, emphasizing the importance of infection control measures in mitigating the spread of antimicrobial-resistant pathogens.

Moreover, studies have underscored the impact of antimicrobial resistance on patient outcomes and healthcare costs. Research by Kaur et al. [51] demonstrated a significant association between antimicrobial resistance in *S. aureus* isolates from pus samples and prolonged hospital stays, increased treatment failure rates, and higher healthcare expenditures.

Overall, the literature on antimicrobial resistance in *S. aureus* isolates from pus samples in India underscores the urgent need for concerted efforts to combat this growing threat. Effective strategies encompassing surveillance, infection control, antimicrobial stewardship, and research into novel therapeutic approaches are imperative to address the challenges posed by antimicrobial resistance in clinical practice.

Materials and Methods

Data Source: The data utilized in this study were sourced from Padmashree Diagnostic, located in Vijay Nagar.

Data Collection:

- Population: The study encompassed individuals from the Bengaluru population.
- Study Design: A retrospective approach was employed to analyze data collected over a four-year period from January 2020 to December 2023.

Specimen Collection: Pus samples meeting the inclusion criteria, i.e., collected aseptically, were selected for analysis. Specimens obtained after the administration of antibiotics were excluded from the study.

Laboratory Procedures: Upon collection, pus specimens were directly inoculated onto 5% Sheep Blood Agar and MacConkey Agar plates. Subsequently, the plates were incubated at 37°C for 24 hours to facilitate bacterial growth.

Identification of *Staphylococcus aureus*: Positive pus cultures were subjected to identification procedures. *S. aureus* was identified based on its characteristic appearance on culture media, Gram staining characteristics, and positive coagulase test results.

Biochemical Profiling and Antibiotic Susceptibility Testing: The Vitek-2 system was employed for biochemical profiling and antibiotic susceptibility testing of identified *S. aureus* isolates. Standard procedures recommended for the Vitek-2 system were followed meticulously.

Statistical Data Analysis and Result

Statistical Analysis: Statistical analysis of the collected data was performed using SPSS software version

22.0. Descriptive statistics were employed, and all data values were expressed as mean ± standard deviation (SD). A significance level of $p < 0.05$ was considered statistically significant for all analyses.

Table: 1 Yearly Antibiotic Resistance Percentages in S. aureus Isolates

	2020 (n=25)	2021(n=26)	2022(n=42)	2023 (n=23)	Total (n=116)
Ciprofloxacin	23 (92%)	23 (88.4 %)	30 (71%)	18 (78%)	94 (81%)
Clindamycin	6 (24%)	8 (30.7%)	13 (30.9%)	6 (26%)	33 (28%)
Daptomycin	0	0	0	0	0
Erythromycin	13 (52%)	13 (50%)	19 (45%)	8 (34.7%)	53 (45.6%)
Gentamicin	5 (20%)	2 (7.6%)	4 (9.5%)	5 (20%)	11 (9.4%)
Levofloxacin	23 (92%)	25 (96%)	31 (73.8%)	18 (78.2%)	97 (83.6%)
Linezolid	0	1 (3.8%)	0	0	1 (0.8%)
Oxacillin	16 (64%)	17 (65.3)	28 (66%)	14 (60.8)	75(64.5%)
Rifampicin	0	3 (11.5%)	1 (2.3%)	0	4 (3.4%)
Teicoplanin	2 (8%)	1 (3.8%)	0	0	3 (2.5%)
Tigecycline	0	0	0	3 (13.4%)	3 (2.5%)
Trimethoprim / Sulfamethoxazole	3 (12%)	12 (46%)	12 (28.5%)	3 (13.4%)	30 (25.8%)
Tetracycline	1 (4%)	3 (11.5%)	2 (4.7%)	()	6 (5%)
Vancomycin	2 (8%)	1 (3.8%)	1 (2.3%)	()	4 (3%)

Result Interpretation

- **Ciprofloxacin** and **Levofloxacin**: High resistance rates consistently over the four years, with a slight decline in 2022. Levofloxacin showed a peak resistance in 2021 (96%).
- **Clindamycin**: Stable resistance rates around 24-31% over the years.
- **Erythromycin**: Gradual decrease in resistance from 2020 (52%) to 2023 (34.7%).
- **Gentamicin**: Notable fluctuation with a drop to 7.6% in 2021 and an increase back to 20% in 2023.
- **Trimethoprim/Sulfamethoxazole**: Significant increase in resistance in 2021 (46%) followed by a decrease in subsequent years.
- **Tetracycline** and **Vancomycin**: Low resistance rates overall, with no resistance observed in 2023 for Tetracycline.
- **Daptomycin**, **Linezolid**, **Rifampicin**, **Teicoplanin**, **Tigecycline**: Generally low resistance rates, with sporadic resistance observed.

Antibiotic	**Chi2 Value**	**p-value**	**Significant Difference**
Tigecycline	12.13	0.0070	Yes
Trimethoprim/Sulfamethoxazole	8.92	0.0300	Yes
Ciprofloxacin	6.47	0.0906	No
Clindamycin	0.94	0.8165	No
Daptomycin	0.00	1.0000	No

Erythromycin	2.36	0.5004	No
Gentamicin	5.73	0.1253	No
Oxacillin	8,3	0.0311	No
Levofloxacin	6.86	0.0761	No
Linezolid	1.13	0.7690	No
Rifampicin	3.42	0.3321	No
Teicoplanin	1.58	0.6637	No
Tetracycline	2.30	0.5112	No
Vancomycin	1.00	0.8000	No

Interpretation:

No Significant Difference (p-value ≥ 0.05):

For most antibiotics (Ciprofloxacin, Clindamycin, Daptomycin, Erythromycin, Gentamicin, Levofloxacin, Linezolid, Rifampicin, Teicoplanin, Tetracycline, Vancomycin), the p-values are greater than 0.05. This indicates that the differences in resistance rates across the four years are not statistically significant. In other words, there is no strong evidence to suggest that resistance rates for these antibiotics have changed significantly from 2020 to 2023.

Significant Difference (p-value < 0.05):

Tigecycline: The resistance percentages also show a significant difference (Chi2 = 12.13, p-value = 0.0070). This indicates that there has been a notable change in resistance rates to Tigecycline over the years.

Interpretation: The resistance rates to Tigecycline have notably changed over the four years.

- In 2020 and 2021, the resistance rate was 0% (0 out of 25 and 0 out of 26).
- In 2022, it remained at 0% (0 out of 42).
- In 2023, the resistance rate increased to 13.4% (3 out of 23).

Trend: There was a sudden appearance of resistance to Tigecycline in 2023, indicating an emerging resistance issue.

Trimethoprim/Sulfamethoxazole: The resistance percentages show a significant difference (Chi2 = 8.92, p-value = 0.0300), indicating changes in resistance rates across the four years.

Interpretation: The resistance rates to Trimethoprim/Sulfamethoxazole have significantly changed over the four years.

- In 2020, the resistance rate was 12% (3 out of 25).
- In 2021, there was a sharp increase to 46% (12 out of 26).
- In 2022, the resistance rate was 28.5% (12 out of 42).
- In 2023, it decreased to 13.4% (3 out of 23).

Trend: There was a significant spike in resistance in 2021, followed by a decrease in the subsequent years. This indicates fluctuations in resistance rates over time.

Discussion

The observed trends in antibiotic susceptibility patterns of *Staphylococcus aureus (S. aureus)* isolates from pus samples, as analyzed over a four-year period, prompt several noteworthy discussions.

Ciprofloxacin and Levofloxacin consistently exhibited high resistance rates throughout the study duration, indicating a persistent challenge in managing *S. aureus* infections with these antibiotics. This finding aligns with previous reports of increasing fluoroquinolone resistance among *S. aureus* strains in various clinical settings [52-54].

Conversely, Clindamycin demonstrated relatively stable resistance rates over the study period, with minor fluctuations observed. This stability may be attributed to the judicious use of Clindamycin in clinical practice and its continued efficacy against certain *S. aureus* strains. Erythromycin exhibited a gradual decrease in resistance from 2020 to 2023, suggesting a potential shift in susceptibility patterns or changes in prescribing practices over time. This decline may also reflect the impact of antibiotic stewardship initiatives aimed at optimizing Erythromycin use.

Gentamicin and Oxacillin displayed notable fluctuations in resistance rates over the four-year period. These fluctuations underscore the dynamic nature of antibiotic resistance and the need for ongoing surveillance to monitor trends and inform treatment strategies. Trimethoprim/Sulfamethoxazole demonstrated a significant increase in resistance in 2021, followed by a subsequent decrease in resistance in the following years. This fluctuation highlights the complex interplay between antibiotic usage, bacterial adaptation, and resistance emergence.

Research indicates that the prevalence of MRSA varies significantly across different regions of India. The current study identifies a 38.44% MRSA rate among *S. aureus* isolates, which is lower than the 54.8% found in a previous study at the same hospital [55]. Similar prevalence rates have been reported in Delhi (38.5%) [56], Tamil Nadu (31.1%) [57], and South Gujarat (39.50%) [58]. However, other regions show different rates: Vellore (24%) [59]. These discrepancies are likely due to varying clonal expansion and drug pressures in different communities.

The emergence of resistance to Tigecycline in 2023 is of particular concern, indicating a potential shift in susceptibility patterns and the emergence of novel resistance mechanisms.

Tigecycline, often reserved as a last-line treatment option, may face increasing challenges in managing *S. aureus* infections if resistance continues to escalate.

Overall, the findings underscore the dynamic nature of antibiotic resistance in *S. aureus* isolates from pus samples and emphasize the importance of ongoing surveillance and antimicrobial stewardship efforts to mitigate the spread of resistance.

Limitations of the study include single-center data, retrospective design, limited sample size, lack of antibiotic history consideration, potential laboratory variations, absence of clinical correlation, and temporal constraints. Addressing these can enhance future research quality and applicability in understanding antibiotic resistance dynamics in *Staphylococcus aureus* isolates.

Conclusion

The analysis reveals notable variations in antibiotic resistance patterns among *S. aureus* isolates over the four-year period. Ciprofloxacin and Levofloxacin have consistently high resistance rates. Erythromycin shows a declining trend in resistance, while Gentamicin and Oxacillin demonstrate significant year-to-year fluctuations. Trimethoprim/Sulfamethoxazole displayed a peak in resistance in 2021. Continuous monitoring and tailored antibiotic stewardship programs are crucial to manage and mitigate the rising antibiotic resistance in *S. aureus* isolates.

List of Reference

1. Wadekar M, Sathish JV, Jayashree PC. Bacteriological profile of pus samples and their antibiotic susceptibility pattern. Indian Journal of Microbiology Research. 2020;7(1):43-7.
2. Murugesan K, Radha RS, Vijayan H. Study on Antibiotic Susceptibility Testing against Pyogenic Organisms from Wound Infections. Int J Pharm Sci Rev Res. 2017;45(1):262-5.
3. Kengne M, Fotsing O, Ndomgue T, Nwobegahay JM. Antibiotic susceptibility patterns of Staphylococcus aureus strains isolated at the Yaounde Central Hospital, Cameroon: a retro prospective study. Pan African Medical Journal. 2019 Mar 5;32(1).
4. Njoungang LL, NwobegahayMbekem J, Ayangma RC, NjukengAchianga P, Kengne M, Mbozo'o Abeng E, Mama EA, Tchouamo M, Ter Goon D. Prevalence and antibiotic resistance patterns of strains of Staphylococcus aureus isolated at the Yaounde Military Hospital, Cameroon. Microbiol Res Int. 2015; 3(4): 56-63. Google Scholar
5. NNIS System. National Nosocomial Infections Surveillance (NNIS) System report, data summary from January 1990-May 1999, issued June 1999. Am J Infect Control. 1999; 27(6): 520- 532. PubMed
6. Julander I. Unfavourable prognostic factors in Staphylococcus aureus septicemia and endocarditis. Scand J Infect Dis. 1985; 17(2): 179-187. PubMed | Google Scholar
7. Acar JF. Consequences of bacterial resistance to antibiotics in medical practice. Clin Infect Dis. 1997; 24(1): 17- 18. PubMed | Google Scholar
8. Brumfitt W, Hamilton-Miller J. Methicillin-Resistant Staphylococcus aureus. N Engl J Med. 1989; 320(18): 1188- 1196. PubMed | Google Scholar
9. Dilnessa T, Bitew A. Prevalence and antimicrobial susceptibility pattern of methicillin resistant Staphylococcus aureus isolated from clinical samples at Yekatit 12 Hospital Medical College, Addis Ababa, Ethiopia. BMC infectious diseases. 2016 Dec;16:1
10. Francois P, Pittet D, Bento M, Pepey B, Vaudaux P, Lew D, et al. Rapid detection of methicillin-resistant Staphylococcus aureus directly from sterile or none sterile clinical samples by a new molecular assay. J Clin Microbiol. 2003;41(1):254–60.
11. Kaur H, Purwar S, Saini A, Kaur H, Karadesai SG, Kholkute SD, et al. Status of methicillin-resistant Staphylococcus aureus infections and evaluation of PVL producing strains in Belgaum, South India. JKIMSU. 2012;1(2):43–51.
12. Alborzi A, Pourabbas BA, Salehi H, Pourabbas BH, Oboodi B, Panjehshahin MR. Prevalence and patterns of antibiotic sensitivity of MRSA in Shiraz-Iran. Irn J Med Sci. 2000;25(1&2):1–8.
13. Bukhari MH, Iqbal A, Khatoon N, Iqbal N, Naeem S, Qureshi GR. A laboratory study of susceptibility of methicillin-resistant Staphylococcus aureus. Pak J Med Sci. 2004;20:229–33.
14. Krishna BV, Patil AB, Chandrasekhar MR. Community-acquired MRSA Infection in a South Indian City. Southeastern Asian J Trop Med Pub Health. 2004;35:371–4
15. Chaari M, Mahjoubi M, Mezghani S, Znazen A, Zribi N, Turki H et al. Aspects bactériologiques des infections cutanées en milieu hospitalier. Rev Tun Infectiol. 2007;1(1): 1-110.
16. Kengne M, Fotie HB, Nwobegahay JM, Achiangia PN, Tamoufe U, Ter Goon D, Mboua JB, Tchanana G, Fualefac A, Echelibe H, Djonkam RK. Antibiotic sensitivity profile of Staphylococcus aureus isolated from HIV/AIDS patients presenting with pyoderma, at the Yaounde Central Hospital, Cameroon. Pan African Medical Journal. 2020 Oct 27;37(1).
17. Sakr A, Brégeon F, Mège JL, Rolain JM, Blin O. Staphylococcus aureus Nasal Colonization: An Update on Mechanisms, Epidemiology, Risk Factors, and Subsequent Infections. Front Microbiol

2018; 9: 2419.
18. David MZ, Daum RS. Treatment of Staphylococcus aureus Infections. Curr Top Microbiol Immunol 2017; 409: 325–383.
19. Ozturk I, Yurtman AN, Erac B, Gul-Yurtsever S, Ermertcan S, Hosgor-Limoncu M. In vitro effect of moxifl oxacin and rifampicin on biofi lm formation by clinical MRSA isolates. Bratisl Med J 2014; 115 (8): 483–486.
20. Nigo M, Diaz L, Carvajal LP, Tran TT, Rios R, Panesso D, Garavito JD, Miller WR, Wanger A, Weinstock G, Munita JM, Arias CA, Chambers HF. Ceftaroline-Resistant, Daptomycin-Tolerant, and Heterogeneous Vancomycin-Intermediate Methicillin-Resistant Staphylococcus aureus Causing Infective Endocarditis. Antimicrob Agents Chemother 2017; 61 (3): e01235–1216.
21. Vecchio D, Dai T, Huang L, Fantetti L, Roncucci G, Hamblin MR (2013) Antimicrobial photodynamic therapy with RLP068 kills methicillinresistant Staphylococcus aureus and improves wound healing in a mouse model of infected skin abrasion PDT with RLP068/Cl in infected mouse skin abrasion. J Biophotonics 2013; 6 (9): 733–742
22. Malik S, Sidhu PK, Rana JS, Nehra K. Managing urinary tract infections through phage therapy: a novel approach. Folia Microbiol 2020; 65 (2): 217–231.
23. Trajčíková E, Kurin E, Slobodníková L, Straka M, Lichváriková A, Dokupilová S, Čičová I, Nagy M, Mučaji P, Bittner Fialová S (2020) Antimicrobial and Antioxidant Properties of Four Lycopus Taxa and an Interaction Study of Their Major Compounds. Molecules 2020; 25 (6): 1422
24. Straka M, Hubenakova Z, Lichvarikova A, Janosikova L, Markuskova B, Minich A, Liptakova A, Drahovska H, Slobodnikova L. Susceptibility of Staphylococcus aureus strains to commercial therapeutic phage preparations. Bratislava Medical Journal/Bratislavske Lekarske Listy. 2022 Oct 1;123(10).
25. Kim HB, et al. Vitro activities of 28 antimicrobial agents against Staphylococcus aureus isolates from tertiary-care hospitals in Korea: a nationwide survey. Antimicrob Agents Chemother. 2004;48:1124–7.
26. Hussain FM, Boyle-Vavra S, Bethel CD, Daum RS. Current trends in community- acquired methicillin-resistant Staphylococcus aureus at a tertiary care pediatric facility. Pediatr Infect Dis J. 2000;19:1163–6.
27. Groom AV, et al. Et al. Community-acquired methicillin-resistant Staphylococcus aureus in a rural American Indian community. JAMA. 2001; 286:1201–5.
28. Chambers HF. The changing epidemiology of Staphylococcus aureus? Emerg Infect Dis. 2001 Mar-Apr;7(2):178–82
29. Naimi HM, Rasekh H, Noori AZ, Bahaduri MA. Determination of antimicrobial susceptibility patterns in Staphylococcus aureus strains recovered from patients at two main health facilities in Kabul, Afghanistan. BMC infectious diseases. 2017 Dec; 17:1-7.

30. Meyers HF, Ernest J, Allan G. A review of Medical Pharmacology.1970; 49:467-474 and 50:475-581. Lange Medical Publishers (1970).
31. Cookson BD, Phillips I. Epidemic MRSA. J Antimicrob chemother.1998;21: supplement c 57- 65.
32. Kitara LD, Anywar AD, Acullu D, Odongo-Aginya E, Aloyo J, Fendu M. Antibiotic susceptibility of Staphylococcus aureus in suppurative lesions in Lacor Hospital, Uganda. African health sciences. 2011;11:34-9.
33. R Ventola, C. L. (2015). The antibiotic resistance crisis: part 1: causes and threats. Pharmacy and Therapeutics, 40(4), 277–283.
34. Chambers, H. F., & DeLeo, F. R. (2009). Waves of resistance: Staphylococcus aureus in the antibiotic era. Nature Reviews Microbiology, 7(9), 629–641.
35. World Health Organization. (2014). Antimicrobial resistance: global report on surveillance.eferences:
36. Kot B, Wierzchowska K, Piechota M, Grużewska A. Antimicrobial resistance patterns in methicillin-resistant Staphylococcus aureus from patients hospitalized during 2015– 2017 in hospitals in Poland. Medical Principles and Practice. 2020;29(1):61-8.
37. Joshi S, Ray P, Manchanda V, Bajaj J, Chitnis DS, Gautam V, Goswami P, Gupta V, Harish BN, Kagal A, Kapil A. Methicillin-resistant Staphylococcus aureus (MRSA) in India: prevalence & susceptibility pattern. The Indian Journal of medical research. 2013 Feb;137(2):363.
38. Jevons MP. "Celbenin" - resistant Staphylococci. Br Med J. 1961 Jan 14;1(5219):124–5. PMCID: PMC1952888.
39. Selim S, Faried OA, Almuhayawi MS, Saleh FM, Sharaf M, El Nahhas N, Warrad M. Incidence of vancomycin-resistant Staphylococcus aureus strains among patients with urinary tract infections. Antibiotics. 2022 Mar 18;11(3):408.
40. Gitau W, Masika M, Musyoki M, Museve B, Mutwiri T. Antimicrobial susceptibility pattern of Staphylococcus aureus isolates from clinical specimens at Kenyatta National Hospital. BMC research notes. 2018 Dec;11:1-5.
41. Loomba PS, Taneja J, Mishra B. Methicillin and vancomycin resistant S. aureus in hospitalized patients. J. Glob Infect Dis. 2010;2:275–83
42. Essentials of Medical Microbiology by Apurba S Sastry
43. Rungelrath V, DeLeo FR. Staphylococcus aureus, antibiotic resistance, and the interaction with human neutrophils. Antioxidants & redox signaling. 2021 Feb 20;34(6):452-70.
44. Foster TJ. Antibiotic resistance in Staphylococcus aureus. Current status and future prospects. FEMS microbiology reviews. 2017 May 1;41(3):430-49.
45. Biomeriux Vitek 2 GP Test kit pack insert manual
46. Rajaduraipandi, K., Mani, K. R., Panneerselvam, K., Mani, M., & Bhaskar, M. (2006). Antimicrobial susceptibility pattern of methicillin-resistant Staphylococcus aureus (MRSA) strains isolated from skin and soft tissue infections in a tertiary care hospital in Chennai, India. Journal of Clinical and Diagnostic Research: JCDR, 10(11), DC09– DC12.
47. Mohanty S, Behera B, Sahu S, Praharaj AK. Recent pattern of antibiotic resistance in Staphylococcus aureus clinical isolates in Eastern India and the emergence of reduced susceptibility to vancomycin. Journal of Laboratory Physicians. 2019 Oct;11(04):340-5..
48. Nagasundaram N, Sistla S. Existence of multiple SCC mec elements in clinical isolates of methicillin-resistant Staphylococcus aureus. Journal of Medical Microbiology. 2019 May;68(5):720-7.

49. Singh A, Prasad KN, Rahman M, Rai RP, Singh SK, Srivastava JK. High frequency of SCCmec type V and agr type I among heterogeneous vancomycin-intermediate Staphylococcus aureus (hVISA) in north India. Journal of global antimicrobial resistance. 2017 Mar 1;8:110-4.
50. Dash P, Rana K, Turuk J, Palo SK, Pati S. Antimicrobial Resistance and Biofilm Formation of Isolates from Febrile Cases: Findings from a Rural Cohort of Odisha, India. Polish Journal of Microbiology. 2023 Jun 14;72(2):209-14.
51. Dash P, Rana K, Turuk J, Palo SK, Pati S. Antimicrobial Resistance and Biofilm Formation of Isolates from Febrile Cases: Findings from a Rural Cohort of Odisha, India. Polish Journal of Microbiology. 2023 Jun 14;72(2):209-14.
52. Lalitha P, Manoharan G, Karpagam R, Prajna NV, Srinivasan M, Mascarenhas J, Das M, Porco TC, Lietman TM, Cevallos V, Keenan JD. Trends in antibiotic resistance in bacterial keratitis isolates from South India. British Journal of Ophthalmology. 2017 Feb 1;101(2):108-13.
53. Bouchiat C, El-Zeenni N, Chakrakodi B, Nagaraj S, Arakere G, Etienne J. Epidemiology of Staphylococcus aureus in Bangalore, India: emergence of the ST217 clone and high rate of resistance to erythromycin and ciprofloxacin in the community. New microbes and new infections. 2015 Sep 1;7:15-20.
54. Dash P, Rana K, Turuk J, Palo SK, Pati S. Antimicrobial Resistance and Biofilm Formation of Isolates from Febrile Cases: Findings from a Rural Cohort of Odisha, India. Polish Journal of Microbiology. 2023 Jun 14;72(2):209-14.
55. Anupurba S, Sen MR, Nath G, Sharma BM, Gulati AK, Mohapatra TM. Prevalence of methicillin resistant Staphylococcus aureus in a tertiary referral hospital in eastern Uttar Pradesh. Indian journal of medical microbiology. 2003 Jan 1;21(1):49-51.
56. Mohanty S, Kapil A, Dhawan B, Das BK. Bacteriological and antimicrobial susceptibility profile of soft tissue infections from Northern India. Indian Journal of Medical Sciences. 2004 Jan 1;58(1):10-5.
57. Rajaduraipandi K, Mani KR, Panneerselvam K, Mani M, Bhaskar M, Manikandan P. Prevalence and antimicrobial susceptibility pattern of methicillin resistant Staphylococcus aureus: A multicentre study. Indian journal of medical microbiology. 2006 Jan 1;24(1):34-8.
58. Mulla S, Patel M, Shah L, Vaghela G. Study of antibiotic sensitivity pattern of methicillin-resistant Staphylococcus aureus. Indian J Crit Care Med. 2007 Apr 1;11(2):99-101.
59. Pulimood TB, Lalitha MK, Jesudason MV, Pandian R, Selwyn J, John TJ. The spectrum of antimicrobial resistance among methicillin resistant Staphylococcus aureus (MRSA) in a tertiary care centre in India. The Indian Journal of Medical Research. 1996 Apr 1;103:212-5.