Current Status and Future Prospective of Vancomycin-Resistant Staphylococcus Aureus (VRSA)

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ABSTRACT

S. aureus is a highly virulent gram-positive bacterium that belongs to the Micrococcaceae family. It possesses a cell wall composed of peptidoglycan, which consists of NAM (N-acetylmuramic) and NAG (N-acetylglucosamine) acid subunits. This bacterium also harbors surface proteins that have virulence factors. S. aureus produces toxins that cause endocarditis, pneumonia, osteomyelitis and bacteremia. The significant mortality and morbidity associated with these diseases make S. aureus a major public health concern. Antibiotic-resistant strains pose a significant challenge for physicians in effectively treating staphylococcal infections. According to available statistics, vancomycin-resistant S. aureus (VRSA) has been reported in Asia, America, and Africa, while no reports have been documented in Oceania. The prevalence rates of VRSA were found to be 1.2% among 5043 isolates in Asia, 3.6% among 140 isolates in America, and 2.5% among 493 isolates in Africa. In Europe, the prevalence rate of VRSA was lower at 1.1% among 179 isolates. Healthcare providers must identify the specific strain of bacteria causing the infection to determine the appropriate treatment regimen. Several alternate approaches to antibiotics against multi-drug resistant S. aureus that have been investigated are i.e., nanoparticles, bacteriophages, bacteriocins, ionized water etc. Clinical trials should be conducted to evaluate efficacy and safety margin of these alternate approaches.

Keywords: Vancomycin-resistant S. aureus, Prevalence, Alternate approaches.

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1. INTRODUCTION

Staphylococcus aureus is a highly virulent gram-positive bacterium that belongs to the Micrococcaceae family. It possesses a cell wall composed of peptidoglycan, which consists of NAM (N-acetylmuramic) and NAG (N-acetylglucosamine) acid subunits (Leonard et al. 2008; Sutton et al. 2021). This bacterium also harbors surface proteins that have virulence factors. S. aureus produces toxins that cause endocarditis, pneumonia, osteomyelitis and bacteremia (Mitchell et al. 2005; Murray 2005; Roberts et al. 2005). The significant mortality and morbidity associated with these diseases make S. aureus a major public health concern. One of the challenges in treating S. aureus infections is the bacterium's ability to develop resistance against multiple antibiotics (Ortega et al. 2010). The development of resistance in S. aureus against antibiotics has been observed since 1942 and continues till today. The first methicillin-resistant strain isolates were identified in 1942, and penicillin-resistant strains in 1961 (McKee et al. 1943; Jevons 1961). Antibiotic-resistant strains pose a significant challenge for physicians in effectively treating staphylococcal infections. Healthcare providers must identify the specific strain of bacteria causing the infection to determine the appropriate treatment regimen (Oli et al. 2017). In this chapter, the general characteristics, pathogenicity, mechanism, and current status of resistance in S. aureus are discussed. Alternative therapeutic approaches to combat vancomycin-resistant Staphylococcus infections have also been explored, considering the limited effectiveness of traditional antibiotics against these strains.

2. STRUCTURE OF STAPHYLOCOCCUS AUREUS

2.1. CELL WALL

The cell wall of S. aureus is composed of approximately 50% peptidoglycan, a structural component of the bacterial cell wall. Peptidoglycan consists of polysaccharide subunits i.e., N-acetylglucosamine (NAG) and N-acetylmuramic acid (NAM). These subunits are connected by 1,4-β linkages, forming the backbone of peptidoglycan chains (Kim et al. 2015). Within the peptidoglycan structure, tetrapeptide bonds and a bridge of pentaglycin connected to NAM form cross-linkages. In addition to peptidoglycan, ribitol teichoic acids are significant components of the S. aureus cell wall. These teichoic acids are linked to peptidoglycan, providing additional structural stability. Lipoteichoic acid, another type of teichoic acid, is found in the cytoplasmic membrane of S. aureus. It is attached to the glycolipid terminus end, contributing to the overall architecture of the cell wall (Mistretta et al. 2019). Peptidoglycan in S. aureus also exhibits endotoxin-like activity that can trigger immune responses in the host organism. Upon recognition by the immune system, peptidoglycan can induce the release of cytokines, leading to the activation of macrophages and complement system with platelet aggregation (Kumar et al. 2020).

3. ENZYMES

Staphylococcus species, including S. aureus, produce several enzymes contributing to their pathogenicity. These enzymes, such as hyaluronidase, lipase, esterase, staphylokinase, deoxyribonuclease, phospholipase, and protease, can break down host tissue and facilitate the spread of bacterium to nearby tissues. Furthermore, enzymes are involved in antibiotic resistance employed by these bacteria. For instance, β-lactamase is an enzyme that can deactivate penicillin, rendering it ineffective. One notable enzyme produced by staphylococci is coagulase. Coagulase can convert fibrinogen, a soluble protein, into fibrin, the main component of blood clots. This enzymatic activity allows staphylococci to form protective barriers, shielding them from the host immune response and promoting bacterial survival. Additionally, coagulase acts as a prothrombin activator, initiating the blood clotting cascade (Quinn et al. 2011; Kobayashi et al. 2015).

4. CAPSULE

Microcapsules are produced by many species of staphylococci. Currently, 11 distinct types of microcapsular serotypes have been identified, which are based on polysaccharides. Among these serotypes, types 5 and 8 are particularly associated with human infections. Type 5 microcapsules are commonly isolated from methicillin-resistant S. aureus (MRSA) strains, indicating their prevalence in these antibiotic-resistant bacteria. Microcapsules are protective layers composed of polysaccharides that surround the bacterial cells. They serve as a defense mechanism against the host immune system, shielding the bacteria from phagocytosis and other immune responses. The presence of microcapsules contributes to the virulence of staphylococci by enhancing their ability to establish and persist in host tissues (O'Riordan et al. 2004).

5. TOXINS

Staphylococcus species are known to produce various toxins that can be categorized based on their mechanisms of action. One category is cytotoxins, specifically a 33-kilo Dalton protein called alpha-toxin. These cytotoxins create pores in mammalian cells and induce proinflammatory changes, leading to cell damage (Otto 2014). Another class of toxins produced by Staphylococcus is pyrogenic toxin super-antigens. These toxins bind to class II proteins of the major histocompatibility complex (MHC) and trigger the release of cytokines, resulting in extensive T-cell proliferation. This immune response can cause harmful effects on the body. Enterotoxins are another group of toxins produced by Staphylococcus. They are responsible for food poisoning. The ingestion of contaminated food or exposure to these toxins can lead to symptoms such as vomiting, diarrhoea, and abdominal pain. Another category of toxins is toxic shock syndrome toxins (TSST). They are responsible for excessive lymphokine production leading to tissue damage. Exfoliative toxins can cause skin erythema (redness) and separation. Examples of exfoliative toxins produced by Staphylococcus include epidermolytic toxins A and B, which affect the skin integrity and can result in the detachment of the upper layers of the skin (Ortega et al. 2010; Pinchuk et al. 2010).

6. SURFACE PROTEINS

Surface proteins, also known as cell wall-anchored (CWA) proteins, play a crucial role in the virulence of S. aureus. Among various staphylococcal spp., S. aureus is known to express 24 different CWA proteins. These proteins are located on the bacterial surface and are covalently bonded to the peptidoglycan layer of the cell wall. The presence of these proteins contributes to both the pathogenic and commensal nature of S. aureus (Lacey et al. 2016). The bacterial growth conditions influence the expression of cell wall-anchored proteins. For instance, most of these proteins are expressed when the bacterium is grown under iron-deficient conditions, although some may also be expressed during the exponential or stationary growth phases. CWA proteins can be classified into four groups based on their structural and functional characteristics. The MSCRAMM (microbial surface component recognizing adhesive matrix molecule) is the most significant group. MSCRAMM proteins play a key role in mediating bacterial adhesion to host tissues. 90% of S. aureus contains protein A (42KD) in their cell wall. Protein A binds with the "Fc and Fab" regions of IgG and B-lymphocytes and inhibits direct phagocytosis and opsonization, respectively (Foster et al. 2014; Speziale et al. 2014; Arora et al. 2016; Hinton-Sheley and Phoebe 2019).

7. GENOME

Staphylococcus bacteria have a circular chromosome in their genome, consisting of approximately 2800 base pairs (bp). In addition to the chromosome, they can also possess plasmids, transposons, and

prophages. These genetic elements are involved in the transfer of many genes, including those responsible for antibiotic resistance. The genes associated with antibiotic resistance can be located on the extrachromosomal elements and the chromosomes. The inherent genetic material of bacteria can carry resistance genes and acquire additional genetic elements via horizontal gene transfer. The extrachromosomal elements, such as plasmids, transposons, and prophages, act as vehicles to transfer genes between various species of Gram-positive bacteria and staphylococcal bacteria. This horizontal gene transfer allows for the spread of genetic traits, including antibiotic resistance, among bacterial populations (Kumar et al. 2020).

8. VANCOMYCIN: BACKGROUND AND IMPORTANCE IN ANTIBACTERIAL TREATMENT

In 1957 E.C Kornfield isolated Vancomycin, a tricyclic glycopeptide antibiotic, from a fungus, Streptomyces orientalis, found in the forests of Borneo. Initially known as "compound 05865" vancomycin exhibited activity against anaerobic and gram-positive bacteria. It is a bactericidal agent and inhibits peptidoglycan's polymerization in the cell wall of the bacterium. This mechanism makes vancomycin effective against many pathogens. It is also effective in combating secondary infections after surgery. FDA has approved Vancomycin against many bacteria, including Pseudomembranous colitis Clostridium difficile, Enterococcal, Staphylococcus enterocolitis, Streptococcal, and Staphylococcal spp. (Aqib et al. 2022).

9. VANCOMYCIN MODE OF ACTION

Vancomycin is primarily effective against Gram-positive bacteria, including Clostridia, Corynebacterium, Staphylococci, Pneumococci, Enterococci, Streptococci, and Listeria. It is commonly employed in treating infections caused by methicillin-resistant S. aureus (MRSA) and in patients allergic to semisynthetic penicillin or cephalosporins (Rubinstein et al. 2014). The mechanism of action of vancomycin involves inhibiting the proper synthesis of the cell wall. There is a structure in bacterial cell wall structure that shields them from being swollen and bursting due to the high osmolarity inside the cell. The cell wall, particularly the peptidoglycan component, undergoes expansion during bacterial growth. This expansion relies on incorporating a lipid II precursor molecule into the developing peptidoglycan chain. Enzymes called penicillin-binding proteins (PBPs) facilitate this process. Vancomycin interacts with D-Ala–D-Ala moieties via hydrogen bonds. When vancomycin binds to the lipid II molecule, it induces a change that hinders the formation of the peptidoglycan chain. This inhibition prevents the subsequent transpeptidation process, which is vital for properly constructing the bacterial cell wall (Hu et al. 2016). By disrupting cell wall synthesis, vancomycin effectively inhibits bacterial growth and division, leading to the death or suppression of susceptible bacteria. As a result, the bacterial cell wall cannot be properly constructed, leading to the decomposition of the cell wall and, ultimately, bacterial lysis, as shown in Fig. 1. Vancomycin's complex structure restricts its ability to penetrate the membrane of the Gram-negative bacteria. Consequently, its bactericidal effect against Gram-negative bacteria is limited (Acharya et al. 2022).

10. DEVELOPMENT OF VANCOMYCIN RESISTANCE IN S. AUREUS

Vancomycin became an important therapeutic option for treating serious infections caused by methicillin-resistant S. aureus (MRSA) in the late 1980s. However, around the same time, a new problem emerged in Europe with the identification of VRE (vancomycin-resistant enterococci). In VRE, vancomycin resistance was primarily intervened by transposons, often present on plasmids that

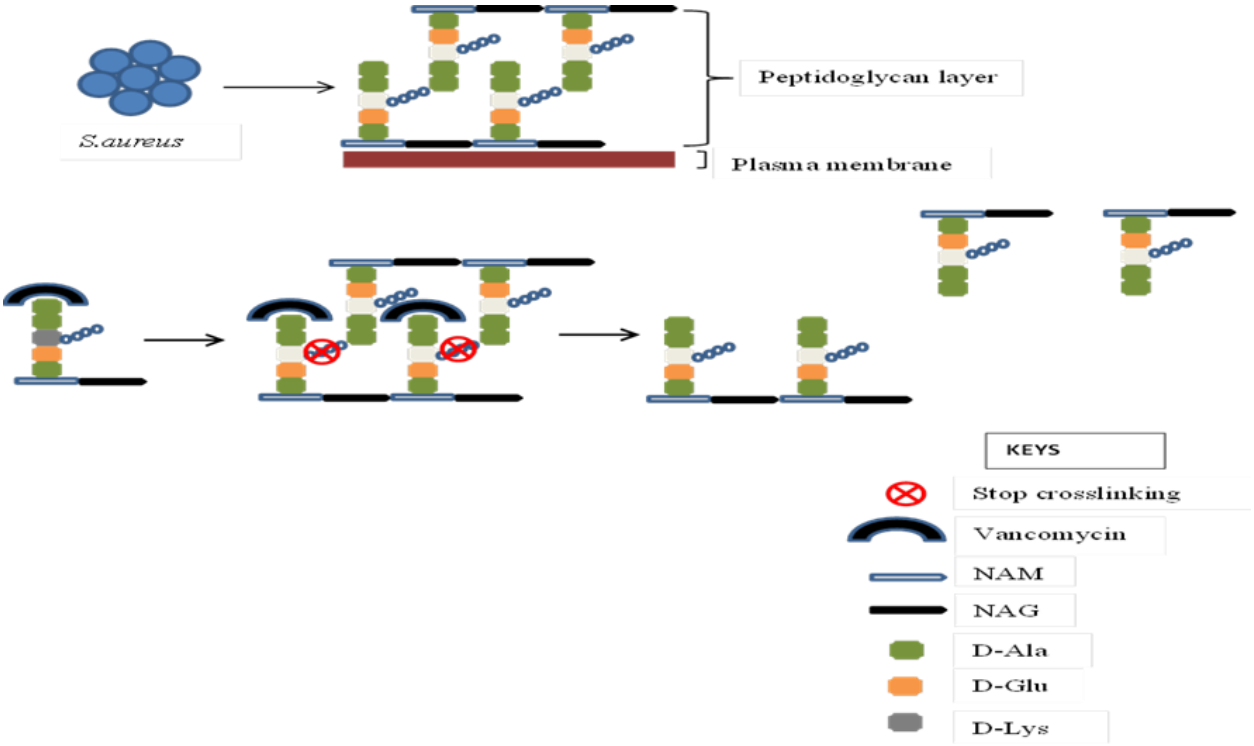

Fig. 1: Mode of action of Vancomycin

enhanced concerns about the potential dissemination of vancomycin resistance to other medically significant microorganisms, particularly S. aureus, which is a major cause of infections. These concerns were validated when the vancomycin resistance determinant was successfully transferred from Enterococcus faecalis to S.aureus in mice co-infected with both bacteria, which confirmed the risk of spreading vancomycin resistance to previously susceptible microorganisms. The first documented case of VRSA occurred in Michigan, USA, in 2002. Subsequently, another VRSA strain was isolated in Pennsylvania, USA, in the same year. Until now, 52 VRSA strains with vancomycin resistance genes have been reported, with 14 in the USA, 11 in Iran, 16 in India, 1 in Brazil, 9 in Pakistan and 1 in Portugal. The emergence of VRSA strains further underscored the urgent need for effective strategies to combat the development of vancomycin resistance and prevent its dissemination (Cong et al. 2020).

11. THE MECHANISM OF VANCOMYCIN RESISTANCE

Bacterial resistance to vancomycin primarily involves van gene clusters, categorized into different types based on DNA sequences. These clusters encode ligase van gene homologs that produce enzymes forming d-alanyl-d-lactate (d-Ala-d-Lac). At least 11 known van gene clusters: VanA, VanB, VanD, VanF, VanI, VanM, VanC, VanE, VanG, VanL, and VanN, play a critical role in vancomycin resistance. Genes like vanA, vanB, vanD, vanF, vanI, and vanM, encoding d-Ala:d-Lac ligases, lead to high-level resistance with MICs exceeding 256 mg/ml. Conversely, genes encoding d-Ala:d-Ser ligases (vanC, vanE, vanG, vanL, and vanN) cause low-level resistance, with MICs ranging from 8 to 16 mg/ml. Enterococcus species are the most common carriers of acquired vancomycin resistance, with the vanA gene cluster specifically linked to vancomycin-resistant S. aureus (VRSA) strains. This cluster contains five crucial proteins i.e., VanS, VanR, VanH, VanA, and VanX, all contributing to vancomycin resistance. The vanA

gene cluster resides within a transposon called Tn1546. VanS and VanR form a two-component system regulating the cluster genes in the presence of vancomycin. VanH, VanA, and VanX modify precursor molecules from D-Ala-D-Ala to the resistant form, D-Ala-D-Lac. Vancomycin's target is the terminal d-Ala-D-Ala moieties of lipid II precursor. However, modification to d-Ala-D-Lac greatly reduces vancomycin's affinity, leading to a nearly 1000-fold decrease in binding affinity and loss of bactericidal effect on strains with modified peptidoglycan precursors (Cong et al. 2020). The brief mechanism of vancomycin resistance is shown in Fig. 2.

12. ZOONOSIS AND HUMANOSIS

The prevalence of MRSA has expanded beyond healthcare settings and is now a concern in the community, particularly in the United States. Community-associated MRSA (CA-MRSA) strains are increasingly replacing the older HA-MRSA (hospital-associated MRSA) strains. MRSA strains in companion animals differ greatly from those in livestock and animals raised for meat production. This distinction is likely because companion animals primarily acquire MRSA from their human owners. In traditional animal husbandry practices, there was less close contact between animals, whereas modern intensive farming methods increase the chances of transmission of MRSA to animals. The emergence of new strains of MRSA, like ST398 in pigs, poses a remarkable zoonotic risk as farm workers may become infected with the new strains. MRSA infections have been reported in various species, including dogs, cats, sheep, chickens, horses, rabbits, seals, and even in one turtle, bat, guinea pig, and chinchilla. Historically, MRSA infections in companion animals were caused by similar strains as in human healthcare settings. When HA-MRSA strains were identified in dogs, it was assumed that transmission had occurred from humans to animals, referred to as "humanosis." (Morgan 2008). Another study reported that VRSA strains isolated from the meat of camel and workers were homologous to each other (Al-Amery et al. 2019).

13. CURRENT STATUS

13.1. VANCOMYCIN RESISTANCE IN S. AUREUS: A SOUTH ASIAN PERSPECTIVE

Following the primary cases of vancomycin-resistant S. aureus (VRSA) in the United States, several other countries have also stated the emergence of vancomycin resistance in clinical isolates of methicillin-resistant S. aureus (MRSA). A graphical picture of the prevalence of VRSA in Pakistan is shown in Fig. 3 (Ghias et al. 2016; Azhar et al. 2017; Hanif et al. 2019; Riaz et al. 2021; Anwaar et al. 2023).
ANSORP (Asian Network for Surveillance of Resistant Pathogens) conducted a study in 2004-2006 and reported that S.aureus with a nosocomial origin is 86.5% prevalent in Sri Lanka (Song et al. 2011). Banerjee et al. (2012) first reported the isolation of the vanA gene in the VISA strain in India. This study enhanced the concerns about the spread of this strain in the hospital staff as patients with VISA strains were asymptomatic. Moses et al. (2020) reported the 6.08% and 46.08% prevalence of VRSA and VISA, respectively, in clinical isolates. Mohanty et al. (2019) conducted a study in Eastern India, isolating 13 hVISA and 18 VISA strains. These remarkable findings show the presence of VISA and VRSA in India and emphasize the urgent control measures to prevent their spread. Chaudhary et al. (2010) conducted a cross-sectional study focusing on dacryocystitis in Nepal and reported an 81.48% prevalence of VRSA strains. Another study was conducted at Allied Sciences and Annapurna Neurological Institute in Nepal and reported the prevalence of VRSA to be 11.11% (Maharjan et al. 2021). However, there is a scarcity of the data regarding research focusing the VISA and VRSA in Nepal. A study conducted in Bangladesh revealed the prevalence of VRSA to be 13.3% in samples of wounds collected from patients in a hospital. They identified the presence of the vanB gene in isolates (Islam et al. 2015).

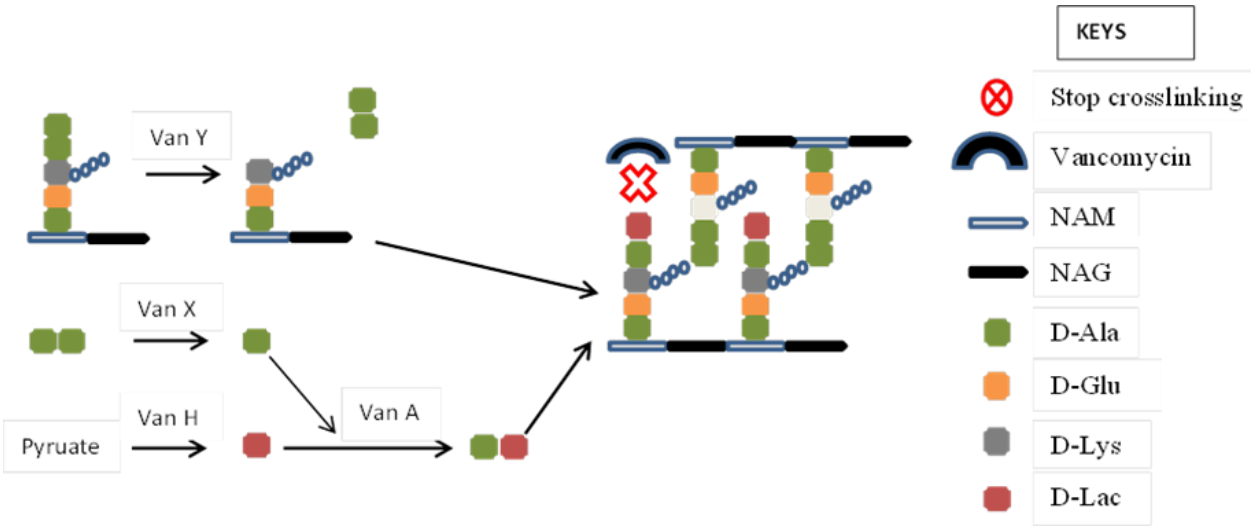

Fig. 2: Mechanism of resistance

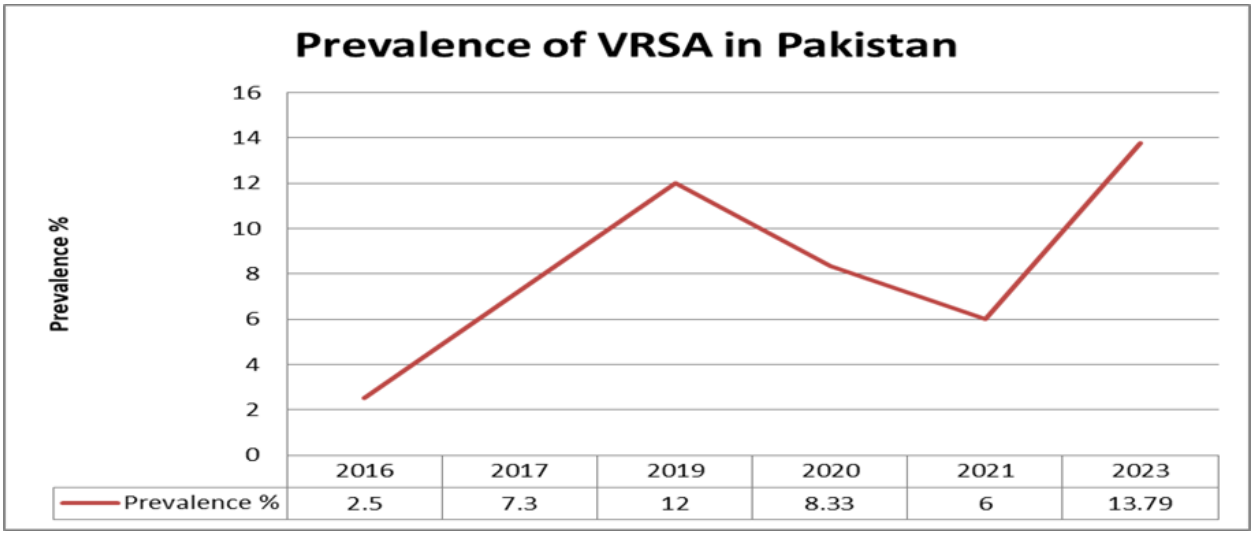

Fig. 3: Prevalence of VRSA in Pakistan

14. GLOBAL PREVALENCE

The prevalence rates of antibiotic-resistant strains of S. aureus vary across different regions. According to available statistics, vancomycin-resistant S. aureus (VRSA) has been reported in Asia, America, and Africa, while no reports have been documented in Oceania. The prevalence rates of VRSA were found to be 1.2% (95% CI 0.7–1.8) among 5043 isolates in Asia, 3.6% (95% CI 0.5–6.6) among 140 isolates in America, and 2.5% (95% CI 0.1–4.8) among 493 isolates in Africa. In Europe, the prevalence rate of VRSA was lower at 1.1% (95% CI 0.0–2.7) among 179 isolates. Regarding vancomycin-intermediate S. aureus (VISA), the prevalence rates were observed to be 2.1% (95% CI 1.6–2.6) among 13,449 isolates in Asia, 1.8% (95% CI 0.8–2.8) among 2198 isolates in Europe, 1.0% (95% CI 0.5–1.4) among 5040 isolates in America, 1.8% (95% CI 0.1–3.4) among 1072 isolates in Africa, and 0.6% (95% CI 0.0–1.3) among 518 isolates in Oceania as shown in Table 1. (Shariati et al. 2020).

Table 1: Continental Prevalence (%) of VRSA and VISA

Continent	Total Isolates	Resistant strains	Country	Prevalence of isolate (%)
			Jordan	4.0
			Bangladesh	4.5
	5043	VRSA	Pakistan	3.3
			Iran	1.3
			India	1.6
			Korea	0.7
			India	4.6
Asia			China	0.5
			Pakistan	5.6
			Iran	3.6
	13,449	VISA	Japan	0.6
			Taiwan	1.9
			Singapore	12.5
			Saudi Arabia	18.0
			Thailand	9.7
	140	VRSA	Brazil	3.6
America	5040	VISA	Brazil	4.1
			USA	0.9
			Nigeria	1.4
	493	VRSA	Algeria	1.4
Africa			Egypt	5.5
			Kenya	4.2
	1072	VISA	Nigeria	15.1
			Algeria	0.6
	179	VRSA	Italy	1.1
			Italy	1.4
Europe			Turkey	2.7
	2198	VISA	Germany	0.7
			France	2.2
			Belgium	2.5
Oceania	518	VISA	Australia	0.7

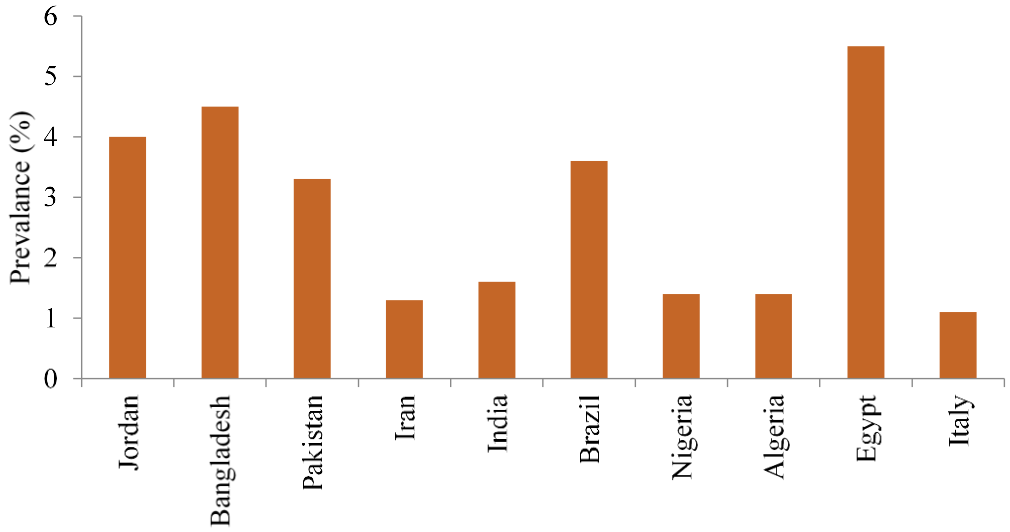

Fig. 4: Prevalence of VRSA in different countries

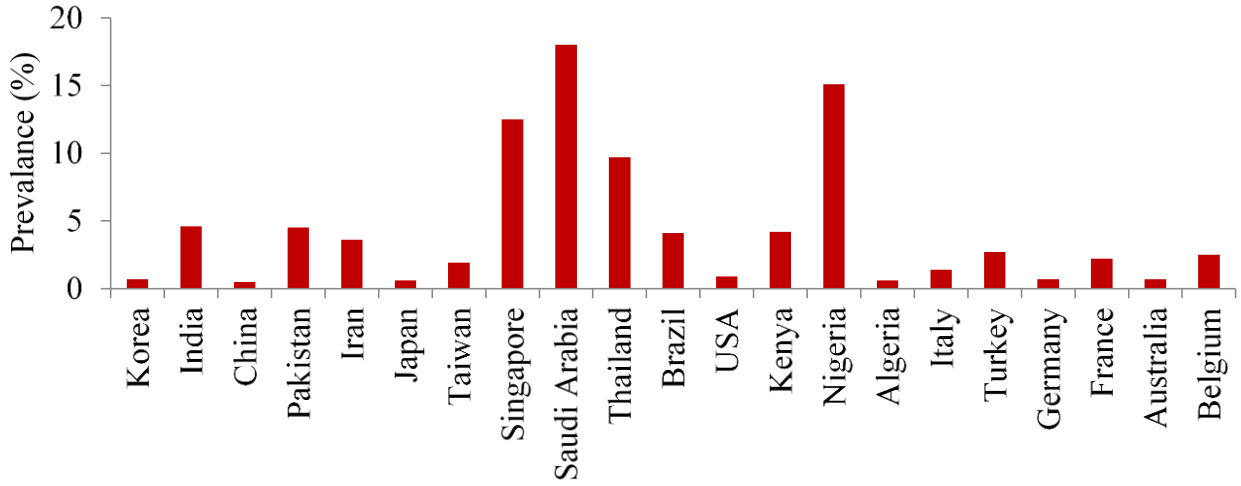

Fig. 5: Prevalence of VISA in different countries

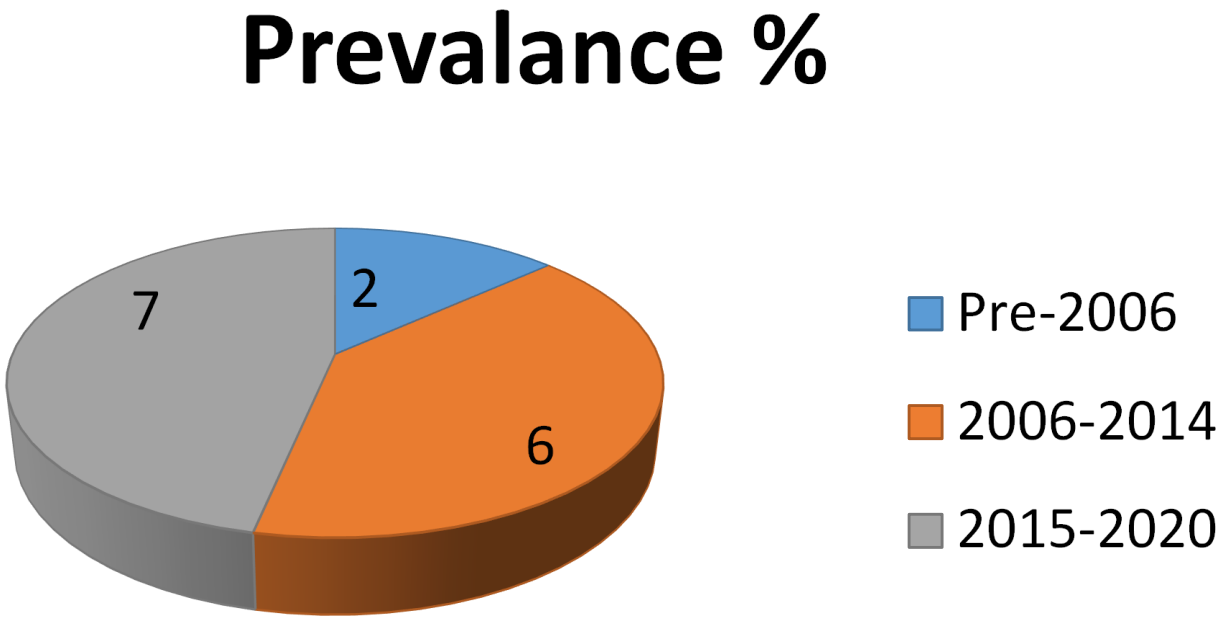

Fig. 6: Prevalence analysis of VRSA in various time periods.

These findings highlight the regional variations in the prevalence rates of VRSA and VISA strains, emphasizing the importance of ongoing surveillance and monitoring of antibiotic-resistant S. aureus strains to inform appropriate prevention and treatment strategies. Fig. 4 and 5 highlights the occurrence of VRSA and VISA across different regions of globe.

15. PREVALENCE ANALYSIS OVER A PERIOD OF TIME

A subgroup analysis was conducted for three periods: pre-2006, 2006-2014 and 2015-2020. The prevalence of VRSA was assessed by examining 11,956 strains of S. aureus.

15.1. PRE-2006 PERIOD

Prior to 2006, the prevalence of VRSA was observed to be 2% (95% CI 0-4) among 466 strains analyzed (Fig. 6). This finding suggests a relatively low occurrence of VRSA during this period.

15.2. 2006-2014 PERIOD

Between 2006 and 2014, the prevalence of VRSA showed a notable increase. Among 6,692 strains examined, VRSA has detected in 6% (95% CI 3-9) cases representing a threefold rise compared to the pre-2006 period, indicating a concerning upward trend (Fig. 6).

15.3. 2015-2020 PERIOD

The most recent period, spanning from 2015 to 2020, has exhibited a further increase in the prevalence of VRSA. Among 5,798 strains analyzed, VRSA was found in 7% (95% CI 4-11) of cases (Fig. 6). Although the rise in prevalence was smaller compared to the previous period, it still signifies a significant progression (Wu et al. 2021).

16. FUTURE PROSPECTIVE

The emergence of antibiotic-resistant S. aureus bacteria, including methicillin-resistant S. aureus (MRSA), has led to exploring alternative strategies to combat these infections. Several approaches that have been investigated are;

Nanoparticles have garnered attention due to their unique physicochemical properties that allow them to inhibit bacterial growth and disrupt biofilm formation. These tiny particles can deliver antimicrobial agents directly to the bacterial cells, making them an attractive option for combating drug-resistant bacteria like S. aureus (Mahal et al. 2023). Bacteriophages, viruses that specifically target bacteria, have shown promise in selectively killing S. aureus strains. Bacteriophage therapy involves using these viruses to infect and destroy bacterial cells, offering a potential alternative to traditional antibiotics (Mohammadian et al. 2022). Bacteriocins, antimicrobial peptides produced by certain bacteria, have exhibited activity against S. aureus. These natural compounds can specifically target and kill the bacteria, making them a potential alternative or adjunct to antibiotics (Xiang et al. 2022). Quorum quenching is a strategy that disrupts bacterial communication systems, which regulate the expression of virulence factors in S. aureus. By interfering with this communication, quorum quenching can impede the ability of the bacteria to cause infections and become resistant (Kaur et al. 2021). Nano needles are microscopic structures that can physically disrupt bacterial membranes, leading to cell death. These tiny needles can deliver antimicrobial agents or physically puncture the bacterial cells, potentially combating antibiotic-resistant S. aureus (Ray et al. 2020). Passive immunization using IgY antibodies or hyperimmune sera has been explored as a potential therapy against S. aureus infections. These antibodies are derived from eggs or animals immunized with S. aureus antigens and can temporarily protect against the bacteria (Tobias et al. 2012). The development of vaccines against S. aureus aims to stimulate an active immune response, providing long-term protection against infection. Various vaccine candidates, including those targeting specific antigens or using novel approaches, are being investigated to prevent S. aureus infections and combat antibiotic resistance (Chand et al. 2023). Certain herbs and natural compounds have demonstrated antimicrobial activity against S. aureus. These natural products, such as essential oils or plant extracts, contain bioactive compounds that can inhibit the growth of drug-

resistant bacteria (Gufe et al. 2023). Phototherapy involves using specific wavelengths of light to kill bacteria. Certain wavelengths, such as blue or ultraviolet light, can have antimicrobial effects and have been investigated as a potential treatment option against S. aureus infections (Woźniak et al. 2022).
Ionized water, produced by ionizing regular tap water, has been explored for its potential antimicrobial properties. Studies have shown that ionized water can exhibit bactericidal effects against S. aureus and may have potential applications in disinfection and wound care (Rahman et al. 2021). The discovery and development of novel antibiotics with activity against VRSA are ongoing. Researchers are exploring alternative treatment options to overcome VRSA resistance mechanisms. Investigating the effectiveness of combination therapy, where multiple antibiotics are used in combination, may help overcome VRSA resistance and improve treatment outcomes (Worthington et al. 2013).
It is important to note that while these alternative approaches hold promise, further research and clinical trials are necessary to fully evaluate their effectiveness, safety, and potential integration into clinical practice. Additionally, a comprehensive approach involving a combination of strategies may be needed to combat antibiotic-resistant S. aureus infections effectively.

17. CONCLUSION

Antibiotic-resistant strains pose a significant challenge for physicians in effectively treating staphylococcal infections. According to available statistics, vancomycin-resistant S. aureus (VRSA) has been reported in Asia, America, and Africa, while no reports have been documented in Oceania. The prevalence rates of VRSA were found to be 1.2% among 5043 isolates in Asia, 3.6% among 140 isolates in America, and 2.5% among 493 isolates in Africa. In Europe, the prevalence rate of VRSA was lower at 1.1% among 179 isolates. Healthcare providers must identify the specific strain of bacteria causing the infection to determine the appropriate treatment regimen. Several alternate approaches to antibiotics against multi-drug resistant S.aureus that have been investigated are i.e., nanoparticles, bacteriophages, bacteriocins, ionized water etc. Clinical trials should be conducted to evaluate efficacy and safety margin of these alternate approaches.

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