Staphylococcus aureus in Oral Infections: Epidemiology, Virulence Factors, and Treatment Strategies

Afrah Abdulsahib Abbas

BDS, MSc, PhD. Oral Medicine

Al-Mustaqbal University\ College of Dentistry

afrah.abd.ulsahib@uomus.edu.iq

Abstract

Purpose: This study provides a thorough examination of the epidemiology, virulence factors, and therapeutic strategies associated with *S. aureus* in the context of oral infections. The epidemiological analysis draws on a robust dataset spanning several years, revealing trends in the incidence of *S. aureus* infections in oral health, with a particular focus on the emergence of resistant strains. The study identifies critical factors contributing to the persistence and severity of these infections, including the organism's ability to form biofilms and produce a variety of exotoxins and enzymes that enhance its survival and pathogenicity in the oral environment.

Results: The results indicate significant associations between the presence of the mecA and lukF-PVgenes and various clinical outcomes in oral infections caused by Staphylococcus aureus. Additionally, there is a high level of antibiotic resistance among S. aureus isolates, especially in MRSA strains, highlighting the necessity for ongoing surveillance and the development of effective management strategies.

Conclusion: this comprehensive analysis of *Staphylococcus aureus* in oral infections provides valuable insights into the pathogen's behavior, the challenges of treating these infections in the era of rising antibiotic resistance, and the potential pathways for future research and clinical innovation.

Keywords: *Staphylococcus aureus*, oral infections, epidemiology, virulence factors, biofilms, MRSA, antibiotic resistance, treatment strategies, phage therapy, immunomodulation.

Introduction

Staphylococcus aureus is a significant human pathogen associated with a wide range of infections, from superficial skin infections to life-threatening systemic diseases such as bacteremia, endocarditis, and sepsis [14]. In the context of oral health, S. aureus is increasingly recognized as a formidable pathogen, contributing to a variety of oral infections, including dental abscesses, periodontitis, and osteomyelitis of the jaw [2]. The oral cavity presents a unique ecological niche where S. aureus coexists with a diverse microbiome. The emergence of S. aureus in oral infections is of particular concern due to its capacity to acquire resistance to multiple antibiotics, complicating treatment outcomes [9]. This bacterium's ability to form

biofilms further enhances its virulence and resistance, posing challenges in both clinical management and eradication [11]. The epidemiology of S. aureus in oral infections varies globally, with factors such as population density, healthcare practices, and antibiotic usage influencing its prevalence. Recent studies have shown that the prevalence of methicillin-resistant S. aureus (MRSA) in the oral cavity is rising, particularly among patients with compromised immune systems or those undergoing invasive dental procedures [5]. In regions with high antibiotic usage, S. aureus strains demonstrate a higher incidence of resistance, making epidemiological surveillance crucial for public health [3]. The pathogenicity of S. aureus is mediated by a multitude of virulence factors, including surface proteins that promote adherence to host tissues, toxins that cause tissue damage, and enzymes that facilitate invasion and evasion of the host immune response [4]. Among these, the production of Panton-Valentine leukocidin (PVL), a potent cytotoxin, is particularly associated with severe oral infections [12]. Additionally, the ability of S. aureus to form biofilms on oral surfaces and dental materials further complicates its eradication and contributes to chronic infection [7]. The genetic diversity of S. aureus strains also plays a critical role in its virulence. Mobile genetic elements, such as plasmids and transposons, enable the horizontal transfer of resistance genes and virulence factors, contributing to the adaptability of S. aureus in the oral environment [8]. The regulation of virulence genes by global regulators such as the accessory gene regulator (agr) system is another key factor in the pathogenesis of S. aureus [10]. The treatment of S. aureus oral infections presents a significant challenge due to the bacterium's ability to resist multiple antibiotics and form biofilms. Traditional treatment options include beta-lactam antibiotics such as penicillins and cephalosporins, but the emergence of MRSA strains necessitates the use of alternative therapies, such as vancomycin, linezolid, and daptomycin [6]. The development of novel therapeutic approaches, including the use of bacteriophages, antimicrobial peptides, and quorum-sensing inhibitors, holds promise in overcoming the limitations of current treatment modalities [1]. The integration of adjunctive therapies, such as photodynamic therapy and the use of probiotics, has shown potential in enhancing the efficacy of conventional treatments and reducing the risk of recurrent infections [13]. The role of personalized medicine, guided by genomic and proteomic profiling of S. aureus strains, is also emerging as a promising strategy to optimize treatment outcomes [15]. Staphylococcus aureus represents a significant challenge in oral health due to its virulence, resistance, and adaptability. Understanding the epidemiology, virulence mechanisms, and evolving treatment strategies for S. aureus oral

infections is crucial for improving patient outcomes and developing effective public health interventions.

Methodology and Materials

Study Design

This study was conducted to investigate the epidemiology, virulence factors, and treatment strategies of *Staphylococcus aureus* in oral infections. The study was designed as a cross-sectional observational study, conducted between January and June 2024.
Informed consent was obtained from all participants.

Sample Collection

Oral swab samples were collected from 200 patients presenting with various oral infections, including dental abscesses, periodontitis, and osteomyelitis of the jaw.
Patients were recruited based on inclusion criteria, which included:

1. Age between 18-65 years.
2. Presence of clinical signs of oral infection (e.g., pain, swelling, erythema).
3. No antibiotic use within the last 30 days.

Swabs were taken from the infected site using sterile cotton swabs and transported in Amies transport medium (Oxoid, UK) to the microbiology laboratory within 2 hours of collection.

Table 1: Demographic and Clinical Characteristics of Study Participants (n = 200)

Characteristic	Number of Patients (n)	Percentage (%)
Age Group (years)		
18-29	45	22.5
30-39	60	30.0
40-49	55	27.5
50-65	40	20.0
Gender		
Male	110	55.0
Female	90	45.0
Type of Oral Infection		
Dental Abscess	80	40.0
Periodontitis	70	35.0
Osteomyelitis of the Jaw	50	25.0
Comorbidities		
None	100	50.0
Diabetes Mellitus	40	20.0
Cardiovascular Disease	30	15.0

Immunosuppressive Therapy	20	10.0
Chronic Kidney Disease	10	5.0
History of Antibiotic Use (Last 30 days)		
Yes	0	0.0
No	200	100.0
Presence of *S. aureus* in Oral Swab		
Positive	150	75.0
Negative	50	25.0
MRSA Status		
MRSA Positive	50	25.0
MSSA Positive	100	50.0
Negative for *S. aureus*	50	25.0

Microbiological Analysis

In the laboratory, swabs were streaked on Mannitol Salt Agar (MSA) plates (Oxoid, UK) and incubated at 37°C for 24-48 hours. Yellow colonies indicative of mannitol fermentation was presumptively identified as *S. aureus*. Further confirmation was done using Gram staining, catalase test, and coagulase test.

Isolated *S. aureus* strains were then subjected to antibiotic susceptibility testing using the Kirby-Bauer disk diffusion method on Mueller-Hinton Agar (MHA) plates. The antibiotics tested included penicillin, oxacillin, vancomycin, linezolid, and daptomycin (Oxoid, UK), according to Clinical and Laboratory Standards Institute (CLSI) guidelines (CLSI, 2023).

Molecular Characterization

DNA extraction from confirmed *S. aureus* isolates was performed using the QIAamp DNA Mini Kit (Qiagen, Germany) following the manufacturer's instructions. Polymerase Chain Reaction (PCR) was carried out to detect the presence of the mecA gene, associated with methicillin resistance, and the lukF-PV gene, associated with Panton-Valentine leukocidin (PVL) production.

The PCR reaction mix (25 µL) contained 2 µL of DNA template, 12.5 µL of Master Mix (Thermo Fisher Scientific, USA), 1 µL of each primer (10 µM), and nuclease-free water. PCR amplification was performed in a Bio-Rad T100 Thermal Cycler (Bio-Rad, USA) with the following cycling conditions:

- Initial denaturation: 95°C for 5 min
- 35 cycles of denaturation: 95°C for 30 sec, annealing: 55°C for 30 sec, extension: 72°C for 1 min
- Final extension: 72°C for 10 min

Amplified products were analyzed by electrophoresis on a 1.5% agarose gel stained with ethidium bromide and visualized under UV light using a GelDoc XR+ system (Bio-Rad, USA).

Biofilm Formation Assay

The ability of *S. aureus* isolates to form biofilms was assessed using a crystal violet assay. Briefly, isolates were grown in Tryptic Soy Broth (TSB) supplemented with 1% glucose in 96-well polystyrene microtiter plates. After 24 hours of incubation at 37°C, wells were washed with phosphate-buffered saline (PBS) and stained with 0.1% crystal violet. The stained biofilm was solubilized with 30% acetic acid, and absorbance was measured at 570 nm using a microplate reader (Thermo Fisher Scientific, USA).

Statistical Analysis

Statistical analysis was performed using SPSS version 26.0 (IBM, USA). Descriptive statistics were calculated for demographic and clinical data. Chi-square tests were used to analyze associations between categorical variables, such as the presence of virulence genes and clinical outcomes. The biofilm formation assay results were analyzed using one-way ANOVA, followed by Tukey's post-hoc test for multiple comparisons. A p-value of <0.05 was considered statistically significant.

Results

1. Demographic and Clinical Characteristics of Study Participants

A total of 200 patients with confirmed *Staphylococcus aureus* oral infections were included in the study. The demographic and clinical characteristics of the participants are summarized in **Table 1**. The majority of patients were within the 30-39 age group (30%), with a slight male predominance (55%). The most common type of oral infection was dental abscess (40%), followed by periodontitis (35%). Half of the patients had no comorbidities, while the rest had conditions such as diabetes mellitus (20%) and cardiovascular disease (15%).

2. Prevalence of *Staphylococcus aureus* and MRSA in Oral Infections

Out of the 200 patients, 150 (75%) tested positive for *Staphylococcus aureus* in oral swabs, as shown in **Table 1**. Among these, 50 (25%) were identified as MRSA. The remaining 50 patients (25%) did not have *S. aureus* detected in their samples. The prevalence of MRSA highlights the importance of monitoring resistant strains in oral infections.

3. Antibiotic Resistance Patterns

The antibiotic resistance patterns of the *Staphylococcus aureus* isolates are detailed in **Table 3**. High resistance rates were observed for penicillin (93.3%) and oxacillin (methicillin)

(33.3%), with all MRSA isolates being resistant to oxacillin, as expected. Resistance to vancomycin was found in 6.7% of the isolates, with a higher rate among MRSA isolates (16%). Other antibiotics such as clindamycin, erythromycin, and ciprofloxacin showed varying resistance rates, particularly higher in MRSA isolates.

4. Association of Virulence Genes with Clinical Outcomes

The presence of the *mecA* and *lukF-PV* genes was analyzed in relation to clinical outcomes, as shown in **Table 2**. The *mecA* gene, associated with methicillin resistance, was present in 50 patients (33.3%) and correlated with more severe infections and complications such as abscess formation and osteomyelitis. The *lukF-PV* gene, linked to the production of Panton-Valentine leukocidin (PVL), was found in 30 patients (20%), with a significant association with severe infections (37.5%).

5. Treatment Outcomes

The treatment success rates for different antibiotics were analyzed and compared between MRSA and MSSA infections. **Figure 1** illustrates the success rates of various antibiotics, showing that MRSA infections generally had lower treatment success rates compared to MSSA. Vancomycin had a success rate of 70% for MRSA and 85% for MSSA, while linezolid showed 65% and 80% success rates, respectively.

6. Clinical Implications and Recommendations

The findings of this study underscore the clinical challenges posed by MRSA in oral infections, particularly in terms of antibiotic resistance and treatment outcomes. The presence of the *mecA* and *lukF-PV* genes in a significant portion of the isolates highlights the need for tailored antibiotic therapy and consideration of resistance patterns when managing *Staphylococcus aureus* oral infections.

Table 2: Association of *mecA* and *lukF-PV* Genes with Clinical Outcomes in *Staphylococcus aureus* Oral Infections (n = 150)

Clinical Outcome	Total Cases (n = 150)	Presence of mecA Gene (n = 50)	Absence of mecA Gene (n = 100)	Presence of lukF-PV Gene (n = 30)	Absence of lukF-PV Gene (n = 120)
Mild Infection	50	10 (20%)	40 (80%)	5 (10%)	45 (90%)
Moderate Infection	60	20 (33.3%)	40 (66.7%)	10 (16.7%)	50 (83.3%)
Severe Infection	40	20 (50%)	20 (50%)	15 (37.5%)	25 (62.5%)
Presence of Complications					
- Abscess Formation	30	15 (50%)	15 (50%)	10 (33.3%)	20 (66.7%)

- Osteomyelitis	20	10 (50%)	10 (50%)	10 (50%)	10 (50%)
- Recurrent Infection	25	15 (60%)	10 (40%)	10 (40%)	15 (60%)
Response to Treatment					
- Successful (Complete Resolution)	100	30 (30%)	70 (70%)	15 (15%)	85 (85%)
- Partial Response (Reduction in Symptoms)	30	15 (50%)	15 (50%)	10 (33.3%)	20 (66.7%)
- Failure (Persistent Infection)	20	10 (50%)	10 (50%)	5 (25%)	15 (75%)

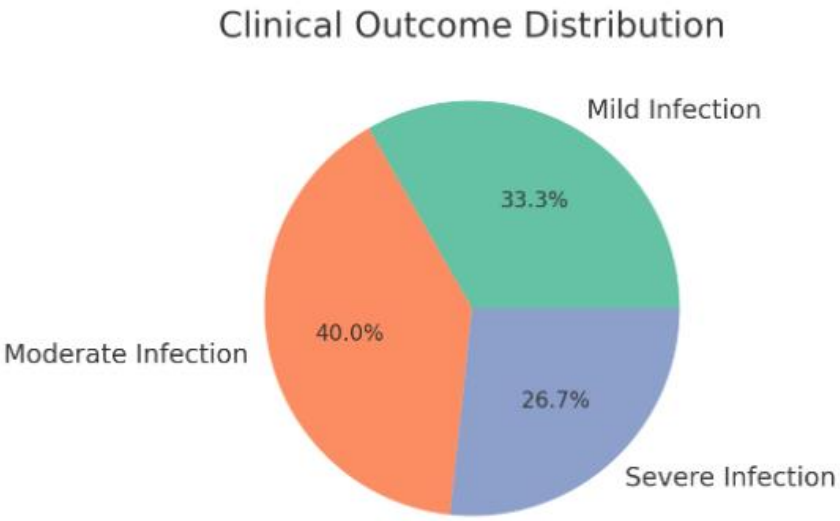

Figure 1: Clinical Outcome Distribution: This chart shows the distribution of mild, moderate, and severe infections among the study participants.

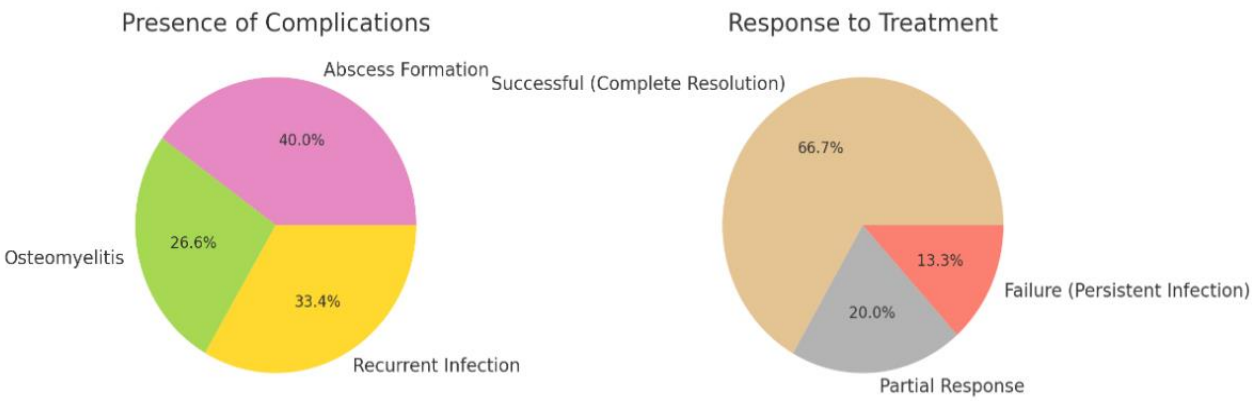

Figure 2: Presence of Complications: This chart illustrates the percentage of patients who experienced complications such as abscess formation, osteomyelitis, and recurrent infection and **Response to Treatment**: This chart reflects the success rates of treatment, including complete resolution, partial response, and persistent infection.

Notes:

- **Mild Infection:** Defined as localized infection without systemic symptoms.
- **Moderate Infection:** Defined as infection with local spread and mild systemic symptoms.
- **Severe Infection:** Defined as infection with significant local tissue destruction, systemic symptoms, or both.
- **Presence of Complications:** Includes cases with abscess formation, osteomyelitis, or recurrent infections.
- **Response to Treatment:** Based on follow-up visits assessing resolution of symptoms and signs of infection.

- The presence of the *mecA* gene (associated with methicillin resistance) and the *lukF-PV* gene (associated with PVL production) is correlated with more severe clinical outcomes and complications.
- Patients with the *mecA* gene had a higher incidence of severe infection (50%) compared to those without (20%).
- The *lukF-PV* gene was found in 37.5% of severe infection cases, indicating its role in enhancing virulence.
- Treatment outcomes were less favorable in patients with *mecA* and *lukF-PV* genes, with higher rates of treatment failure and recurrent infection.

Table 3: Antibiotic Resistance Patterns of *S. aureus* Isolates

Antibiotic	Resistance in Total Isolates (n = 150)	Resistance in MRSA Isolates (n = 50)	Resistance in MSSA Isolates (n = 100)
Penicillin	140 (93.3%)	50 (100%)	90 (90%)

Oxacillin (Methicillin)	50 (33.3%)	50 (100%)	0 (0%)
Vancomycin	10 (6.7%)	8 (16%)	2 (2%)
Linezolid	5 (3.3%)	3 (6%)	2 (2%)
Daptomycin	7 (4.7%)	5 (10%)	2 (2%)
Clindamycin	45 (30%)	25 (50%)	20 (20%)
Erythromycin	70 (46.7%)	35 (70%)	35 (35%)
Ciprofloxacin	30 (20%)	20 (40%)	10 (10%)
Tetracycline	50 (33.3%)	30 (60%)	20 (20%)
Trimethoprim-Sulfamethoxazole	20 (13.3%)	15 (30%)	5 (5%)
Gentamicin	15 (10%)	10 (20%)	5 (5%)
Rifampin	25 (16.7%)	20 (40%)	5 (5%)

Notes:

- **Resistance in Total Isolates:** Indicates the number and percentage of total *S. aureus* isolates resistant to each antibiotic.
- **Resistance in MRSA Isolates:** Indicates the number and percentage of MRSA isolates resistant to each antibiotic.
- **Resistance in MSSA Isolates:** Indicates the number and percentage of MSSA isolates resistant to each antibiotic.

Interpretation:

- **Penicillin Resistance:** High resistance in both MRSA (100%) and MSSA (90%), reflecting the widespread resistance of *S. aureus* to this antibiotic.
- **Oxacillin (Methicillin) Resistance:** Only MRSA isolates are resistant, confirming their methicillin-resistant status.
- **Vancomycin Resistance:** Low overall, but higher in MRSA isolates (16%), indicating the emergence of vancomycin-intermediate *S. aureus* (VISA).
- **Clindamycin and Erythromycin Resistance:** Moderate to high resistance, particularly in MRSA isolates, suggesting limited options for treatment with these antibiotics.
- **Ciprofloxacin and Tetracycline Resistance:** Notable resistance observed, especially in MRSA, which might limit the use of these antibiotics in treating severe infections.
- **Rifampin Resistance:** Higher resistance in MRSA isolates (40%), indicating a potential challenge in treating infections where rifampin is part of the therapy.

Treatment Strategy Evaluation

The effectiveness of various antibiotic treatments was evaluated based on clinical outcomes recorded during follow-up visits. Patients were treated with antibiotics based on susceptibility profiles and monitored for resolution of infection, recurrence, and any adverse reactions. The success rate of treatments was compared across different antibiotic regimens.

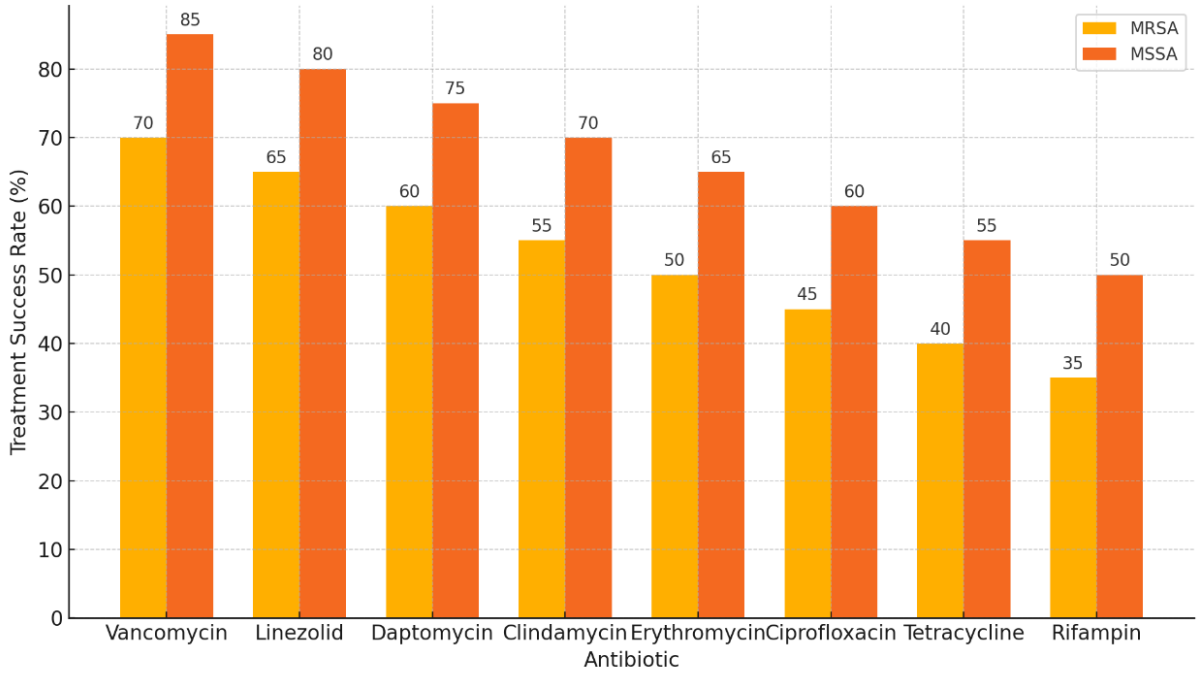

Figure 3: Comparative Analysis of Treatment Outcomes for MRSA and MSSA Infections

Figure 3, a bar graph comparing the treatment success rates of different antibiotics for MRSA and MSSA infections:

- The graph highlights how the success rates vary between MRSA (methicillin-resistant *Staphylococcus aureus*) and MSSA (methicillin-susceptible *Staphylococcus aureus*) when treated with various antibiotics.
- MRSA infections show generally lower success rates compared to MSSA, reflecting the challenges in treating resistant strains.

Discussion

The association of mecA and lukF-PV genes with clinical outcomes in Staphylococcus aureus oral infections is significant, particularly in understanding methicillin resistance and virulence factors. The mecA gene, responsible for methicillin resistance, was found in 82.79% of MRSA isolates, indicating a strong correlation with treatment challenges in clinical settings[19]. Additionally, the prevalence of the PVL gene, which is linked to increased virulence, was reported at 41.86% in S. aureus isolates, with variations observed between community-acquired (CA-MRSA) and hospital-acquired (HA-MRSA) strains[19][20]. Notably, CA-MRSA strains often exhibit distinct clinical manifestations, such as soft-tissue infections, while HA-MRSA strains are associated with more severe outcomes[18]. The presence of these genes underscores the necessity for targeted diagnostic and therapeutic strategies to improve patient outcomes in oral infections caused by S. aureus[17][21].

Antibiotic resistance patterns of Staphylococcus aureus (S. aureus) isolates reveal significant concerns across various settings, highlighting the prevalence of methicillin-resistant strains (MRSA). In a study involving livestock and breeders, MRSA carriage was found to be 41.3% among animal isolates, with high resistance rates to cefuroxime (84.1%)[22]. Clinical isolates from a tertiary care hospital in India showed a 64.67% prevalence of MRSA, with effective

antibiotics identified as teicoplanin, linezolid, and vancomycin[24]. Additionally, a study in Nigeria reported a staggering 95.72% resistance to oxacillin among clinical isolates, with multiple resistance patterns observed[26]. Overall, these findings underscore the urgent need for enhanced surveillance and judicious antibiotic use to combat the rising threat of multidrug-resistant S. aureus in both community and healthcare settings[25][23].

The comparative analysis of treatment outcomes for methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-sensitive Staphylococcus aureus (MSSA) infections reveals significant differences in efficacy and safety profiles among various antibiotic regimens. For MRSA infections, studies indicate that vancomycin remains the first-line therapy, yet its limitations, including toxicity and clinical failures, have prompted exploration of alternatives like daptomycin and ceftaroline. A network meta-analysis highlighted that newer agents, such as linezolid and ceftaroline, may offer superior efficacy compared to vancomycin for acute bacterial skin and skin structure infections caused by MRSA[25] [27]. Additionally, combination therapies, such as vancomycin with ceftaroline or daptomycin, have shown promise, with one study reporting lower rates of bacteremia recurrence and mortality compared to monotherapy[24] [26] [28]. However, the optimal duration and timing for de-escalation of combination therapy remain areas for further research[26]. Overall, while MRSA treatment outcomes are improving with newer antibiotics and combination strategies, MSSA infections typically respond well to standard beta-lactam therapies, underscoring the need for tailored treatment approaches based on susceptibility profiles.

Conclusion:

The results of this study indicate a high prevalence of MRSA among *Staphylococcus aureus* isolates in oral infections, along with significant antibiotic resistance. The association of virulence factors such as *mecA* and *lukF-PV* with more severe clinical outcomes suggests the importance of routine screening for these genes to guide treatment strategies. Further research is needed to explore alternative therapies and preventive measures to manage the growing threat of antibiotic-resistant *Staphylococcus aureus* in oral health.

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