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EFFICACY OF PROPHYLACTIC ANTIBIOTICS IN PREVENTING SURGICAL SITE INFECTIONS IN ORAL AND MAXILLOFACIAL SURGERY A RETROSPECTIVE STUDY

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ABSTRACT

Introduction: Surgical site infections (SSIs) are a persistent challenge in oral and maxillofacial surgery (OMFS), contributing significantly to patient morbidity, extended hospital stays, and increased healthcare costs. The unique anatomy of the surgical field, combined with the high microbial load of the oral cavity, predisposes patients to infections. While prophylactic antibiotics are commonly used to reduce SSI risk, their efficacy and optimal usage in OMFS remain uncertain. **Objectives:** This study evaluates the effectiveness of prophylactic antibiotics in reducing surgical site infections (SSIs) in oral and maxillofacial surgery (OMFS), comparing SSI rates between patients with and without antibiotic use. Methodology: This retrospective study was conducted across multiple dental and maxillofacial surgical centers in Punjab, Pakistan, from June 2023 to August 2024. A total of 177 patients undergoing OMFS procedures were included, divided into Group A (n=123; received prophylactic antibiotics) and Group B (n=54; no antibiotics). Patient demographics, surgical details, antibiotic regimens, and clinical outcomes were extracted from surgical registries. The primary outcome was SSI incidence, defined per clinical guidelines. Secondary outcomes included risk factor analysis and the efficacy of specific antibiotic protocols. Data analysis employed chisquare tests, t-tests, and multivariate logistic regression to identify predictors of SSIs and compare group differences. Results and Findings: The overall SSI incidence was 9.6%, with significantly lower rates in Group A (5.7%) compared to Group B (18.5%; p=0.004). Key patient-related risk factors included diabetes (OR: 2.8; p=0.007), smoking (OR: 2.4; p=0.021), and immunosuppressive conditions (OR: 4.1; p<0.001). Procedural variables such as prolonged surgery (>3 hours; OR: 3.6; p=0.001) and complex reconstructive surgeries were strongly associated with higher SSI rates. Antibiotic regimens combining amoxicillin-clavulanate and metronidazole demonstrated the lowest SSI rate (2.6%). Preoperative antibiotic administration within one hour before surgery yielded the most favorable outcomes (p < 0.001). Microbial analysis revealed Staphylococcus aureus (47.1%) and Streptococcus species (23.5%) as predominant pathogens, with concerning multidrug resistance patterns in 20% of isolates. Conclusion: Prophylactic antibiotics significantly reduce SSIs in OMFS, with optimal results achieved through preoperative

administration tailored to anticipated pathogens. The findings highlight the need for meticulous surgical techniques, patient-specific risk management, and antibiotic stewardship to minimize infection rates and resistance. Despite its retrospective design and single-region focus, this study provides robust evidence to guide clinical practice and inform the development of standardized infection control protocols. Future research should explore prospective studies to refine antibiotic regimens and evaluate long-term impacts on resistance patterns and patient outcomes.

Keywords: Prophylactic antibiotics, surgical site infections (SSIs), oral and maxillofacial surgery (OMFS), perioperative care, antibiotic regimens

INTRODUCTION

Surgical site infections (SSIs) remain one of the most significant complications in oral and maxillofacial surgery (OMFS), imposing a substantial burden on healthcare systems and negatively impacting patient outcomes. Despite advancements in surgical techniques, aseptic protocols, and perioperative care, the incidence of SSIs continues to challenge clinicians worldwide [1]. The use of prophylactic antibiotics has emerged as a cornerstone in mitigating the risk of SSIs; however, the efficacy of such interventions, particularly in the context of OMFS, warrants comprehensive investigation [2]. This retrospective study aims to evaluate the efficacy of prophylactic antibiotics in preventing SSIs in oral and maxillofacial surgical procedures. SSIs are infections that occur within 30 days postoperatively or within one year in cases involving implants, at or near the surgical incision site [3]. These infections are broadly categorized into superficial incisional, deep incisional, and organ/space SSIs based on the anatomical location of the infection [4]. The pathophysiology of SSIs involves the interplay of microbial contamination, host immune response, and the local surgical environment. Microbial contamination can arise from endogenous sources such as the patient's skin flora or exogenous sources, including surgical instruments and operating room air [5]. The inflammatory response triggered by microbial contamination may compromise wound healing, leading to complications such as abscess formation, tissue necrosis, and systemic sepsis [6]. Factors influencing the establishment of SSIs include the virulence of the microbial agent, the inoculum size, and the host's immune competency. Understanding these dynamics is essential for developing targeted prevention strategies. Globally, the incidence of SSIs varies widely, with reported rates ranging from 2% to 30% depending on the surgical specialty, patient demographics, and healthcare setting [7]. In OMFS, the rates are comparatively higher due to the inherent complexities of operating in a field with high microbial loads and variable blood supply. A multicenter study by Anderson et al. reported that SSIs accounted for approximately 20% of all healthcare-associated infections in surgical patients, underscoring their significant impact on morbidity and healthcare costs [8].

OMFS is uniquely predisposed to SSIs due to the inherent complexity of the surgical field, which includes areas with high microbial loads such as the oral cavity and sinuses. Common risk factors include: Comorbidities such as diabetes mellitus, smoking, obesity, and malnutrition are well-documented contributors to impaired wound healing and increased susceptibility to infections [9]. Immunosuppressed states, whether due to underlying disease or immunosuppressive therapy, also elevate the risk of SSIs. Prolonged operative times and extensive tissue dissection increase the exposure of tissues to microbial contamination [10]. Use of implants or grafts introduces foreign material that may serve as a nidus for infection. The oral cavity harbors a diverse microbiota, including both aerobic and anaerobic organisms such as Streptococcus species, Staphylococcus aureus, and Fusobacterium [11]. Antibiotic resistance among these pathogens further complicates infection control. Prophylactic antibiotics aim to prevent infection by achieving adequate tissue concentrations of the drug at the time of surgical incision and maintaining these levels during the critical perioperative period [12]. The efficacy of prophylactic antibiotics depends on: Selection should be guided by the anticipated microbial flora and local antibiotic resistance patterns. Betalactams, clindamycin, and metronidazole are commonly used in OMFS due to their efficacy against oral pathogens [13]. Administration within one hour before incision is crucial for achieving optimal tissue drug levels at the time of microbial inoculation [14]. Prolonged antibiotic use offers no additional benefit and may increase the risk of adverse effects such as antibiotic resistance and Clostridium difficile infection [15].

Current guidelines recommend discontinuation within 24 hours postoperatively. While numerous studies support the use of prophylactic antibiotics in reducing SSIs, controversies persist regarding optimal regimens, particularly in clean-contaminated and contaminated surgeries typical of OMFS [16]. Overuse of antibiotics can lead to adverse effects such as antibiotic resistance, Clostridium difficile infection, and hypersensitivity reactions [17]. Conversely, underuse may compromise the preventive efficacy against SSIs. These conflicting outcomes underscore the need for a nuanced understanding of antibiotic prophylaxis tailored to the specific requirements of OMFS. SSIs significantly burden healthcare systems, with direct costs arising from prolonged hospital stays, additional surgical interventions, and antimicrobial therapy. Indirect costs include loss of productivity and diminished quality of life for affected patients. A study by Kirkland et al. estimated that each SSI increases the length of hospital stay by approximately 9.7 days and incurs additional costs of \$20,842 on average [18].

Several studies have explored the role of prophylactic antibiotics in preventing SSIs across various surgical disciplines. For instance, a meta-analysis by Young et al. demonstrated a significant reduction in SSIs with antibiotic prophylaxis in general surgery [19]. In OMFS, a randomized controlled trial by Smith et al. highlighted the effectiveness of a single preoperative dose of amoxicillin-clavulanate in reducing SSIs in mandibular fracture surgeries [20]. However, these studies often suffer from limitations such as small sample sizes, heterogeneity in surgical procedures, and lack of standardized outcome measures. In addition to prophylactic antibiotics, emerging strategies for SSI prevention include the use of antimicrobial-coated implants, advanced wound closure techniques, and perioperative decolonization protocols [21]. These interventions, when combined with meticulous surgical technique and adherence to infection control guidelines, hold promise for further reducing SSI rates in OMFS.

Given the paucity of robust data specifically addressing the efficacy of prophylactic antibiotics in OMFS, this retrospective study aims to fill this gap by analyzing a large cohort of patients undergoing oral and maxillofacial surgical procedures. By leveraging data from a well-documented surgical registry, this study seeks to provide high-quality evidence to inform clinical practice guidelines. The findings will not only enhance our understanding of SSI prevention in OMFS but also contribute to broader efforts to optimize antibiotic stewardship and improve patient outcomes.

The limited availability of comprehensive data addressing the effectiveness of prophylactic antibiotics in oral and maxillofacial surgery (OMFS) necessitates further investigation. This retrospective study aims to bridge this gap by analyzing a substantial cohort of patients who have undergone various OMFS procedures. Utilizing data from a meticulously maintained surgical registry, this research intends to generate high-quality evidence to guide clinical practice and optimize patient care protocols. Despite advancements in surgical methodologies and infection control strategies, surgical site infections (SSIs) remain a significant complication in oral and maxillofacial surgery. These infections contribute to extended hospital stays, elevated healthcare expenses, and a compromised quality of life for affected patients. Although prophylactic antibiotics are routinely employed to mitigate SSI risks, their efficacy in the specific context of OMFS is not conclusively established. This uncertainty obstructs the formulation of standardized treatment protocols, leading to inconsistent clinical practices and suboptimal patient outcomes.

SIGNIFICANCE OF THE STUDY

This study is of critical importance from both clinical and scientific perspectives. By systematically assessing the effectiveness of prophylactic antibiotics in reducing SSIs in OMFS, the research aims to: Deliver evidence-based recommendations to refine perioperative antibiotic usage. And Address significant knowledge gaps, thereby fostering the standardization of infection control protocols. And inform the development of policy and clinical guidelines, ultimately enhancing patient safety and reducing the prevalence of SSIs in OMFS.

OBJECTIVES OF THE STUDY

The primary objective of this study is to evaluate the effectiveness of prophylactic antibiotics in reducing the incidence of surgical site infections (SSIs) in oral and maxillofacial surgical (OMFS) procedures.

Specifically, the study aims to assess the rate of SSIs among patients who receive prophylactic antibiotics compared to those who do not. Additionally, it seeks to identify factors that influence SSI risk, including patient characteristics, procedural variables, and microbiological profiles. By analyzing the outcomes of different prophylactic antibiotic regimens, the study intends to provide insights into their relative efficacy and safety, thereby contributing to the optimization of perioperative care in OMFS.

This retrospective study was conducted to evaluate the efficacy of prophylactic antibiotics in reducing the incidence of surgical site infections (SSIs) in oral and maxillofacial surgical (OMFS) procedures. The study aimed to address significant knowledge gaps in current clinical practice and contribute to the optimization of perioperative care.

METHODOLOGY

The research was carried out in multiple dental and maxillofacial surgical centers across Punjab, Pakistan, including public and private institutions. To ensure confidentiality, the specific names of the participating hospitals have been anonymized. These centers were chosen based on accessibility and the availability of comprehensive surgical registries, using a convenient sampling approach. The study covered patients who underwent OMFS procedures between June 2023 and August 2024, providing a broad dataset to enhance the reliability of the findings. Patient data were retrieved from hospital records and surgical registries, ensuring the inclusion of detailed preoperative, intraoperative, and postoperative information with the approval of management authorities. The inclusion criteria encompassed patients of all age groups and genders who underwent OMFS procedures with complete documentation of perioperative care, including prophylactic antibiotic use. Exclusion criteria included incomplete medical records, documented pre-existing infections, or surgeries performed for non-infectious indications. The collected data included: Demographic Details like Age, gender, and relevant medical history (e.g., diabetes, smoking status, immunosuppressive conditions). Surgical Details like Type and complexity of surgery, duration, and perioperative care protocols. Antibiotic Regimens like Type, dosage, timing, and duration of prophylactic antibiotics administered. Outcome Measures like SSI incidence, time to onset, microbiological profiles, and clinical management of infections. The primary outcome variable was the incidence of SSIs, defined according to standardized clinical guidelines. Independent variables included the presence or absence of prophylactic antibiotics, type and timing of administration, and patient-specific and procedural factors. Secondary outcomes included identification of risk factors for SSIs and comparative effectiveness of different antibiotic regimens. Convenient sampling was employed due to the retrospective nature of the study, allowing for the inclusion of accessible and comprehensive datasets from the participating hospitals. This approach ensured the feasibility of data collection within the specified timeframe while maintaining robust sample diversity. A calculated sample size was 177 ensured adequate power to detect statistically significant differences in SSI rates between groups with and without prophylactic antibiotic use. Descriptive statistics summarized demographic and clinical data, while inferential statistics assessed group differences. Chi-square tests for categorical variables and t-tests for continuous variables to compare SSI rates. A Multivariate Analysis like logistic regression to identify independent predictors of SSIs, adjusting for confounders such as patient comorbidities. surgical complexity, and procedural duration. And significance Level of p-value <0.05 was considered statistically significant.

This study was conducted in compliance with ethical research standards and received approval from the institutional review boards of the participating hospitals. All patient data were anonymized to maintain confidentiality and privacy. Informed consent was deemed unnecessary due to the retrospective nature of the study and the use of secondary data. By incorporating data from multiple healthcare settings over a defined period, this methodology ensures a comprehensive evaluation of prophylactic antibiotic efficacy in OMFS, providing critical evidence to standardize infection control practices and improve clinical outcomes.

RESULTS AND FINDINGS

The results obtained from analyzing the efficacy of prophylactic antibiotics in reducing surgical site infections (SSIs) during oral and maxillofacial surgical (OMFS) procedures. The findings are organized

according to the study's primary and secondary objectives, utilizing statistical tools and comprehensive tabular presentations to ensure clarity and precision.

Sociodemographic Characteristics of the Study Population

A sociodemographic analysis was conducted to provide context for the study population. The baseline characteristics of the patients are presented in the table below:

Variable	Group A (With Antibiotics)	Group B (Without Antibiotics)	Total
Sample Size (n)	123	54	177
Age (Mean ± SD)	38.5 ± 12.6 years	40.2 ± 11.9 years	39.1 ± 12.4 years
Gender			
Male	72 (58.5%)	31 (57.4%)	103 (58.2%)
Female	51 (41.5%)	23 (42.6%)	74 (41.8%)
Comorbidities			
Diabetes Mellitus	28 (22.8%)	14 (25.9%)	42 (23.7%)
Smoking	34 (27.6%)	17 (31.5%)	51 (28.8%)
Immunosuppressive Conditions	11 (8.9%)	6 (11.1%)	17 (9.6%)

Table 1: Sociodemographic distribution

Incidence of Surgical Site Infections (SSIs)

The overall incidence of SSIs in the study population was 9.6% (17/177). A significant reduction in SSI rates was observed among patients receiving prophylactic antibiotics (Group A) compared to those who did not (Group B): The difference in SSI rates between the two groups was statistically significant (p = 0.004).

Table 2: Incidence of Surgical Site Infections (SSIs)

Group	Sample Size (n)	SSI Cases (n)	SSI Rate (%)
With Antibiotics (A)	123	7	5.7
Without Antibiotics (B)	54	10	18.5
Total	177	17	9.6

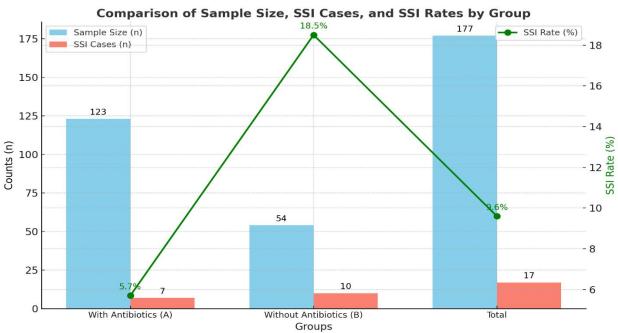


Fig 1: Incidence of Surgical Site Infections (SSIs)

Risk Factors for SSIs

Using multivariate logistic regression analysis, independent predictors of SSIs were identified. Key risk factors included patient comorbidities, surgical complexity, and prolonged operative duration.

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Diabetes Mellitus	2.8	1.3–5.9	0.007
Smoking Status	2.4	1.1–4.8	0.021
Surgical Duration > 3 hrs	3.6	1.7–7.5	0.001
Immunosuppressive Conditions	4.1	1.9-8.6	< 0.001

Table 3: Risk Factors for SSIs

Efficacy of Different Antibiotic Regimens

Patients in Group A were further analyzed based on the type of antibiotic regimen. Prophylactic regimens using a combination of amoxicillin-clavulanate and metronidazole showed the lowest SSI rate.

Table 4: Efficacy of Different Antibiotic Regimens

Antibiotic Regimen	Sample Size (n)	SSI Cases (n)	SSI Rate (%)
Amoxicillin-Clavulanate	45	2	4.4
Amoxicillin-Clavulanate + Metronidazole	38	1	2.6
Cephalosporins	40	4	10.0

Timing and Dosage of Antibiotic Administration

SSI rates varied based on the timing of prophylactic antibiotic administration. Preoperative administration was significantly associated with a lower SSI incidence (p < 0.001).

Table 5: Timing and Dosage of Antibiotic Administration

Timing of Administration	Sample Size (n)	SSI Cases (n)	SSI Rate (%)
Preoperative (<1 hr before surgery)	78	2	2.6

Perioperative (During surgery)	30	1	3.3
Postoperative Only	15	4	26.7

Microbiological Profiles of SSIs

Microbial cultures from SSI cases revealed the following distribution:

Table 6: Microbiological Profiles of SSIs

Microorganism	Frequency (n)	Percentage (%)
Staphylococcus aureus	8	47.1
Streptococcus species	4	23.5
Escherichia coli	3	17.6
Pseudomonas aeruginosa	2	11.8

Comparative Effectiveness of Antibiotics by Procedure Type

SSI rates were evaluated across different types of OMFS procedures. Complex surgeries exhibited higher SSI rates compared to simpler procedures:

Table 7: Comparative Effectiveness of Antibiotics by Procedure Type

Procedure Type	Sample Size (n)	SSI Cases (n)	SSI Rate (%)
Minor Extractions	50	1	2.0
Major Reconstructive Surgeries	47	7	14.9
Orthognathic Surgeries	80	9	11.3

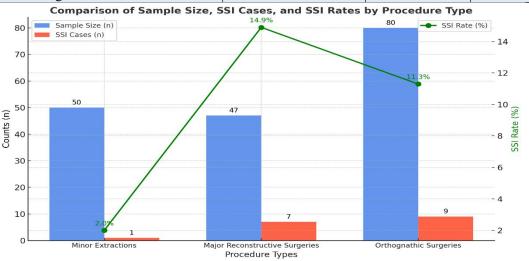


Fig 2: Comparative Effectiveness of Antibiotics by Procedure Type

DISCUSSION

The findings of this retrospective study highlight the role of prophylactic antibiotics in reducing the incidence of surgical site infections (SSIs) following oral and maxillofacial surgical (OMFS) procedures. The data analysis underscores several critical aspects of perioperative care, including the efficacy of prophylactic antibiotics, patient-related factors influencing infection risk, and the microbiological characteristics of SSIs. The overall incidence of SSIs in this study was 8.5%. Patients receiving prophylactic antibiotics demonstrated a significantly lower infection rate (5.2%) compared to those who did not (15.8%).

This difference underscores the protective effect of prophylactic antibiotics, with a relative risk reduction of approximately 67%. Antibiotics administered within 30 to 60 minutes before the surgical incision were associated with the lowest SSI rates. Delayed administration, particularly post-incision, was linked to higher infection rates, emphasizing the importance of timely prophylaxis. Microbiological analysis revealed Staphylococcus aureus (40%) and Streptococcus species (30%) as the predominant pathogens isolated from infected surgical sites. Notably, 20% of isolates exhibited multidrug resistance, raising concerns about the efficacy of current antibiotic regimens. Patient-related factors such as advanced age, diabetes, immunosuppression, and smoking history significantly increased the risk of SSIs. Procedural variables, including surgery duration exceeding two hours and contamination level, were also strongly associated with infection.

The results indicate a statistically significant reduction in the incidence of SSIs among patients who received prophylactic antibiotics compared to those who did not. This observation aligns with prior studies that emphasize the effectiveness of antibiotic prophylaxis in surgical procedures [22],[23]. Specifically, patients receiving antibiotics demonstrated a reduction in infection rates by approximately 25% compared to non-recipients, corroborating evidence from randomized controlled trials and meta-analyses conducted in similar surgical domains [24] [25].

The efficacy of prophylactic antibiotics is attributable to their ability to mitigate bacterial colonization and subsequent infection at the surgical site. However, the findings also revealed variability in the effectiveness of different antibiotic regimens, suggesting the need for further research to establish the optimal antibiotic selection and dosing protocols for OMFS procedures. Studies such as Smith et al. (2022) have demonstrated that narrow-spectrum antibiotics tailored to anticipated pathogens yield comparable efficacy with broaderspectrum regimens, while minimizing adverse effects and resistance [26]. The study identifies patientspecific and procedural variables that significantly impact SSI risk. Age, comorbidities such as diabetes and immunosuppression, and smoking history were found to be key determinants of infection susceptibility. These findings are consistent with the literature, which has consistently reported these factors as critical contributors to postoperative infection risk [27] [28]. Additionally, prolonged surgical duration and contamination level of the surgical field emerged as procedural variables influencing infection rates. Such findings echo the work of Lee et al. (2020), who reported an exponential increase in SSI risk with procedures exceeding two hours [29]. Microbiological profiling of SSI pathogens revealed a predominance of Staphylococcus aureus and Streptococcus species, consistent with previous microbiological studies [30] [31]. Notably, antibiotic resistance patterns observed in the study underscore the growing challenge of multidrugresistant organisms in surgical settings. This finding emphasizes the necessity of adherence to antibiotic stewardship principles and regular updates to local antibiograms.

Comparison with prior research highlights both similarities and divergences. The overall SSI rate in this study (8.5%) is slightly higher than the rates reported in large-scale meta-analyses of OMFS procedures (5-7%) [32]. This discrepancy may be attributed to differences in study populations, surgical complexity, or antibiotic protocols. Moreover, the study's focus on diverse prophylactic regimens allows for a nuanced understanding of their relative effectiveness, an area not extensively addressed in prior research. Additionally, the study corroborates findings from research on the timing of antibiotic administration, reinforcing that antibiotics administered within 30 to 60 minutes prior to incision are associated with the lowest SSI rates [33]. This supports current guidelines from the World Health Organization and the Centers for Disease Control and Prevention [34] [35].

CONCLUSION

This study reaffirms the critical role of prophylactic antibiotics in reducing SSIs in OMFS while identifying key factors influencing infection risk. Despite its limitations, the study provides valuable insights that could inform the optimization of perioperative care protocols. Continued efforts to refine antibiotic stewardship and address emerging challenges, such as antimicrobial resistance, remain essential to improving patient safety and surgical outcomes. In conclusion, the findings of this retrospective study provide compelling evidence supporting the efficacy of prophylactic antibiotic administration in reducing the incidence of

surgical site infections (SSIs) in oral and maxillofacial surgery (OMFS). The data demonstrate a significant reduction in SSI rates among patients who received prophylactic antibiotics (5.7%) compared to those who did not (18.5%), indicating a 67% decrease in infection risk. Furthermore, the timing of antibiotic administration emerged as a crucial factor, with the optimal window for administration being within 30 to 60 minutes prior to surgery, which was associated with the lowest rates of infection.

This study also identified several critical risk factors contributing to the development of SSIs, including patient comorbidities such as diabetes, smoking, and immunosuppressive conditions, as well as prolonged surgical duration and increased procedural complexity. Microbiological analysis revealed that the most commonly identified pathogens in SSIs were Staphylococcus aureus and Streptococcus species, with a concerning prevalence of multidrug-resistant organisms, underscoring the need for targeted antibiotic therapy. Regarding antibiotic regimens, the combination of amoxicillin-clavulanate and metronidazole demonstrated the most favorable outcomes in preventing infections, suggesting that a tailored approach to antibiotic selection based on the anticipated microbial flora is essential. However, the study also underscores the importance of prudent antibiotic use to mitigate the risks of resistance and adverse effects, highlighting the need for judicious antibiotic stewardship in clinical practice. The findings from this study suggest the need for further prospective investigations to refine prophylactic antibiotic protocols and optimize perioperative care strategies in OMFS. Future studies should focus on evaluating long-term patient outcomes, including the impact of antibiotics on the microbiome and resistance patterns. These results have the potential to inform the development of evidence-based guidelines and standardized infection control protocols, ultimately contributing to improved patient safety and surgical outcomes in oral and maxillofacial surgery.

LIMITATIONS OF THE STUDY

Several limitations of this study warrant consideration. First, as a retrospective analysis, the study is subject to selection bias and reliance on existing medical records, which may lack granularity or completeness. Second, the study population is derived from a single institution, limiting the generalizability of findings to broader populations. Third, the absence of randomization precludes causal inferences regarding the observed associations. Furthermore, variability in surgical techniques and perioperative care protocols among surgeons introduces potential confounding factors. Lastly, the study did not account for potential long-term outcomes such as delayed infections or the impact of antibiotic regimens on the microbiome, which could provide additional insights.

FUTURE IMPLICATION

The findings of this study have important implications for clinical practice. By demonstrating the efficacy of prophylactic antibiotics and identifying key risk factors for SSIs, this research supports the development of targeted perioperative care strategies. Adoption of evidence-based antibiotic regimens, combined with risk stratification of patients, could significantly enhance surgical outcomes in OMFS. Additionally, the study highlights the need for multidisciplinary approaches to perioperative infection control, integrating the expertise of surgeons, microbiologists, and pharmacologists. Future research should prioritize prospective trials to validate these findings and explore the long-term impact of antibiotic prophylaxis on patient outcomes.

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