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Microbiological profile and antibiotic sensitivity of maxillofacial infections in an emergency hospital

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Aim: To investigate the bacteriological profile of oral and maxillofacial infections and the pattern of sensitivity to a specific group of antibiotics in a reference emergency hospital in Brazil. **Methods:** This is a prospective cohort institutional study that studied patients affected by oral and/or maxillofacial infections in a Brazilian emergency hospital, over a 12-month period, of different etiologies, through data collection, culture and antibiogram tests, and monitoring of the process of resolution of the infectious condition. The variables were analyzed using the chi-square and Mann-Whitney tests, using a significance level of 5%. **Results:** The sample consisted of 61 patients, 62.3% male. The mean age of participants was 34.3 years. Odontogenic infection was the most frequent etiology and the submandibular space was the most affected. The bacterial species *Streptococcus viridans* was isolated in 21.6% of cases. Levofloxacin, vancomycin and penicillin were the antibiotics with the highest frequency of bacterial sensitivity, while clindamycin and erythromycin showed the highest percentages of resistance. **Conclusions:** The results suggest that, among the most used antibiotics for the treatment of these infections, penicillin remains an excellent option of choice for empirical therapy.

Keywords: Bacteria. Anti-bacterial agents. Focal infection, dental. Surgical wound infection. Oral and maxillofacial surgeons.

Introduction

Severe infections in the oral and maxillofacial regions are among the most frequent emergency situations that are cared by Oral and Maxillofacial Surgeons. Due to the rapid progress from a single primary space to the deep spaces of the head and neck, it can cause serious complications such as respiratory obstruction, meningitis, mediastinitis, sepsis and death[1]. The accelerated clinical worsening of maxillofacial infections can be the result of several factors, such as the patient's immune status, virulence and antibiotic resistance of pathogenic organisms, inappropriate antibiotic choice or an ineffective surgical approach[2].

It is known that most infections found in the head and neck region, odontogenic and non-odontogenic, are polymicrobial, predominantly by streptococcus[3-5]. Although there are numerous other causes for infections in this region, the main etiology are odontogenic infections and in most of the cases the infection will progress to resolution if the incision and drainage procedures, removal of the infectious focus and the administration of antibiotic therapy are performed effectively[6-8]. Generally, the choice of the antibiotic is empiric in mild and moderate infections or until the antibiogram result is obtained[9]. Since the microbial flora and bacterial resistance varied greatly antibiogram is considered mandatory and has an extreme impact on the empirical choice of antibiotics[10-12]. Concern about the development of multidrug-resistant bacteria, as resistant infections have higher rates of morbidity and mortality and the study of antibiotic sensitivity aim at the clinical improvement of patients and lower hospital costs. Knowing that the behavior of infections differs geographically, local health services aim to reduce the inappropriate prescription of antibiotics and rationalize their use[13-15].

The aim of this study is to investigate the bacteriological profile of oral and maxillofacial infections and their pattern of sensitivity to a specific group of antibiotics in a Brazilian trauma hospital. This information should help surgeons choose the appropriate antibiotic to treat these infections.

Materials and methods

This study is a prospective, observational and analytical cohort study, which was performed at the department of Oral and Maxillofacial Surgery at the Emergency Hospital of the Northwest Region of Goiânia Governador Otávio Lage de Siqueira (HUGOL), located in the city of Goiania in Brazil. Patients with oral and maxillofacial infections were recruited between September 2020 and September 2021. The research was approved by the Ethics Committee of Leide das Neves Ferreira (CAAE: 32548620.7.0000.5082). The inclusion criteria was defined by the presence of infections in the oral and maxillofacial region of any etiology, in the stage of abscess with drainable collection. Exclusion criteria were presence of non-bacterial infections, infections in early stages, impossibility of collecting material for analysis and patients who had already undergone the incision and drainage procedure for the same infection.

The diagnosis of the infection was based on clinical or tomographic images. Swelling, hyperemia and local erythema, presence of image suggestive of a drainable collection on contrast-enhanced facial computed tomography, and a positive result on a fine needle aspiration. All patients or relatives were informed and consented to participate in the research by signing the Consent Form. Demographic data as gender and age, detailed medical history, and outcomes of each participant were collected.

For sample collection, aspiration puncture procedures or tissue fragment removal from the deepest region of the infected site were performed, after decontamination of the area with saline solution, preferably by an extraoral approach and, when not possible, by an intraoral approach. The sample was stored in a sterile and dry container and transported within 1 hour of collection to the hospital's laboratory. The tissue fragments collected were immersed in BHI broth (brain heart infusion) for 24 hours in an oven at a temperature of 36°C and the broth, as well as the collected secretions, were seeded with disposable loops in a tripartite plate, which contained the media of chocolate agar, blood agar and MacConkey agar and on a single plate with chocolate agar medium. The single plate was placed in an anaerobic jar, and both plates were placed in an oven at 36°C. After 48 hours, the material was removed from the oven and, if there was growth, the identification of the microorganism and the antibiogram were performed through automation, by the Microscan method, according to the criteria established by the CLSI (Institute of Clinical and Laboratory Standards). The frequency of isolated species, identification by Gram stain and oxygen tolerance were performed. Cultures were tested for the following antibiotics: Penicillin, amoxicillin plus clavulanic acid, clindamycin, erythromycin, levofloxacin, vancomycin, ampicillin, ceftriaxone, cefuroxime, linezolid, meropenem, tetracycline, ciprofloxacin, gentamicin, and trimethoprim plus sulfamethoxazole.

Data were organized and analyzed using the SPSS software (version 25.0; SPSS Inc., Chicago, IL, USA). Descriptive and bivariate analyzes were performed. Chi-square test was used to verify the association between previous antibiotic use and resistance. The length of hospital stay was compared between participants with and without resistance, with and without a positive result in the culture test using the Mann-Whitney test. A significance level of 5% was adopted.

Results

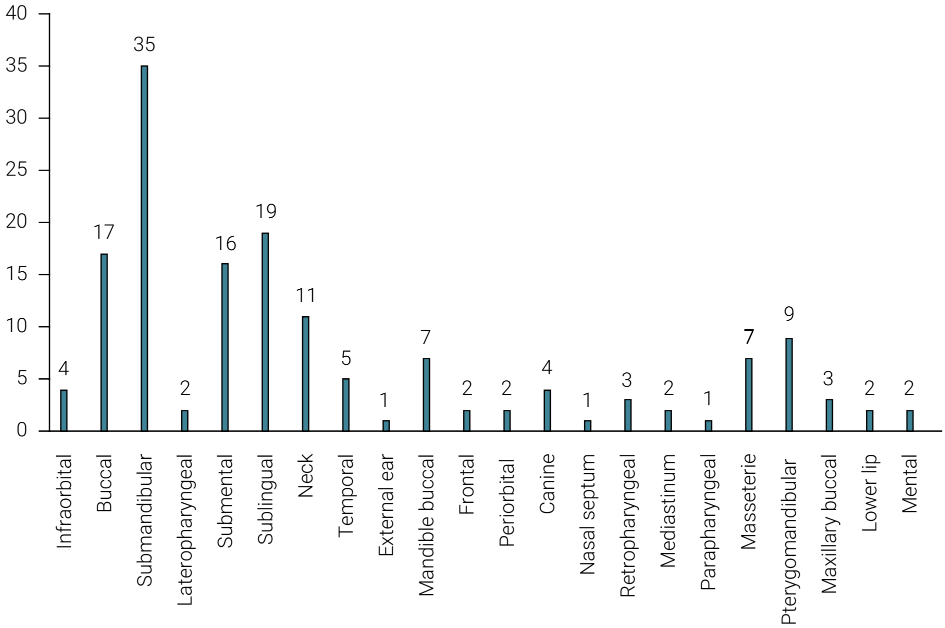
A total of 61 patients with oral and/or maxillofacial infections participated in this study. The medical history study revealed that from 18 participants that had some systemic disease. The most frequent condition was Diabetes mellitus (n=7, 11.5%). Arterial hypertension, cardiovascular and respiratory diseases were other reported conditions. More than half of the participants (67.2%) reported using antibiotics for their current infection prior to hospital admission. The characteristics of the participants were presented in Table 1.

Table 1. Characteristics of study participants (*n*=61).

Variables	n (%)
Gender	
Male	38 (62,3)
Female	23 (37,7)
Age (yo)	Mean: 34,3 (SD:14,4)
<17	4 (6,6)
18-35	31 (50,8)
36-60	24 (39,3)
>60	2 (3,3)
Systemic disease	
No	43 (70,5)
Yes	18 (29,5)
Previous antibiotic use	
No	20 (32,8)
Yes	41 (67,2)
Etiology	
Fracture postoperative infections	7 (11,5)
Post extraction infections	9 (14,8)
Odontogenic infections	30 (49,2)
Infected wounds after suturing	5 (8,2)
Infected cystic lesions	5 (8,2)
Skin or mucosal infections	5 (8,2)

n: absolute frequency; %: relative frequency.

Anatomical single space infections occurred in 20 patients (32.8%), while infections involving multiple spaces occurred in 41 patients (67.2%). The submandibular space was most frequently affected (57.4%) (Graph 1).

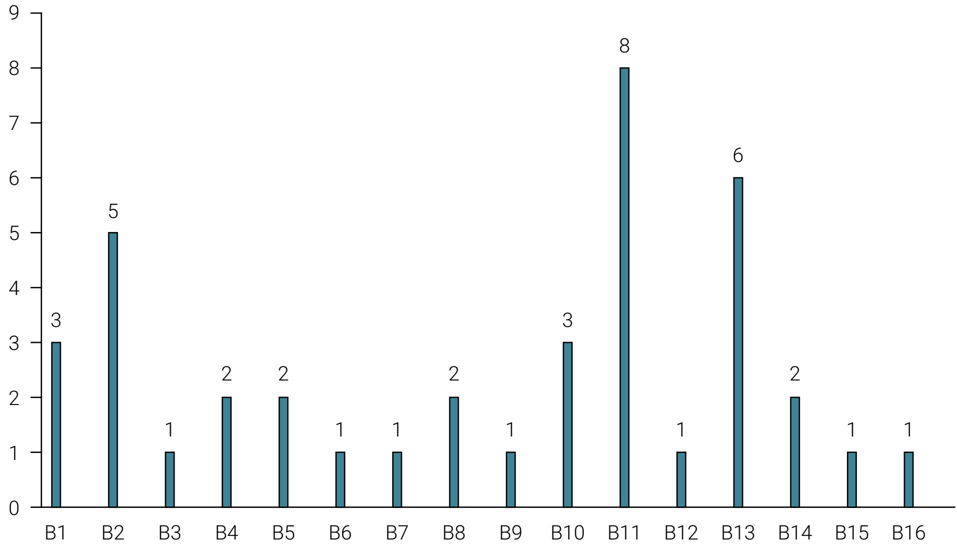


Graph 1. Absolute frequency of affected anatomical regions.

All patients underwent incision and abscess drainage procedure under local or general anesthesia, removal of the cause of infection and empirical antibiotic therapy. Patients with severe infection were initially prioritized for airway maintenance. 39 patients required hospitalization for treatment of the infection (63.9%), while 22 patients were followed up on an outpatient basis (36.1%). The length of hospital stay averaged 5.4 days (SD: 7.9; 0-44), 6 patients (9.8%) required intensive care and only 1 patient died.

Regarding empirical antibiotic therapy, 9 different antibiotic protocols were used in the treatment of 61 participants. Ceftriaxone/clindamycin (55%), clindamycin (13.3%) and amoxicillin associated to clavulanic acid (13.3%) were the most frequent prescriptions.

The culture test and antibiogram were positive in 37 cases (60.7%) and in 21 cases (56.7%) bacterial resistance to at least 1 antibiotic was found. Forty bacteria were identified, 16 of which were different species (Graph 2). *Streptococcus viridans* (21.6%; *n*=8) and *Streptococcus anginosus* (16.2%; *n*=6) were the most frequently isolated bacteria. Of the bacterial species found, 34 were Gram-positive (85%) and 6 were Gram-negative (15%). The percentage of facultative anaerobic bacteria was 95%, followed by aerobics at 5%.



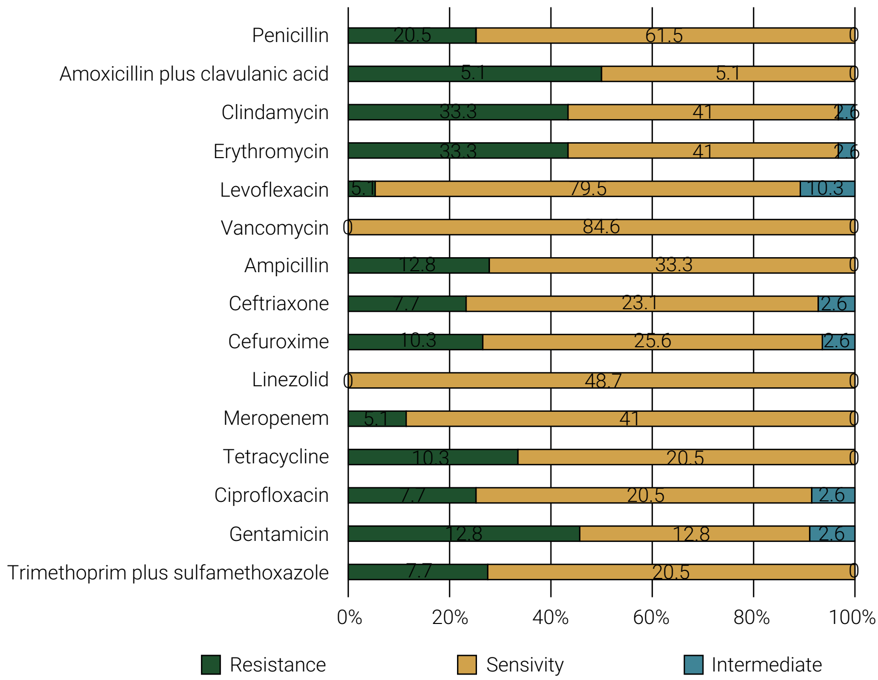
Graph 2. Absolute frequency of bacteria isolated in the culture test. B1: *Enterococcus faecalis*; B2: *Streptococcus constellatus*; B3: *Pseudomonas aeruginosa*; B4: *Streptococcus pneumoniae*; B5: *Streptococcus intermedius*; B6: *Escherichia coli*; B7: *Proteus mirabilis*; B8: *Staphylococcus epidermidis*; B9: *Streptococcus oralis*; B10: *Staphylococcus aureus*; B11: *Streptococcus viridans*; B12: *Klebsiella oxytoca*; B13: *Streptococcus anginosus*; B14: *Klebsiella pneumoniae*; B15: *Streptococcus sinensis*; B16: *Micrococcus sp*.

Regarding the etiology, the bacteria isolated in odontogenic infections were: *Streptococcus pneumoniae*, *Streptococcus viridans*, *Streptococcus sinensis*, *Streptococcus constellatus*, *Streptococcus anginosus*, *Enterococcus faecalis*, *Klebsiella pneumoniae* e *Micrococcus sp*. In post extraction infections, the bacteria *Streptococcus intermedius* and *Klebsiella oxytoca* were isolated. And in the postoperative infections of fractures of the facial bones were isolated: *Streptococcus viridans*, *Streptococcus constellatus*, *Staphylococcus aureus*, *Staphylococcus epidermidis* e *Enterococcus faecalis*.

Levofloxacin (*n*=31) and vancomycin (*n*=33) were the antibiotics with the highest absolute frequency in terms of sensitivity, followed by penicillin (*n*=24) and linezolid (*n*=19). Clindamycin and erythromycin were the antibiotics with the highest absolute frequency of bacterial resistance (13 cases each). One patient identified with Klebsiella pneumoniae was resistant to all antibiotics tested.

Among the most common Gram-positive bacteria, *Streptococcus viridans* and *Streptococcus constellatus* were 100% sensitive to penicillin, vancomycin and levofloxacin. *Streptococcus viridans* was resistant to clindamycin and tetracycline in 25% of cases, while *Streptococcus constellatus* was resistant to clindamycin, erythromycin and ceftriaxone in 60%, 40% and 20% of cases, respectively. *Streptococcus anginosus* was also sensitive to levofloxacin and vancomycin in 100% of cases and to penicillin in 83.3%. Its resistance was 16.6% for penicillin, clindamycin, erythromycin and ampicillin. Among the 6 Gram-negative bacteria found, it was possible to identify resistance to ampicillin, cefuroxime, ciprofloxacin and gentamicin in 2 cases each and resistance to amoxicillin/clavulanic acid, ceftriaxone and meropenem in 1 case each.

Staphylococcus aureus and *Staphylococcus epidermidis* were resistant to penicillin, clindamycin and erythromycin in all cases. They showed satisfactory sensitivity to levofloxacin, vancomycin, linezolid and ciprofloxacin. Graph 3 shows the percentages of resistance, sensitivity and intermediate observed for each antibiotic administered.



Graph 3. Relative frequency (%) of resistance, sensitivity and intermediate observed for each antibiotic.

In the evaluation of factors associated with antimicrobial resistance, it was observed that the period of hospitalization was similar between participants with (median 4.0 [minimum-maximum 0-31]) and without resistance (4.0 [minimum-maximum 0-44] (p=0.852). There was no significant association between antimicrobial resistance and previous use of antibiotics. The frequency of previous antibiotic use was similar between participants with (52.4%) and without resistance (47.6%) (p=0.074). The length of hospital stay was similar between participants with positive (4.0 [0-44]) and negative (4.0 [0-11]) results in the culture test and antibiogram (p=0.495). There was no significant difference in the median of hospitalization between the types of bacteria isolated in each participant (p=0.230).

Discussion

Oral and maxillofacial infections often require hospital care when not treated in their initial course. The present study evaluated patients affected by these infections in an emergency hospital in order to present their characteristics and standardize the prescription of antibiotics during treatment. Most articles are limited to the study of infections of odontogenic origin[7], since they are the most commonly diagnosed and treated infections by Oral and Maxillofacial Surgeons[16,17]. In this study, other etiologies were also included, such as postoperative infections, infected cystic lesions and skin infections, since they are also frequent clinical situations in emergency services and can progress to a severe stage if not treated correctly[6,7,18,19]. Another limitation of some studies is the inclusion of patients who were followed up only during hospitalization[20]. Our study evaluated inpatients and outpatients.

The sample was predominantly composed of male individuals (62.3%) aged between 18-35 (50.8%). This patient profile is consistent with the characteristics found in other studies[6,16,21]. Diabetes mellitus is an immunosuppressive systemic disease closely related to the worsening of the clinical picture of oral and maxillofacial infections, dissemination to deep spaces, emergence of complications, increased length of stay and the need for intensive care[1,8,18,22]. In our study, this condition was present in 7 patients (11.5%), 4 of whom required intensive care and 1 died. The mean hospital stay for these patients was 15.4 days and all of them had infections that involved multiple anatomical spaces. However, it was not possible to identify whether the severity was related to diabetes mellitus, the spread of the disease or the proposed treatment plan for each patient.

The indiscriminate use of antibiotics is evidenced by the fact that 67.2% of the patients recruited for the study used some antibiotic prior to hospital admission as the only method of treatment. Most of these individuals did not have the prescription in hand and did not remember the name of the medication used. Therefore, it was not possible to obtain information about these drugs and continue the therapeutic regimen already started, nor to know if the patients were self-medication.

The submandibular space was the most affected anatomical region, confirming the information reported in several studies[13,23-26]. Then, the most frequent spaces were: sublingual, buccal and submental. Some infections have spread to high-severity spaces that directly threaten the airways and vital structures, such as the deep spaces of the neck and the mediastinum.

Aspiration puncture or tissue fragment removal from infected sites were performed in all patients before the surgical procedure and the beginning of antibiotic therapy to avoid changes in the pathogenic microbiota. The swab collection method is not accepted by the hospital protocol, due to the high risk of contamination that this method offers[27]. In the entire sample, only 37 patients (60.7%) were positive for bacterial culture and 39.3% of the samples were sterile. The factors that possibly caused this large number of samples that did not have bacterial growth include incorrect collection or transport technique, presence of bacteria sensitive to previously used antibiotics, failures in laboratory processing and lack of supplies to perform more specific methods for the identification of bacteria. , such as molecular techniques[16,21,28]. The aspiration collection method is able to capture more anaerobic bacteria than the swab method, however, some microorganisms may not have supported the aspiration, transport and culture process[17,23].

For many years, the microbiology of infections remained inconsistent, but nowadays it is possible to identify the polymicrobial nature of these infections, their constantly changing flora and resistance pattern. Our study concluded that *Streptococcus viridans* remains the most common pathogen found in head and neck infections, as reported in previous studies[4,9,11,23,24,28,29]. After them, *Streptococcus anginosus* and *Streptococcus constellatus* were the most frequently found microorganisms in our sample. *Streptococcus constellatus* is associated with the formation of satellite abscesses and more aggressive infectious processes[10]. *Staphylococcus aureus* and *Enterococcus faecalis* were identified in 3 cases each, and *Staphylococcus aureus* is characterized by being present in skin infections, oral mucosal abscesses and secondary infections, while *Enterococcus faecalis* is more commonly found in oral mucosal infections[19]. *Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Escherichia coli* were identified in smaller numbers and are characterized by being pathogens found in the respiratory system, oral mucosa and skin infections, especially in immunocompromised individuals[19].

In the present study, it was possible to test the sensitivity of the bacteria found to 15 types of antibiotics, of different classes, including beta-lactams, cephalosporins, quinolones and others. All bacteria were sensitive to linezolid and vancomycin. These results were supported by Sebastian et al.[11] (2019) and by Kim et al.[2] (2017), respectively.

Bacterial sensitivity to clindamycin is quite varied among studies published in the literature. This antibiotic is often used to treat oral and maxillofacial infections, but high resistance has been observed in recent years. Some recent articles report that clindamycin is still highly indicated for the treatment of infections, due to its excellent coverage against Gram+ cocci and anaerobic bacteria[11,14,16,25,27]. Adversely, the present study concluded that clindamycin was the antibiotic that presented the highest frequency of bacterial resistance, among the most used antibiotics, information that is also compatible with several other studies found in the literature[5,12,22,29,30]. What justifies this difference between the reports are the variations in the techniques used for the culture and identification of bacteria and the gradual changes that occur in the microbiota due to the reckless use of the drug, according to the reflection of local practice[31].

In previous studies, bacterial resistance to erythromycin was compatible with that of clindamycin[2,12,22], as well as in ours. The association of clindamycin with ceftriaxone was presented in the study by Gómez-Arámbula et al.[5] (2015), which concluded that clindamycin showed great resistance and that ceftriaxone is more indicated as a prophylactic therapy for mandibular fractures than for infections already installed.

The use of penicillin was considered the first choice in the treatment of these infections for decades, until the emergence of several bacteria resistant to this antibiotic[2,9,14,21]. Penicillin was the third antibiotic with the highest frequency of antibiotic sensitivity in the present study. These results, added to those found in the literature[12,17,27,30], suggest that the use of penicillin as the first choice should be continued, due to its good susceptibility to aerobic and anaerobic microorganisms[3].

Therapy with amoxicillin, a semisynthetic antibiotic derived from penicillin, is an excellent choice due to its high effectiveness, minimal side effects, low cost, patient tolerability and availability in most public services[17]. Amoxicillin associated with clavulanic acid, a broad-spectrum combination, can be used in cases of severe infections due to the high level of resistance to beta-lactams, previously reported[20,22,25]. The use of clindamycin should be reserved for patients allergic to penicillin[3,12,20].

The patients studied showed clinical improvement and cure of the infection in 98.3% of the cases, even with the presence of bacteria resistant to the antibiotics frequently prescribed. Liau et al.[14] (2018) concluded that patients who presented antibiotic resistance had a worse clinical response, increased length of stay, need for intensive care and surgical re-approach. These results were not similar to those found in the present study, as well as in the studies by Kim et al.[2] (2017) and from Yuvaraj et al.[27] (2012). Some factors must be raised as hypotheses of clinical worsening of patients, such as ineffective surgical approaches, failure to identify and remove the causative infectious focus, spread of infection to deep spaces, presence of immunosuppressive systemic diseases, among others. Antibiotic therapy works as an adjuvant therapy for surgical approaches to remove the infectious focus, incision and drainage of the abscess and copious irrigation[16,32], which are of valuable importance in reducing the concentration of microorganisms and the infectious biological load in the patient[3,7,25].

There are some limitations in our study, such as the small sample size, the frequent use of antibiotics prior to the study, the presence of several samples with negative results for culture, in addition to the lack of specific culture medium for transporting restricted anaerobic samples and lack of inputs to carry out molecular methods of identification of bacteria. Our results can be used to decrease antibiotic misuse in the local population and further studies, including time and larger samples, will confirm and extend our results.

Conclusion

Antibiotic therapy is one of the requirements for the management of infections of the maxillofacial region, as it has the role of preventing bacteremia and helps the immune system to fight infections. The standardization of empirical antibiotic therapy used in a local population can be established through knowledge of the characteristics and sensitivity pattern of the local pathological flora, through culture and antibiogram tests.

Conflicts of interest

None.

Data Availability

Datasets related to this article will be available upon request to the corresponding author.

Author Contribution

Laiz Moreira de Paula: conceptualization, methodology, formal analysis, investigation, manuscript writing, project administration. **Eduardo Zancopé:** validation, manuscript writing, review and editing, visualization, supervision. All authors actively participated in discussing the manuscript's findings and have revised and approved the final version of the manuscript.

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