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RESEARCH ARTICLE

ANTIBIOTIC RESISTANCE OF DENTAL ABSCESS INFECTION IN PAEDODONTIC PATIENTS: A PROSPECTIVE STUDY IN A TERTIARY CARE DENTAL HOSPITAL

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ABSTRACT

Background: Dental abscesses are a common infection in paedodontic patients and are often managed with antibiotics in conjunction with dental interventions. However, the increasing prevalence of antibiotic resistance presents a significant challenge in effective treatment, leading to prolonged infections, complications, and increased healthcare burden.

Objective: This study aimed to evaluate the patterns of antibiotic resistance in bacterial isolates from dental abscesses in paedodontic patients attending Mahe Institute of Dental Sciences & Hospital.

Methods: A prospective cross-sectional study was conducted over a period of 3 months. Paedodontic patients presenting with clinical signs of dental abscesses were included. Pus samples were aseptically collected and cultured for bacterial isolation. Identified isolates underwent antibiotic susceptibility testing using the Kirby-Bauer disk diffusion method following CLSI guidelines.

Results: In the 25 samples collected, revealed the presence of multiple microorganisms, with a total of 25 isolates identified. *Streptococcus oralis/mitis* was the most prevalent organism, accounting for 6 isolates (24% of the total). Other significant organisms included *Staphylococcus hominis*, *Klebsiella pneumoniae*, *Citrobacter koseri*, *Peribacillus simplex*, and *Enterobacter cloacae*, each contributing 3 isolates (12% each). Additionally, *Enterobacter aerogens* and *Bacillus altitudinis* were identified, each comprising 2 isolates (8% each).

Conclusion: The study highlights a concerning level of antibiotic resistance among pathogens causing dental abscesses in children. These findings underscore the necessity for culture-guided antibiotic therapy and the development of local antibiotic stewardship protocols to prevent the escalation of resistance and ensure optimal patient outcomes.

Keywords: Dental abscess, paedodontics, microbiota, antibiotic resistance

INTRODUCTION

Apical abscess is the most common form of dental abscess and is caused by infection of the root canal of the tooth. It is usually localized intraoral, but in some cases the apical abscess may spread and result in severe complications or even mortality. The reasons why dental root canal infections can become symptomatic and evolve to severe spreading and sometimes life-threatening abscesses remain elusive.¹ Studies using culture and advanced molecular microbiology methods for microbial identification in apical abscesses have demonstrated a multispecies community conspicuously dominated by anaerobic bacteria. Species/phylotypes commonly found in these infections belong to the genera *Fusobacterium*, *Pavimonas*, *Prevotella*, *Porphyromonas*, *Dialister*, *Streptococcus* and *Treponema*.¹

Most commonly prescribed drugs in pediatric dentistry are “Antibiotics.” Among Dentists, there is a trend toward overuse of antibiotics for non-indicated clinical conditions. This insufficient knowledge of the appropriate clinical indications for antibiotic prescriptions promotes the overuse of antibiotics and contributes to the emergence of antibiotic resistance among children. According to the various surveys done on the dental students, dentists and pediatric dentists on the antibiotic prescribing practices, overall, adherence to the professional clinical guidelines was low.²

The American Academy of Pediatric Dentistry (AAPD) recognizes the increasing prevalence of antibiotic-resistant microorganisms and potential for adverse drug reactions and interactions. These recommendations are intended to provide guidance in the proper and judicious use of antibiotic therapy in the treatment of oral conditions. The use of antibiotic prophylaxis for dental patients at risk for infection is addressed in a separate best practices document. Information regarding commonly prescribed antibiotics can be found in AAPD’s useful medications for oral conditions.³

All of the above factors might contribute to the emergence of antibiotic resistance among children. Children as young as 4 years were found to harbor multidrug resistant bacteria in their oral cavities.^{4,5} Further, patients who received frequent prescriptions of amoxicillin, a common antibiotic in dental prescriptions also exhibited a higher rate of amoxicillin-resistant oral *Streptococci*.^{6,7} In addition to the problem of antibiotic resistance, there are other complications associated with antibiotic prescribing in paediatric population. A significant proportion of

practitioners prescribe mostly sugar-containing formulations at frequencies inconsistent with manufacturers recommendations, and for prolonged periods of time, that may reach 10 days.⁸ The risk of developing diabetes in children due to sugar-containing medications cannot be overlooked. Moreover, generally, there is risk of development of allergy and asthma in children treated with antibiotics.^{9,10} Early-life exposure to antibiotics is also thought to change intestinal microbiota, with subsequent adverse long-term effects like obesity.¹¹ Other complications include superinfections with *Candida* species¹² and photosensitivity.^{11,13} Children are also at risk of gastrointestinal disturbances, like diarrhoea, which is generally more frequent with three-times-daily than twice-daily regimens.¹²

There are many reports on the complications associated with antibiotics abuse during the treatment of paediatric patients, particularly those related to antimicrobial resistance. The dental profession is no exception; there is growing evidence that dental practitioners are misusing antibiotics in the treatment of their paediatric patients.

Considering the above facts, this study is planned to identify the common micro-organisms in dental abscess and to pinpoint the best suitable antibiotic for those infections.

METHODOLOGY

This prospective cross-sectional study was conducted for a period of 3 months at Mahe Institute of Dental Sciences, Mahe. The ethical clearance for the study was obtained from the Institutional Review Board before starting the study. Informed consent was obtained and documented in standard proforma from consented subjects after individual counselling and providing information on the purpose of study, method of sample collection and their right of refusal. Demographic information such as age, gender, and oral hygiene, dietary habits was gathered in the standard proforma before the collection of samples. The samples were collected from 25 subjects.

Inclusion criteria: All consented patients with dental abscess in the paedodontic department was included for this study, irrespective of gender and age. The control group consisted of age and gender matched subjects in good oral health.

Exclusion criteria: Children with genetic disorders and parents who were not willing to give the consent was excluded from the study.

Sample Collection: Oral swabs were collected by Hilton method of abscess drainage and control samples by using a sterile dry cotton swab. The sample was immediately sent to microbiology laboratory for analysis.

Procedure: The oral samples collected was immediately processed in microbiology laboratory and placed in Brain heart infusion (BHI) broth. The broth was incubated at 37° C for overnight aerobically and was inoculated into Blood agar, Chocolate agar and Mac Conkey agar, culture media plates and incubated at 37° C. The mixed culture growths on the primary culture plates were the sub cultured individually in blood agar and chocolate agar, and each type of colonies grown was subjected for rapid phenotypic identification by automated bacterial identification system (MALDI TOF-MS).

Antimicrobial susceptibility testing: Antibiotic sensitivity testing was carried out by Kirby-Bauer disc diffusion method. Standard suspensions of the isolates were made and turbidity was matched to 0.5 McFarland standards. The isolates were inoculated on Mueller-Hinton agar (MHA) plates to perform a lawn culture using sterile cotton swabs and was allowed to dry for 5 – 10minutes. Antibiotic discs were then placed on the agar surface with appropriate spacing. The plates were inverted and incubated at 37°C for 18 – 24 hours. After incubation, the diameter of the zone of inhibition was measured and interpreted according to the Clinical Laboratory Standards Institute (CLSI) 2011.

Statistical analysis:

Statistical analysis was done by using SPSS software 2.0 version.

RESULT

Dental abscess samples were obtained from 25

individuals belonging to age group 7-12 years. Among the 25 samples 15 were female and 10 were males. The analysis of pediatric dental abscess samples was done using automated bacterial identification system (MALDI TOF- MS) revealed the presence of multiple microorganisms, with a total of 25 isolates identified. *Streptococcus oralis/mitis* was the most prevalent organism, accounting for 6 isolates (24% of the total). Other significant organisms included *Staphylococcus hominis*, *Klebsiella pneumoniae*, *Citrobacter koseri*, *Peribacillus simplex*, and *Enterobacter cloacae*, each contributing 3 isolates (12% each). Additionally, *Enterobacter aerogens* and *Bacillus altitudinis* were identified, each comprising 2 isolates (8% each) (Figure 1). All clinical specimens in the present study exhibited bacterial growth; majority of the organisms were Gram-positive organism. The growth observed was predominantly of Gram-positive cocci such as *Streptococcus mitis/oralis* (24%) followed by *Staphylococcus hominis*(12%). These samples were investigated for their antibiotic resistance pattern.

Antibiotic sensitivity testing was carried out by Kirby-Bauer disc diffusion method. After incubation and culturing, the diameter zone of inhibition was measured and interpreted according to the clinical laboratory standards unit (CLSI) and required data with traffic light chart was prepared.

The most commonly tested antibiotics against all the studied bacterial pathogen were amoxicillin/ clavulanic acid, ciprofloxacin, tigecycline, gentamicin, and clindamycin and others (as listed in the Fig 1). Other classes of antibiotics were often tested for diverse infection – colistin, fosfomycin, amikacin and cefoperozone were tested against *Staphylococcus*, *Peribacillus simplex*, *Enterobacter* and *Citrobacter*.

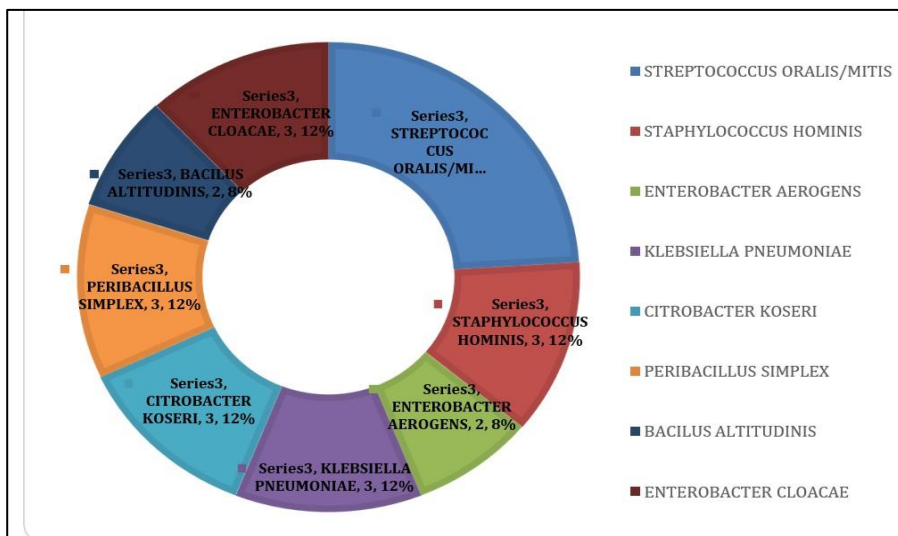


Figure 1. Identification and distribution of microorganisms isolated from pediatric dental abscesses.

Table 1. Antibiotic resistance pattern of Gram-positive microorganisms isolated from pediatric dental abscesses.

	Gram positive microorganisms (n=14)			
	<i>Streptococcus oralis/mitis</i> (n=6)	<i>Staphylococcus hominis</i> (n=3)	<i>Bacillus altitudinis</i> (n=2)	<i>Peribacillus simplex</i> (n=3)
Amoxicillin/clavulanic acid	-	-	-	R
Piperacillin/tazobactam	-	-	-	S
Cefuroxime	-	-	-	R
Cefuroxime axetil	-	-	-	R
Ceftriaxone	I	-	-	S
Cefoperazone/sulbactam	-	-	-	S
Cefepime	-	-	-	S
Ertapenem	-	-	-	S
Imipenem	-	-	-	S
Meropenem	-	-	-	S
Amikacin	-	-	-	S
Gentamicin	-	S	S	S
Ciprofloxacin	-	S	S	S
Tigecycline	S	S	S	S
Fosfomycin	-	-	-	R
Colistin	-	-	-	I
Trimethoprim/sulfamethoxazole	-	R	R	S
Benzympenicillin	-	R	R	-
Ampicillin	-	-	-	-
Cefotaxime	S	-	-	-
Levofloxacin	R	S	S	-
Moxifloxacin	S	-	-	-
Inducible clindamycin resistance	-	-	-	-
Erythromycin	-	R	R	-
Clindamycin	S	S	S	-
Linezolid	S	S	S	-
Teicoplanin	-	S	S	-
Vancomycin	-	S	S	-
Tetracycline	R	S	S	-
Chloramphenicol	S	-	-	-
Rifampicin	-	S	S	-
Cefoxitin screen	-	R	R	-
Ampicillin	-	R	R	-
Oxacillin	-	R	R	-
Cefazolin	-	R	R	-
Gentamicin high level	-	-	-	-
Daptomycin	-	S	S	-
Nitrofurantoin	-	S	S	-

Note: The chart uses a traffic light color scheme to indicate the resistance patterns of various organisms against selected antibiotics: red represents resistance (R), yellow indicates intermediate susceptibility (I), and green denotes susceptibility (S). This color-coded format provides a quick and clear visual representation of the antimicrobial effectiveness, highlighting critical areas of resistance and guiding therapeutic decisions.

Table 2. Antibiotic resistance pattern of Gram-negative microorganisms isolated from pediatric dental abscesses.

Antibiotics	Gram negative microorganisms(n=11)			
	<i>Enterobacter aerogens</i> (n=2)	<i>Klebsiella pneumoniae</i> (n=3)	<i>Citrobacter koseri</i> (n=3)	<i>Enterobacter cloacae</i> (n=3)
Amoxicillin/clavulanic acid	R	S	S	R
Piperacillin/tazobactam	S	S	S	S
Cefuroxime	R	S	S	R
Cefuroxime axetil	R	S	I	R
Ceftriaxone	S	S	S	S
Cefoperazone/sulbactam	S	S	S	S
Cefepime	S	S	S	S
Ertapenem	S	S	S	S
Imipenem	S	S	S	S
Meropenem	S	S	S	S
Amikacin	S	S	S	S
Gentamicin	S	S	S	S
Ciprofloxacin	S	S	S	S
Tigecycline	S	S	S	S
Fosfomycin	-	S	S	-
Colistin	I	I	I	I
Trimethoprim/sulfamethoxazole	S	S	S	S
Benzylnicillin	-	-	-	-
Ampicillin	-	-	-	-
Cefotaxime	-	-	-	-
Levofloxacin	-	-	-	-
Moxifloxacin	-	-	-	-
Inducible clindamycin resistance	-	-	-	-
Erythromycin	-	-	-	-
Clindamycin	-	-	-	-
Linezolid	-	-	-	-
Teicoplanin	-	-	-	-
Vancomycin	-	-	-	-
Tetracycline	-	-	-	-
Rifampicin	-	-	-	-
Cefoxitin screen	-	-	-	-
Ampicillin	-	-	-	-
Oxacillin	-	-	-	-
Cefazolin	-	-	-	-
Gentamicin high level	-	-	-	-
Daptomycin	-	-	-	-
Nitrofurantoin	-	-	-	-

Note: The chart uses a traffic light color scheme to indicate the resistance patterns of various organisms against selected antibiotics: red represents resistance (R), yellow indicates intermediate susceptibility (I), and green denotes susceptibility (S). This color-coded format provides a quick and clear visual representation of the antimicrobial effectiveness, highlighting critical areas of resistance and guiding therapeutic decisions.

Predominant Gram-positive Organisms in dental abscess:

The Gram-positive isolates included *Streptococcus oralis/mitis* (n=6), *Staphylococcus hominis* (n=3), *Bacillus altitudinis* (n=2), and *Peribacillus simplex* (n=3). Resistance patterns among these organisms revealed high resistance to amoxicillin/clavulanic acid, cefuroxime, cefuroxime axetil, and fosfomycin. All isolates demonstrated sensitivity to tigecycline, ertapenem, imipenem, meropenem, linezolid, and chloramphenicol. Notably, *Streptococcus oralis/mitis* displayed resistance to tetracycline and levofloxacin, while *Staphylococcus hominis* showed resistance to erythromycin, ceftioxin, and oxacillin, indicating potential methicillin resistance.

Predominant Gram-negative Organisms in dental abscess:

The Gram-negative isolates included *Enterobacter aerogens*(n=2), *Klebsiella pneumoniae* (n=3), *Citrobacter koseri*(n=3), and *Enterobacter cloacae* (n=3). These organisms exhibited a high level of susceptibility to piperacillin/tazobactam, ceftriaxone, cefoperazone/sulbactam, ertapenem, imipenem, meropenem, amikacin, and ciprofloxacin. However, resistance to amoxicillin/clavulanic acid and cefuroxime was observed in *Enterobacter cloacae* and *Enterobacter aerogens*, suggesting variability in susceptibility among *Enterobacter* species. Intermediate susceptibility to colistin was observed across all Gram-negative isolates. Amoxicillin/clavulanic acid exhibited the highest resistance rates, with resistance observed in all tested Gram-positive isolates and a significant proportion of Gram-negative isolates, including *Enterobacter cloacae* and *Enterobacter aerogens*. Similarly, cefuroxime displayed high resistance across multiple organisms, particularly among Gram-positive isolates. The limited efficacy of these antibiotics suggests their reduced suitability for empirical therapy in pediatric dental abscess cases.

The high resistance rates to amoxicillin/clavulanic acid may reflect its frequent use in outpatient settings, leading to selection pressure and the emergence of resistant strains. These findings underscore the importance of performing antibiotic susceptibility testing to guide clinical decision-making and avoid overreliance on antibiotics with established resistance trends.

Antibiotic Susceptibility

Carbapenems (ertapenem, imipenem, and meropenem), tigecycline, and amikacin demonstrated the highest efficacy, with universal sensitivity among both Gram-positive and Gram-negative isolates. In

contrast, amoxicillin/clavulanic acid and cefuroxime were the least effective, with widespread resistance observed in both groups.

DISCUSSION

Despite the increased incidence of odontogenic infections, there is a paucity of data on the bacteriological profile and the antimicrobial resistance pattern of the isolates. Such data are a prerequisite for the development of clinical recommendations and guidelines on the antibiotic prescribing practices to be adopted by dentists for the therapeutic management of odontogenic infections. In this study, Gram-positive bacteria dominated over Gram-negative bacteria, which is consistent with the previous report by Brescó Salinas et al in 2006.¹⁴

The most predominant organism isolated was similar to the study by Brescó-Salinas et al. in 2006, where *Streptococcus* species were the predominant organisms isolated.¹⁴ Samples from the periapical region were collected, and when compared to abscesses in other regions (i.e., pericoronal and periodontal), the antibiotic resistance pattern was studied more conveniently from periapical abscesses. This is similar to the study conducted by Kuriyama et al in 2000, where periapical abscesses accounted for 78%, while the rest were 26%.¹⁵

Previous reports suggest that unnecessary antibiotic prescriptions significantly contribute to the development of antibiotic resistance. Furthermore, antibiotic prophylaxis is rarely addressed in dentistry. Hence, periodic surveillance for antibiotic resistance, education on antibiotic stewardship, routine audits, and feedback could serve as essential interventions in hospital dental care and outpatient dental settings.

Brescó Salinas et al. in 2006 reported susceptibility rates of 91.4%, 34.2%, and 91.4% for *E. faecalis* against amoxicillin, azithromycin, and linezolid, respectively.¹⁴ *Streptococcus oralis* showed 37% sensitivity to amoxicillin, according to Mahalle et al. in 2014.¹⁶ While 76.95% were sensitive to azithromycin, according to Jagadish Chandra et al in 2017.¹⁷ 60% sensitivity for linezolid was observed, according to Jindal et al in 2019.¹⁸ For *Enterobacter* species, Abdulla et al in 2009 reported 0% sensitivity to amoxicillin, which was also observed by Prakash et al in 2016 for amoxicillin-clavulanate.^{19,20} These findings align with our study results.

Amoxicillin and amoxicillin-clavulanic acid are the empirical drugs commonly used for facultative anaerobes and aerobes. Tigecycline showed the highest

susceptibility rate of 100% in our study, followed by a 75% susceptibility rate for gentamicin, ciprofloxacin, linezolid, and teicoplanin in Gram-positive bacteria. Erythromycin or azithromycin are commonly used when patients are allergic to penicillin group antibiotics²¹ Linezolid, an oxazolidinone and a recent reserve drug, is used against multidrug-resistant Gram-positive organisms.²¹ Hence, linezolid was also tested alongside the commonly prescribed drugs. Linezolid is not recommended for Gram-negative bacteria, and no interpretation criteria were provided by both CLSI and EUCAST guidelines.²²

For Enterobacter species, which were 100% susceptible to amoxicillin, prescribing amoxicillin and clavulanic acid is unnecessary as it may contribute to the emergence of drug-resistant strains. Recent reports have also shown an emergence of beta-lactamase-producing *K. pneumoniae*, which aligns with our study results.²³

Chien et al. in 2021 concluded in their systematic review of eight studies that there are no ideal antibiotic regimens for treating orofacial infections.²⁴ They also stated that broad-spectrum antibiotics should not be prescribed indiscriminately, as narrow-spectrum antibiotics also offer effective results for otherwise healthy individuals.²⁵ In concurrence with Chien et al, our study suggests that evaluating the antibiotic resistance pattern of a patient's dental microbiota is crucial for effective antibiotic therapy and minimizing resistance development.

Pharmacologically, the selection of antibiotics should be based on their mechanism of action and the pharmacokinetic properties of the drug to ensure effective penetration into infected tissues. Beta-lactam antibiotics, such as amoxicillin and cephalosporins, act by inhibiting bacterial cell wall synthesis, making them highly effective against Gram-positive bacteria. However, resistance mechanisms, such as beta-lactamase production, have led to the need for beta-lactamase inhibitors like clavulanic acid. Macrolides, including erythromycin and azithromycin, function by inhibiting bacterial protein synthesis and are often used as alternatives in penicillin-allergic patients. Fluoroquinolones, such as ciprofloxacin, target bacterial DNA replication and have demonstrated efficacy against Gram-negative bacteria, although their use in dentistry is limited due to concerns over resistance.²⁶⁻²⁹

Following are the most commonly used antibiotics in dentistry:³⁰⁻³²

1. Amoxicillin: Most frequently prescribed due to

- broad-spectrum activity; adverse effects include
2. gastrointestinal disturbances and hypersensitivity reactions.
 3. Amoxicillin-Clavulanic Acid: Effective against beta-lactamase-producing bacteria; contraindicated in patients with liver disease. Azithromycin: Used for penicillin-allergic patients; may cause QT prolongation and gastrointestinal issues.
 4. Metronidazole: Effective against anaerobic infections; common side effects include nausea, metallic taste, and potential neurotoxicity.
 5. Clindamycin: Alternative for penicillin-allergic patients; associated with a high risk of *Clostridium difficile* infection.
 6. Ciprofloxacin: Used for Gram-negative infections; contraindicated in pregnant women and children due to cartilage toxicity.
 7. Linezolid: Reserved for multidrug-resistant infections; may cause myelosuppression with prolonged use.

Mechanisms of Resistance:

- Beta-lactamase production – Enzymatic breakdown of beta-lactam antibiotics.
- Efflux pumps – Actively pump out antibiotics, reducing intracellular drug concentration.
- Target site mutations – Alteration of antibiotic binding sites, reducing drug efficacy.
- Biofilm formation – Creates a protective environment that limits antibiotic penetration.

Contraindications and Cost:

Amoxicillin: Contraindicated in severe renal impairment; cost-effective.

Azithromycin: Caution in cardiac patients due to QT prolongation; moderately expensive.

Metronidazole: Avoid alcohol due to disulfiram-like reaction; inexpensive.

Amoxicillin: Contraindicated in severe renal impairment; cost-effective.

Azithromycin: Caution in cardiac patients due to QT prolongation; moderately expensive. Metronidazole:

Avoid alcohol due to disulfiram-like reaction; inexpensive.

Clindamycin: High risk of antibiotic-associated colitis; moderately priced. Linezolid: High cost; reserved for resistant infections.²⁷⁻³⁰

Pharmacotherapy of Antibiotic-Resistant Strains:

- Combination Therapy: Utilizing synergistic antibiotic combinations, such as beta-lactam antibiotics with beta-lactamase inhibitors (e.g., piperacillin-tazobactam) to combat resistant strains.
- Reserve Antibiotics: Linezolid, daptomycin, and tigecycline are used for resistant Gram-positive

- bacteria, whereas colistin and carbapenems (e.g., meropenem) are employed against resistant gram-negative bacteria
- Bacteriophage Therapy: Investigating the use of bacteriophages to target drug-resistant bacteria as an alternative treatment approach.
- Antimicrobial Peptides: Developing novel peptides that can disrupt bacterial membranes and evade resistance mechanisms.
- Adjunctive Therapies: The use of probiotics and immunomodulators to enhance host defense and reduce bacterial colonization.³³⁻³⁵

Antibiotic-resistant bacterial strains associated with dental and oral maxillofacial infections are a significant cause of morbidity and mortality worldwide and pose severe health concerns.²⁶⁻²⁸

Hence, patient education and public awareness about the proper use of antibiotics should be promoted to prevent misuse, such as over-the-counter drug purchases and self-medication. Additionally, implementing antibiotic stewardship programs, strict adherence to prescribing guidelines, and alternative therapeutic strategies, including adjunctive therapies like probiotics or antimicrobial peptides, should be explored in future research to combat the rising trend of antibiotic resistance effectively.

Continued research pertaining to orofacial infection of odontogenic origin with larger sample size is needed periodically as different bacterial strains emerge and the bacterial resistance to various antibiotics may vary from time to time. Advanced, rapid, feasible, cost-effective, less tedious, and technique sensitive laboratory procedures to process and to identify the bacterial strains and their sensitivity to antibiotics are required to combat emerging resistant strains.

CONCLUSION

The antimicrobial susceptibility testing revealed concerning levels of resistance to commonly prescribed antibiotics such as amoxicillin/clavulanic acid and cefuroxime, particularly among Gram-positive isolates. However, broad-spectrum antibiotics like tigecycline, carbapenems, and amikacin displayed high efficacy across all isolates, suggesting their potential role as reliable therapeutic agents in severe or resistant cases.

These findings emphasize the need for targeted antibiotic therapy informed by susceptibility testing to ensure effective treatment and to reduce the risk of antimicrobial resistance development. The wide

spread resistance observed in this study also underscores the importance of judicious antibiotic use in pediatric dental cases and advocates for continuous surveillance to monitor resistance trends. Future research should focus on evaluating alternative treatment strategies and exploring novel antimicrobial agents to manage resistant infections effectively.

DECLARATIONS

Ethical statement

This study was performed in line with the principles of the Declaration of Helsinki.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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