ORAL HEALTH AND MAXILLOFACIAL RESEARCH
Jan-Mar 2025, VOL. 2, ISSUE 1, pp. 20-25
https://doi.org/10.61577/ohmr.2025.100004

RESEAPRO JOURNALS

REVIEW

OPEN ACCESS

Emerging antibiotic resistance and its impact on dental and orofacial infection management

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ABSTRACT

Antibiotic resistance in odontogenic infections has become a critical challenge within dental and maxillofacial practice, compromising the effectiveness of established antimicrobial protocols. The inappropriate and excessive prescription of antibiotics, often administered empirically without microbiological confirmation, has facilitated the rise of multidrug-resistant oral pathogens, leading to increased morbidity, treatment failures, and higher healthcare costs. A targeted literature search was performed using PubMed, ScienceDirect, and Scopus, focusing on publications from 2010 to 2024. Keywords included "odontogenic infections," "antibiotic resistance," "oral microbiota," and "antimicrobial stewardship." Eligible studies were limited to human clinical research, systematic reviews, and meta-analyses; experimental and non-English studies were excluded. Key resistant pathogens identified include *Streptococcus* spp., methicillin-resistant *Staphylococcus aureus* (MRSA), *Prevotella* spp., and *Fusobacterium* spp., showing decreased susceptibility to penicillin, amoxicillin, and clindamycin. Resistance mechanisms involve β-lactamase production, efflux pumps, biofilm formation, and target modifications. Clinically, these patterns complicate management, requiring broader-spectrum or adjunctive therapies and increasing disease burden and costs. Antimicrobial stewardship initiatives have proven essential in optimizing antibiotic use and preserving efficacy. Limitations include the lack of standardized dental prescribing guidelines and insufficient resistance surveillance. Future research should emphasize rapid diagnostics and the development of novel therapeutics to improve infection management in dental practice. This review aims to provide dental professionals with an updated understanding of antibiotic resistance in odontogenic infections, emphasizing the importance of required antibiotic use and the potential of novel therapeutic approaches to mitigate resistance development.

KEYWORDS

Antibiotic resistance; Dental infections; Penicillin; Antimicrobial peptides; Odontogenic infections

ARTICLE HISTORY

Received 22 January 2025; Revised 28 February 2025; Accepted 07 March 2025

Introduction

Antibiotic resistance has become a major global health threat, significantly affecting infection management across medical and dental disciplines. In dentistry, antibiotics are routinely prescribed to manage odontogenic infections such as periapical abscesses, periodontitis, pericoronitis, and postoperative wound infections. However, the indiscriminate use of antibiotics, particularly empirical prescribing without microbiological confirmation, has facilitated the emergence of resistant oral pathogens. This has led to treatment failures, prolonged disease courses, and increased healthcare burdens, undermining the efficacy of standard antimicrobial therapies in dental and orofacial care [1].

Historically, the introduction of penicillin revolutionized the management of odontogenic infections, dramatically reducing the morbidity and mortality associated with orofacial infections. Over time, agents such as amoxicillin, metronidazole, and clindamycin became standard choices in dental antimicrobial therapy. Yet, despite their initial success, decades of misuse, often without clear clinical indication or diagnostic support, have created selective pressures that favor resistant strains [2]. Current evidence indicates that common oral pathogens, including *Streptococcus* spp., methicillin-resistant *Staphylococcus aureus* (MRSA), *Prevotella* spp., *Fusobacterium* spp., and *Enterococcus faecalis*, increasingly exhibit reduced susceptibility to penicillin, amoxicillin, macrolides, and clindamycin [3].

Globally, antibiotic resistance in dental pathogens has reached concerning levels. Reports estimate that nearly 60-70% of dental antibiotic prescriptions may be unnecessary, contributing directly to resistance trends. In some regions, penicillin resistance in oral anaerobes exceeds 30%, and MRSA colonization in the oral cavity is no longer rare, particularly in immunocompromised or elderly populations. The unchecked spread of resistance not only complicates routine dental treatments but also elevates the risk of systemic complications, hospitalization, and increased healthcare costs [4].

This review aims to provide an updated analysis of antibiotic resistance in dental and orofacial infections, focusing on the epidemiology, resistance mechanisms, and clinical impact. Additionally, it explores emerging management strategies, including antimicrobial stewardship, novel antimicrobials, and adjunctive therapies, intended to mitigate resistance development and improve patient outcomes. By consolidating current evidence, this review seeks to guide dental professionals in adopting evidence-based, judicious antibiotic use and in anticipating future directions for effective infection management in dental practice.

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Methodology

A systematic literature search was conducted to identify relevant clinical evidence addressing antibiotic resistance in dental and orofacial infections. The search was performed using three major biomedical databases: PubMed, Scopus, and Web of Science. The search strategy incorporated a combination of controlled vocabulary (MeSH terms) and free-text keywords, including "antibiotic resistance," "odontogenic infections," "dental pathogens," "biofilm," "oral microbiome," "antimicrobial stewardship," and "alternative therapies." Boolean operators were applied to combine terms and refine the search for maximum relevance.

Inclusion criteria were defined as human clinical studies, systematic reviews, and meta-analyses published between January 2010 and March 2024, focusing on antibiotic resistance patterns, mechanisms, prescribing trends, stewardship practices, or alternative treatments related to dental infections. Only articles published in peer-reviewed journals and available in English were considered. Exclusion criteria included in vitro studies, animal studies, case reports, editorials, conference abstracts, and non-English publications.

The search initially yielded approximately 550 articles. After removing duplicates, titles and abstracts were screened for relevance to antibiotic resistance in dental practice, narrowing the selection to 130 articles for full-text review. Following detailed eligibility assessment, 72 studies fulfilling the inclusion criteria were retained for synthesis in this review. The screening process was conducted by two independent reviewers to minimize selection bias. Disagreements were resolved through discussion and consensus. No formal risk of bias assessment or quality grading tool was applied, as the review aimed to provide a broad synthesis of current clinical evidence rather than perform a quantitative meta-analysis.

Antibiotic Use in Dentistry

Common dental infections requiring antibiotics

Odontogenic infections are among the most frequent bacterial infections encountered in dental practice. Antibiotic therapy is indicated primarily when infections extend beyond local tissue boundaries or present with systemic signs such as fever, lymphadenopathy, or spreading cellulitis. Periapical abscesses, originating from pulpal necrosis, can result in localized pus accumulation at the apex of the tooth root; while drainage remains the primary management, antibiotics are warranted if systemic involvement is present [5]. Periodontal infections, including periodontal abscesses and necrotizing periodontal diseases, affect the periodontium and may progress rapidly in immunocompromised or systemically compromised patients, requiring adjunctive antibiotic therapy. Post-surgical infections, though less common in routine dental practice, can occur following extractions, implant placements, or bone grafting, particularly in patients with diabetes, immunosuppression, or poor wound healing capacity, necessitating systemic antibiotic administration alongside local debridement [6].

Commonly prescribed antibiotics

Amoxicillin remains the first-line agent for odontogenic infections due to its broad spectrum and favorable pharmacokinetic properties. In cases of penicillin allergy, clindamycin is frequently used for its robust anaerobic and Gram-positive coverage. Metronidazole, with potent anaerobic activity, is often combined with amoxicillin for severe or refractory infections. Macrolides, such as azithromycin, are alternatives in select cases, particularly for patients unable to tolerate β-lactam or lincosamide antibiotics. Selection of antibiotics should be guided by clinical presentation, suspected pathogens, and regional resistance patterns [7].

Misuse and over prescription

Despite established guidelines, antibiotics are often overprescribed in dentistry. Commonly observed inappropriate practices include prophylactic antibiotic use in low-risk patients undergoing minor dental procedures, prescribing antibiotics for irreversible pulpitis or localized infections amenable to operative treatment, and unnecessarily prolonged treatment durations [8]. Patient-driven demand, diagnostic uncertainty, time pressures, and medicolegal concerns are key contributors to this misuse. Such practices not only provide little to no clinical benefit but also accelerate the development of antimicrobial resistance, complicating future treatment options [9]. Table 1 explains the dental infections, required antibiotics, their dosage and side effects of overdosage.

Table 1. Overview of dental infections, prescribed antibiotics, dosage and side effects of overdosage.

Dental Infection	Antibiotics	Dosage	Duration	Dosage Mode	Common Side Effects
Periapical Abscess	Amoxicillin	500 mg every 8 hours	3–7 days	Oral	Diarrhea, rash, nausea, hypersensitivity reactions
	Clindamycin (if penicillin-allergic)	300 mg every 8 hours	3–7 days	Oral	Diarrhea, pseudomembranous colitis, metallic taste
	Metronidazole (adjunct)	500 mg every 8 hours	5–7 days	Oral	Metallic taste, gastrointestinal upset, dizziness
Periodontal Infections	Amoxicillin + Metronidazole	500 mg amoxicillin + 500 mg metronidazole every 8 hours	7 days	Oral	Metallic taste, gastrointestinal upset, dizziness
	Clindamycin (alternative)	300 mg every 8 hours	7 days	Oral	Metallic taste, gastrointestinal upset, dizziness
Post-Surgical Infections	Amoxicillin/Clavulanate	875/125 mg every 12 hours	5–7 days	Oral	Diarrhea, gastrointestinal upset, allergic reactions
	Clindamycin (if penicillin-allergic)	300 mg every 8 hours	5–7 days	Oral	Diarrhea, gastrointestinal upset, allergic reactions
	Azithromycin (alternative)	500 mg once daily	3 days	Oral	Gastrointestinal upset, QT prolongation, headache

https://doi.org/10.61577/ohmr.2025.100004

Global prescribing trends

Antibiotic prescribing patterns in dental practice vary internationally. Data show that dental prescriptions account for approximately 7-10% of all outpatient antibiotic use in high-income countries. In the United States, amoxicillin and clindamycin dominate dental antibiotic prescribing, while metronidazole use is more prevalent in the United Kingdom and Australia, reflecting local microbial profiles and prescribing guidelines. In low and middle-income countries, over-the-counter antibiotic access and lack of stewardship frameworks further exacerbate inappropriate use [4]. Global efforts to harmonize prescribing practices and implement antibiotic stewardship interventions in dentistry are critical to reducing resistance and safeguarding the efficacy of available antimicrobial agents [10].

Mechanisms of Antibiotic Resistance

Genetic mechanisms of resistance

Oral pathogens employ several genetic strategies to evade antibiotic action, reducing the clinical efficacy of standard antimicrobial therapies. One prominent mechanism is enzymatic inactivation, where bacteria produce β-lactamases that hydrolyze the β-lactam ring of penicillins and cephalosporins, neutralizing their antibacterial activity [11]. This mechanism is widespread among anaerobic oral bacteria, including *Prevotella* and *Porphyromonas* species. Another major resistance pathway involves target site modification. Alterations or mutations in penicillin-binding proteins (PBPs) lower the binding affinity of β-lactam antibiotics, effectively rendering them ineffective. This mechanism has been documented in oral streptococci and staphylococci, contributing to the persistence of infections despite therapy [12]. Additionally, bacterial efflux pumps actively transport antibiotics out of the cell, reducing intracellular drug concentrations below therapeutic levels. These pumps, which span multiple antibiotic classes, play a significant role in resistance to tetracyclines, macrolides, and fluoroquinolones among oral isolates [13] [Figure 1].

Role of biofilms in resistance

Biofilms play a critical role in dental infections and significantly enhance bacterial survival against antibiotics. The biofilm matrix acts as a physical barrier, limiting antibiotic penetration and creating concentration gradients. Furthermore, biofilm-associated bacteria exhibit altered metabolic states, including slow growth or dormancy, reducing their susceptibility to antibiotics that target active cellular processes [14]. The close proximity of cells within biofilms also facilitates horizontal gene transfer, promoting the spread of resistance genes across bacterial populations. Dental plaque, a natural oral biofilm, serves as a key reservoir for resistant organisms, complicating the management of periodontal and endodontic infections [15].

Major resistant pathogens in dentistry

Several clinically important oral pathogens have demonstrated notable antibiotic resistance. *Streptococcus mutans*, a primary agent in dental caries, has shown increasing resistance to tetracyclines and erythromycin, complicating adjunctive antibiotic strategies in caries control. Porphyromonas gingivalis, implicated in chronic periodontitis, exhibits resistance to macrolides and β-lactams, driven by both β-lactamase production and robust biofilm formation [16]. Methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as a concerning oral colonizer, particularly in immunocompromised individuals and patients with healthcare exposure; its multidrug resistance profile includes resistance to β-lactams and several non-β-lactam agents. *Enterococcus faecalis*, frequently isolated in persistent root canal infections and failed endodontic treatments, displays intrinsic resistance to several antibiotics, including cephalosporins and, in some strains, vancomycin, making eradication particularly challenging [17] [Table 2].

Table 2. Oral Antibiotics and resistant pathogens.

Oral Disease	Antibiotics	Mode of Application	Resistant Pathogen	Mode of Resistance
Dental caries	Amoxicillin, Erythromycin	Oral	*Streptococcus mutans*	Efflux pumps, PBPs modification, macrolide target site changes
Periodontitis	Metronidazole, Clindamycin	Oral / Topical	*Porphyromonas gingivalis*	β-lactamase production, biofilm-mediated tolerance, ribosomal protection
Endodontic infections (root canals)	Penicillin, Clindamycin	Oral	*Enterococcus faecalis*	Intrinsic vancomycin resistance, biofilm formation, efflux pump mechanisms
Peri-implantitis	Doxycycline, Amoxicillin	Local irrigation / Oral	*Aggregatibacter actinomycetemcomitans*	Outer membrane changes, β-lactamase, biofilm resistance
Postoperative dental infections	Amoxicillin–Clavulanate	Oral	Methicillin-resistant *Staphylococcus aureus*	mecA gene encoding PBP2a, β-lactamase, multidrug efflux pumps
Necrotizing periodontal disease	Metronidazole, Penicillin	Oral	*Fusobacterium nucleatum*	β-lactamase, metronidazole resistance (nitroreductase mutation)
Chronic gingivitis	Tetracycline, Doxycycline	Topical / Oral	*Prevotella intermedia*	Tetracycline-specific efflux pumps (tetQ), ribosomal protection proteins

https://doi.org/10.61577/ohmr.2025.100004

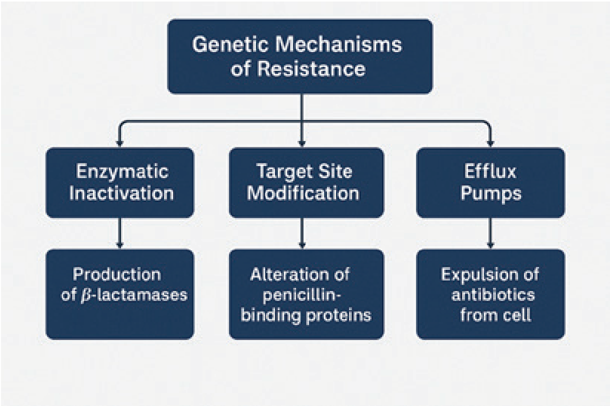

Figure 1. Flowchart representing Genetic Mechanisms of Resistance.

Antibiotic Stewardship in Dentistry

Principles of antibiotic stewardship in dental practice

Antibiotic stewardship in dental care involves coordinated strategies to promote the proper use of antimicrobial agents, aiming to optimize clinical outcomes while minimizing the risk of antimicrobial resistance. Dentists contribute a notable share of outpatient antibiotic prescriptions, with studies indicating that up to 80% of these prescriptions may be unnecessary. Core stewardship principles in dental settings include prescribing antibiotics only when bacterial infections are confirmed or strongly suspected, selecting narrow-spectrum agents tailored to the pathogens, and determining the shortest effective treatment duration. Dentists are encouraged to integrate evidence-based prescribing into routine practice, document indications and rationale for antibiotic use, and continuously evaluate prescribing patterns to identify areas for improvement [18].

International and national guidelines

Professional organizations have established evidence-based guidelines to standardize antibiotic prescribing in dental care. The European Society of Endodontology (ESE) advises that antibiotics are not needed for routine endodontic cases and should be reserved for patients exhibiting systemic signs such as fever, lymphadenopathy, or cellulitis. The American Association of Endodontists (AAE) similarly recommends limiting antibiotic use to situations involving systemic spread or immunocompromised status, emphasizing that antibiotics are not a substitute for definitive dental treatment [19]. The World Health Organization (WHO) highlights dentistry as a key target in its global action plan on AMR, urging national dental bodies to align with antimicrobial stewardship goals. National guidelines, such as those by the National Institute for Health and Care Excellence (NICE) in the UK and the American Dental Association (ADA), reinforce these recommendations, providing clinicians with standardized, context-specific prescribing frameworks [20].

Education and awareness among dental professionals

Surveys reveal that many dental professionals possess limited formal training in antimicrobial stewardship but demonstrate a willingness to improve prescribing behaviors when supported by targeted education. Incorporating stewardship training into undergraduate and postgraduate dental curricula, offering regular education programs, and providing access to updated prescribing guidelines are essential measures to enhance practitioner competence. Educational initiatives should cover local resistance trends, the rationale for restricted antibiotic use, and non-antibiotic management strategies to ensure dentists remain current and confident in stewardship practices [21].

Challenges in implementation

Despite global efforts, several barriers complicate stewardship implementation in dentistry. Many dental clinics lack access to rapid microbiological diagnostics, leading to reliance on empirical treatment. Additionally, localized surveillance data on oral pathogen resistance patterns are often scarce, making it difficult for clinicians to select antibiotics based on regional susceptibility profiles. In low and middle-income countries, financial constraints and limited health infrastructure further burden stewardship efforts [22]. Moreover, repeated prescribing habits, patient expectations for antibiotics, and medicolegal concerns contribute to unnecessary antibiotic use. Addressing these challenges requires coordinated action, including the development of region-specific guidelines, investment in diagnostic resources, integration of stewardship principles into clinical protocols, and public education to reduce patient-driven demand for antibiotics. Strengthening these measures is essential to preserving antibiotic efficacy and safeguarding future dental treatment outcomes [23].

Emerging Alternatives and Future Directions

Antimicrobial peptides

AMPs are small, naturally occurring molecules produced by the host immune system, known for their potent activity against bacteria, fungi, and viruses. In dental applications, AMPs such as human β-defensins and cathelicidin (LL-37) disrupt microbial membranes, leading to bacterial lysis and death. Studies have shown AMPs to be particularly effective against *Streptococcus mutans* and Porphyromonas gingivalis, key pathogens in dental caries and periodontitis, respectively [24]. Beyond direct antimicrobial action, AMPs also modulate local immune responses and promote tissue repair. However, their clinical use faces limitations, including rapid degradation by proteases in the oral cavity, potential cytotoxicity at high concentrations, and high manufacturing costs. Research is currently focused on developing synthetic AMP analogs and encapsulated delivery systems to improve stability and targeted application [25].

Probiotics and microbiome modulation

Probiotic therapies aim to restore microbial balance in the oral cavity by introducing beneficial bacteria that outcompete pathogenic species. Strains such as Lactobacillus reuteri, Streptococcus salivarius, and Bifidobacterium spp. have demonstrated capacity to reduce plaque accumulation, lower gingival inflammation, and inhibit the growth of periodontal pathogens. Clinical trials report reductions in P. gingivalis and Aggregatibacter actinomycetemcomitans levels following probiotic supplementation [26]. Mechanistically, probiotics work through competitive exclusion, production of bacteriocins, and modulation of local immune responses. Despite promising findings, challenges remain, including variability in strain-specific efficacy, inconsistent dosing

https://doi.org/10.61577/ohmr.2025.100004

regimens, and lack of long-term safety data. Standardized protocols are needed before routine clinical use can be recommended [27].

Photodynamic Therapy (PDT)

PDT uses a photosensitizing agent, such as methylene blue or toluidine blue, activated by a specific wavelength of light to generate reactive oxygen species that destroy bacterial cells. PDT has been successfully applied as an adjunct in the treatment of periodontitis, peri-implantitis, and root canal disinfection. Reported bacterial load reductions range from 50% to 85% depending on treatment parameters. Advantages of PDT include minimal systemic toxicity, absence of resistance development, and targeted application. However, its clinical adoption is limited by factors such as the need for specialized light sources, variability in photosensitizer effectiveness, and additional treatment time [28].

Novel delivery systems and materials

Nanotechnology offers innovative strategies to overcome biofilm-related antimicrobial resistance in the oral cavity. Nanoparticles, such as silver, chitosan, and zinc oxide, exhibit intrinsic antimicrobial properties and can penetrate biofilm matrices, delivering drugs directly to infection sites. Additionally, antimicrobial coatings on dental implants and restorative materials have been developed to prevent bacterial adhesion and secondary infections. Controlled-release nanoparticle systems offer the advantage of sustained drug delivery, reducing the need for repeated applications. Despite promising laboratory results, concerns regarding biocompatibility, potential cytotoxic effects, and long-term environmental impact must be addressed through rigorous in vivo studies and clinical trials [29].

While emerging antimicrobial strategies in dentistry show significant promise, several research gaps remain. There is a need for large-scale, randomized clinical trials to evaluate the long-term efficacy and safety of AMPs, probiotics, PDT, and nanomaterials in diverse patient populations. Standardization of dosages, delivery methods, and treatment protocols is essential for reproducibility. Additionally, understanding the interactions between these novel therapies and the host immune system will inform the development of personalized, precision-based approaches. Future research should also focus on cost-effectiveness analyses and strategies to integrate these technologies into routine clinical practice while ensuring patient compliance and acceptance [30].

Conclusion

Antibiotic resistance has become a critical threat in dental and orofacial infection management, undermining the effectiveness of standard antimicrobial treatments. This review highlights how inappropriate antibiotic prescribing, particularly without microbiological confirmation, has accelerated the emergence of resistant pathogens such as Streptococcus mutans, Porphyromonas gingivalis, Enterococcus faecalis, and MRSA. These organisms, through mechanisms like β-lactamase production, efflux pump activity, and biofilm formation, now frequently resist first-line therapies, leading to prolonged infections and higher treatment costs.

Despite clear international guidelines, studies report that up to 60-70% of dental antibiotic prescriptions remain unnecessary, often issued for self-limiting conditions or prophylactic purposes in low-risk procedures. Organizations such as the European Society of Endodontology and the American Association of Endodontists emphasize that antibiotics should be restricted to cases with systemic signs or confirmed bacterial spread, with priority given to operative interventions. Emerging solutions such as antimicrobial peptides, probiotics, photodynamic therapy, and nanoparticle-based systems show promise in overcoming resistance barriers, but require further clinical validation before routine integration into practice.

Dentists play a central role in controlling antimicrobial resistance by applying evidence-based prescribing, engaging in ongoing education, and guiding patients toward appropriate antibiotic use. However, progress requires global cooperation aligning dental practice within broader antimicrobial stewardship efforts, improving local resistance surveillance, and supporting research into novel therapeutics. In conclusion, addressing antibiotic resistance in dentistry demands immediate, coordinated action combining clinical vigilance, innovation, and international partnership to preserve the effectiveness of antimicrobial therapies for future dental care.

Disclosure statement

No potential conflict of interest was reported by the author.

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