World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

Check for updates

Antimicrobial Resistance (AMR) and Dentistry: A lethal connect

C.S. Baiju [1] and Diya Pandey [2,*]

[1] *Department of Periodontics and Oral Implantology, Sudha Rustagi College of Dental Sciences and Research, Faridabad, Haryana, India.*
[2] *Sudha Rustagi College of Dental Sciences and Research, Faridabad, Haryana, India.*

World Journal of Advanced Research and Reviews, 2024, 22(03), 1600–1610

Publication history: Received on 18 May 2024; revised on 25 June 2024; accepted on 27 June 2024

Article DOI: https://doi.org/10.30574/wjarr.2024.22.3.1905

Abstract

In the unfolding narrative of global health, the ominous spectre of antimicrobial resistance (AMR) looms large, presenting an ever more urgent challenge to public health systems worldwide. Antibiotics are a primary tool in the field of therapeutic medicine & dentistry & they saturate the Indian pharmaceutical markets. Dentistry places substantial reliance on use of antibiotics in prophylaxis & therapy, but this dependence contributes to the overuse & misuse of these drugs. A significant number of prescriptions are frequently deemed superfluous. Furthermore, antibiotics are readily accessible over the counter in addition to being subject to notable instances of overprescription. The absence of timely antibiotic culture & susceptibility tools accelerates the dissemination of resistance, resembling a wildfire.

Given current trends, it appears we are unwittingly fostering a situation akin to Frankenstein's monster. But is this foresight or mere paranoia? Our focus must centre not only on bolstering surveillance but also on the understanding of the need of antibiotics in dental treatment, advocating for responsible antibiotic usage & advancing research into innovative treatments, in return fortifying healthcare systems. Failure to curb the spread of antimicrobial resistance, at best- jeopardises individual health to a point of no return, & at its worst- undermines the sustainability of modern medicine as we know it. This article is aimed to depict the contemporary landscape of antimicrobial resistance within the realm of dentistry ,speculate on its potential detrimental trajectory.

Key words- Antimicrobial resistance (AMR); Overprescription; Dental treatment; Impending pandemic

1. Introduction

Antimicrobials are a group of medications that either eradicate or restrain the growth of microorganisms. This category includes antibiotics, antivirals, antifungals, and antiparasitics. They are essential drugs used to combat infectious diseases in humans, animals, and plants.Antimicrobial Resistance (AMR) arises when microorganisms like bacteria, viruses, fungi, and parasites develop insensitivity to these medicines. This renders antimicrobial drugs ineffective, making their infections challenging or impossible to treat. Consequently, there's an elevated risk of disease transmission, severe illness, morbidity and mortality.(1)

Upon the introduction of antimicrobials, most bacteria are eradicated, yet some persist. Development of resistance is an inherent process that unfolds gradually due to genetic shifts in pathogens.Through repeated cycles of exposure to antimicrobials, only the fittest survive, leading to the development of highly resistant strains. Human actions, especially the overuse and abuse of antimicrobials for treating, preventing, or controlling infections , hence, accelerate the emergence and spread of AMR.(1)

* Corresponding author: Diya Pandey

2. Evolution and Identification of resistant bacteria

AMR is one of the WHOs major global health concerns(1). Over time, bacteria have evolved various adaptive mechanisms to resist antibiotics. The primary methods of AMR include enzymatic inactivation of antimicrobial compounds, alteration of a drug target, reduced permeability of the outer membrane, and active drug efflux (13).Hydrolases, passivation, and modified enzymes are among the critical drug-inactivating enzymes. The modification of target sites is a significant factor in the development of drug resistance in Gram-positive bacteria, such as gene PBP2a in methicillin-resistant Staphylococcus aureus (MRSA), MRSA by the acquisition of the mecA gene and similar variants, as well as in polymyxin-resistant bacterial strains.Altering the bacterial envelope by reducing porin production or enhancing the expression of efflux pump systems has also been reported(14). Current testing modalities include the contemporary methods like broth dilution, agar dilution, disk diffusion and newer methods like chromogenic media and genomic methods. Their disadvantage being common- they all are time consuming methods. Some other methods include automated systems for susceptibility testing, genetics methods and Matrix-assisted laser desorption ionisation-time of flight mass spectrometry (MALDI-TOFMS) but being either highly technical or high cost procedure they can not be used routinely(13). The PA-100 AST System by Sysmex Astrego has recently won the Longitude Prize for its advanced point-of-care test for Urinary Tract Infections (UTIs). This technology swiftly identifies the UTI-causing bacteria and conducts antibiotic susceptibility testing in less than 45 minutes, aiding in personalised antibiotic selection.(30) This provides promising prospects for future advancements and the application of comparable technology to combat antibiotic resistance in the oral environment.

3. Present situation and statistics

According to the World Health Organization (WHO) in 2019, AMR was directly responsible for a staggering 1.27 million deaths, disproportionately impacting socioeconomically vulnerable regions.About 410,000 children under five years old die from pneumonia in India each year, representing nearly a quarter of all child deaths. The current crude mortality rate from infectious diseases in India is 417 per 100,000 people, indicating a potentially greater impact of AMR in this context(18).

Recently, Global AMR and Use Surveillance System (GLASS) report 2022 indicate a concerning trend, with 76 countries exhibiting significant rates of resistance, particularly evident in third-generation cephalosporin-resistant E. coli (42%) and methicillin-resistant Staphylococcus aureus (35%) .Klebsiella pneumoniae, a frequently found bacterium in the intestines, has demonstrated higher resistance to essential antibiotics. This resistance escalation may necessitate the increased use of last-resort medications such as carbapenems, resistance to which has also started spreading across various areas.(1) This is often referred to as ‘Resistome’ which is the total compilation of antibiotic resistance genes (ARGs) and their precursor. It includes genes from both harmful and harmless bacteria, like the ones that cause diseases, the ones that produce antibiotics themselves, and the ones that don't harm us. It is present in the living beings and the ecosphere beyond the living body- the land, air and water.(2)

In the oral ecosystem it has emerged as the oral resistome. A recent research project used shotgun metagenomics to analyse oral and gut samples collected from healthy individuals across various countries. They discovered variations in the prevalence of antibiotic resistance genes (ARGs) both among countries and between oral and stool samples. Specifically, they observed that oral samples had a higher abundance but lower diversity of ARGs compared to gut samples(3). Forces us to think if we are treading the path of resistance just a few steps behind Klebsiella pneumoniae.It isn't a trend limited to bacteria , drug resistant fungi and viruses have also seen a surge recently, specially in the post COVID-19 era.

Where may it lead us? According to forecasts from the Organization for Economic Cooperation and Development (OECD), there is an expected doubling in resistance to last-resort antibiotics by 2035 compared to levels seen in 2005. This highlights the pressing necessity for strong antimicrobial stewardship measures and improved surveillance globally.(1).

4. Anticipated Catastrophe

Consider a scenario where an individual is afflicted with a debilitating ailment, and the responsible bacteria are classified as highly resistant to nearly all medications except a limited few. Regrettably, these select treatments are either unavailable or financially unfeasible for the patient. Consequently, as the disease advances unabated, the only recourse may be to await the patient's eventual demise from sepsis. This underscores the profound severity of the problem.

In India, the prevalence of methicillin-resistant Staphylococcus aureus (MRSA) increased from 29% in 2008 to 47% by 2014(18).Gram-positive bacteria like MRSA and vancomycin-resistant Enterococcus were significant areas of concern ten years ago. However, the focus has now shifted towards multidrug-resistant Gram-negative bacteria, which are developing resistance more rapidly and have fewer treatment options available.(5). Historically, strain named CTX-M-15 (Cefotaximase-Munich) extended-spectrum β-lactamase (ESBL) encoded by *blaCTX-M-15* gene was reported in India in mid 1990s which showed resistance to third gen cephalosporins in enterobacteriaceae .Recent studies have found ESBLs present in 70–90% of Enterobacteriaceae in India. The Indian Network for Surveillance of Antimicrobial Resistance (INSAR) found that MRSA had a prevalence rate of 41% across 15 tertiary care centres. Additionally, the study revealed significant resistance rates to antibiotics such as ciprofloxacin, gentamicin, cotrimoxazole, erythromycin, and clindamycin.(18)

The newer strain New Delhi metallo-β-lactamase 1 (NDM-1) has been the object of extensive scientific study and it has been concluded that most of the strains are resistant to all antibiotics except colistin and tigecycline.(15) A recent article talks about how many people in India are using antibiotics without a prescription, which is causing a big problem(6). This can make the issue of NDM-1 much worse in the future. It's worrying as the speed with which the plasmids are being transferred, is much higher than the speed with which scientific bodies can come up with new antibiotics and agents.Additionally, it's concerning that many isolates from India, particularly in Chennai and Haryana, are from community-acquired infections, indicating that strain *bla NDM-1* is prevalent in the environment.(7) The prevalence of the strain in community actually poses a risk to the tourists as well. Some UK patients infected with blaNDM-1 had elective surgeries, including cosmetic procedures, in India or Pakistan. India offers cosmetic surgery to people globally, indicating the potential worldwide spread of blaNDM-1.Encouraging UK patients to seek corrective surgery in India with the aim of saving NHS costs could result in unforeseen expenses.(15) In the recent update of the Bacteria Priority Pathogens List 2024 by the World Health Organization, certain resistant bacteria that have recently shown a rise in occurrence have been categorized as follows:(29) [FIGURE 1.]

Figure 1 Adapted from WHO-BPPL 2024(29)

5. Clinical relevance of AMR in dentistry & its presence

Dentistry is as causative as afflicted by AMR. Overprescription prevails in dentistry of which allegedly 66% of antibiotics prescribed are deemed unnecessary.(9) But the total number of antibiotics being used for dental treatments is very

high, accounting to informal health care providers(ICHP) including Providers of medications, traditional birth assistants, unlicensed allopathic practitioners, traditional medicine practitioners, spiritual healers, and practitioners of homoeopathy and self medication. Khare et al.'s research found that while dental patients comprised 8% of all patients visiting ICHP they comprise 10% of the total antibiotic prescriptions.(8)

Ongoing research to understand AMR from a dental standpoint is based on results obtained from the sequence-based and functional metagenomics. Utility of new gene sequencing has also been studied.(12) Presently, there is limited understanding regarding how antibiotics impact the oral resistome. Early investigations suggest that antibiotics may exert only a minimal influence on the oral microbiome, which appears to be more robust and stable compared to other microbiomes in the human body. Initial findings even suggest that after antibiotic use, the oral microbiota rebounds easily and rather quickly, unlike the gut microbiome.(11).

6. Areas of concern

One of the primary worries regarding AMR revolves around the potential emergence of bacteria that demonstrate high levels of resistance to current therapeutic options, rendering healthcare providers and patients without effective tools to combat infections. The lack of effective treatment options for multidrug resistant pathogens can severely compromise the success of medical interventions ranging from routine surgeries to complex procedures such as organ transplants.

6.1. Overcoming Shortcomings of Antibiotic Understanding and Testing

A fundamental concern lies in the criteria governing the prescription of antimicrobial drugs. Currently, there are limited guidelines available, such as those provided by the American Dental Association (ADA) and certain ministries in South Asian countries like Malaysia and the Philippines. However, within the Indian Dental Community, there is a notable absence of such guidelines, leading many practitioners to rely on personal judgement when prescribing drugs.Reasons for prescription among dentists remain as varied as therapeutic, prophylactic , lack of knowledge or simply from the fear of losing patients (10). The National Action Plan on Antimicrobial Resistance (NAP-AMR) 2017 – 2021 of India mentions Dental Council of India (DCI) as one of the key stakeholders , however, the understanding of AMR in dentistry and related substantial research is miles behind in comparison to other medical sectors.(18)

Another significant issue revolves around the administration of suboptimal doses of drugs. Whether due to shortcomings in sterilisation processes, incomplete administration of antimicrobials, or the use of ineffective antibiotics, bacteria that manage to survive are more likely to develop AMR. Therefore, the comprehension of antimicrobials by dentists becomes increasingly crucial in addressing this concern.Another significant issue is the absence of rapid methods for assessing antibiotic susceptibility. Current testing methods often take significantly longer than the time it takes for bacterial colonies to prosper. Consequently, by the time susceptibility is determined and a more suitable treatment regimen is implemented, the patient may have already suffered considerable harm.

6.2. Antimicrobial agents being misused

Overuse of certain drug classes undeniably increases the threat of AMR.The WHO's AWaRe classification system for antibiotics, devised in 2017, aids antibiotic stewardship efforts globally. It categorises antibiotics into Access, Watch, and Reserve groups based on their impact on AMR , advocating for their appropriate use. This classification undergoes biennial updates to ensure relevance and effectiveness in combating AMR .(17).A study found that among the 23 most commonly used antibiotics in Indian dental setups, twelve were classified as "Access" and eleven as "Watch" by the World Health Organization (WHO). [FIGURE:2]

Thirteen of these antibiotics were listed in India's National List of Essential Medicines (NLEM) for 2015. Among the nine fixed-dose combinations (FDCs) used, only two (amoxicillin/clavulanic acid and co-trimoxazole) were categorised as "Access" and included in India's NLEM(10). Indian clinicians commonly tend to favour specific drugs or combinations of drugs. Due to the excessive use of these agents, there's a theoretical possibility that resistance could emerge prematurely. Research on the same topic needs to be conducted.[FIGURE 3]

Figure 2 Adaptation from WHO AWaRe classification(17)

Figure 3 The list of drugs/ drug combinations not recommended by WHO

6.3. Contribution of Dentistry in One Health Concept

According to WHO, addressing AMR requires coordinated efforts across various sectors including human health, food production, animal welfare, and the environment. The One Health approach integrates these sectors to achieve optimal and sustainable health outcomes for humans, animals, and ecosystems. It recognizes the interconnectedness of human health, animal health, plant health, and environmental health. (1). The role of dentists extends beyond merely reducing antibiotic prescriptions; it also involves understanding their contribution to antimicrobial pollution. A significant concern lies in the inadequate disposal of antibiotics, particularly antiplaque and anticalculus mouthwashes utilised in dental clinics or prescribed by dentists, which often enter the common sewage system without proper monitoring. This presents a substrate for bacteria to engage in evolutionary processes, facilitating their adaptation and potential development of resistance. Secondly, it is important to understand how the left over or expired antibiotics are disposed of. In a study aimed to understand antibiotic awareness of parents of paediatric patients, It was observed that many parents either discard antibiotics by throwing them into household bins, leading to their eventual deposition in landfills, or pour liquid antibiotics down the drain. Alternatively, some parents return unused antibiotics to pharmacies and some simply pass them on to the next needy.(15). These patterns of poor disposal and misuse of antibiotics would accelerate the emergence of superbugs in the environment, particularly in densely populated countries like India, where high population density increases the ease of cross-contamination (1).[FIGURE 4]

7. Possible solutions

Insufficient focus on dental contributions and potentially underestimated antibiotic usage highlight the distant prospect of effective solutions to India's AMR . Tailored, context-specific approaches are crucial for meaningful progress in the country with the largest population.

7.1. Governance and Strategic Initiatives

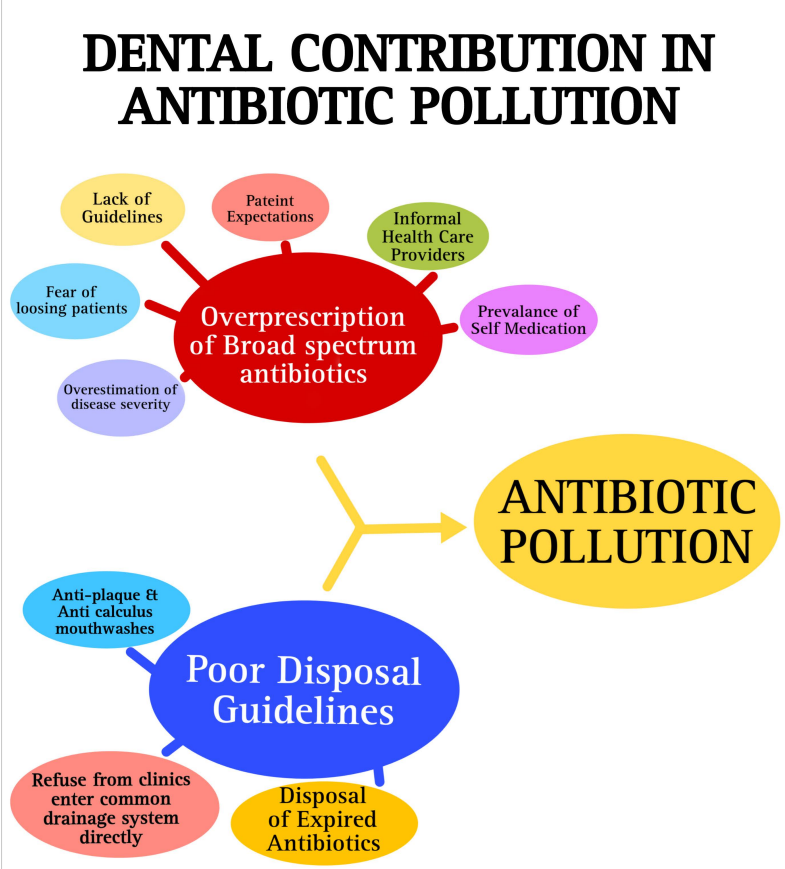

Figure 4 Flowchart summarising how dentists contribute to antibiotic pollution

The current governance framework includes three key components: an intersectoral coordinating committee to oversee and align policies across all sectors related to AMR and public health goals, a Technical Advisory Group on AMR to

review and recommend initiatives, and a Core Working Group on AMR to provide technical and operational support to India's national coordinating centre for AMR.

This was the result of a bilateral discussion between the premiers of India & US to tackle AMR in Indian Scenario(18).[FIGURE 5]

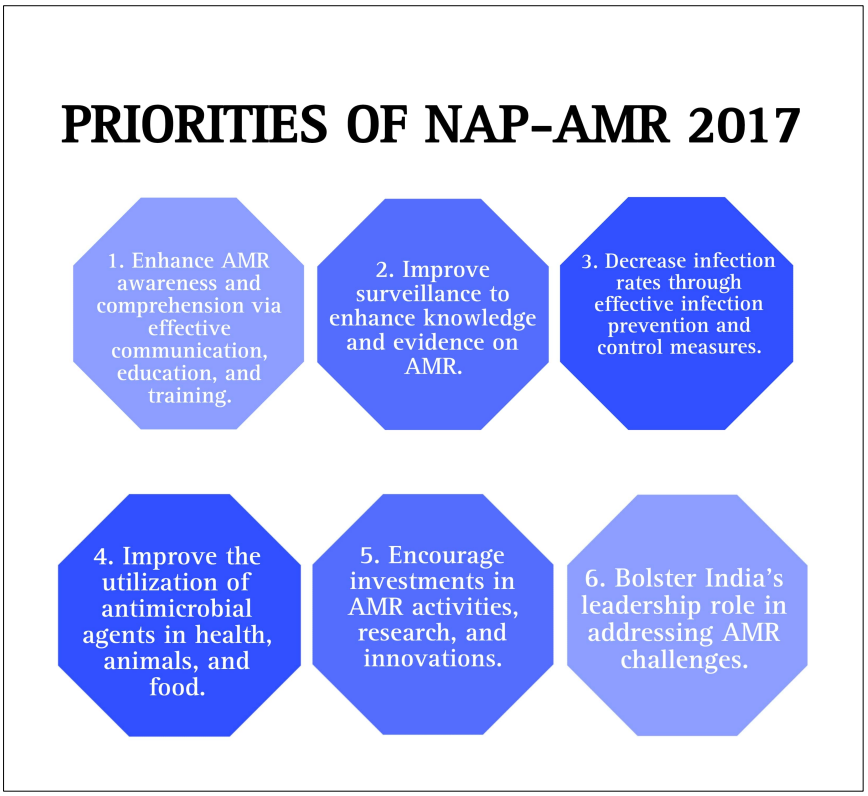

Figure 5 The priorities as formulated by NAP-AMR (18)

7.2. Approaches from a dental standpoint

Overuse of antibiotics in dentistry is a critical issue driven largely by the misconception that antibiotics are a universal remedy for all dental conditions, leading to their widespread self-prescription. The educated guesswork by many dental clinicians exacerbates the issue. But it would be another episode of negligence to address it as the only problem that requires significant attention. Each stage, from prescription to usage to disposal, represents a critical factor to potentially contribute to antibiotic pollution and concurrent AMR .

To keep prescription practices in check, it is crucial to establish long-overdue guidelines for prescribing antimicrobial drugs in dental sciences. Implementing practices such as reclaiming leftover antibiotics from patients or establishing systems similar to directly observed therapy short course (DOTS) could help mitigate this challenge as well. In fact, This practice alone can effectively monitor all three crucial stages - prescription, usage and disposal.

Implementing stewardship in densely populated countries like India poses challenges, but it is essential to regulate the dispensing of these drugs by pharmacists. Furthermore, raising awareness among the general public about the fact that antibiotics are not universally applicable and should only be used under the guidance of a licensed doctor is crucial.

It's concerning that non-chemical methods like heat treatment of dental refuse for bacterial inactivation have received insufficient research attention, possibly due to inadequate recognition of antimicrobial introduction into the environment by the dental community. Similar to the issue of antimicrobial agents ending up in landfills, improper management of dental waste is a significant contributor to antimicrobial pollution caused by the dental community.

Addressing these gaps in research and improving waste management practices are crucial steps towards reducing dentistry induced antibiotic pollution and safeguarding environmental and public health. Research in every relevant field must intensify if we are to effectively combat resistant bacteria.

7.3. Current methods for the prevention and treatment of oral infections

To combat oral infections associated with biofilms, improving oral hygiene with fluoride toothpaste is crucial but insufficient alone.(4) Antimicrobial dental materials have been developed for procedures such as restorations and implants to address this challenge effectively.According to Jiao et al(20), antimicrobial dental materials have been advanced through three mechanisms: releasing antimicrobial agents, contact killing, and multifunctional strategies. Nanoengineering has significantly boosted the development of new or enhanced dental nanomaterials with antibiofilm properties. Despite promising results in vitro, the clinical application of these materials faces challenges, particularly in terms of biocompatibility. Ramburrun et al.(19) recently provided a comprehensive review of emerging trends and advancements in antimicrobial materials for dental restorative, reconstructive, and replacement purposes.

Alternative strategies such as - antimicrobial photodynamic therapy (APDT), cold atmospheric plasma (CAP), probiotics, natural products, inhibitors of virulence factors, antimicrobial peptides have been investigated and clinically tested. These methods have been summarised in table.

Table 1 Summary of alternative strategies for treatment of oral infections.

S. no	Name of methodology	Mechanism	Remarks
1.	Antimicrobial Photodynamic Therapy (APDT)	- It utilises a photosensitizer and low-energy laser light with oxygen to produce reactive oxygen species (ROS), effective in bactericidal action. - APDT is studied extensively both in vitro and clinically. - It is applied independently and adjunctively in treating dental caries, endodontic diseases, periodontal diseases, and peri-implantitis. (21)	- research in this field is ongoing.
2.	Cold Atmospheric Plasma (CAP)	- CAP (Cold Atmospheric Plasma), an innovative approach, offers significant advantages over conventional antibiotics in dental clinical settings for managing biofilm infections. - CAP generates reactive oxygen and nitrogen species that infiltrate the biofilm, causing oxidative damage to bacterial membranes, extracellular DNA, and proteins.(20)	-
3.	Natural Products	- Plant-derived natural compounds such as phenolics, quinones, flavonoids, alkaloids, and terpenoids are recognized as valuable sources of quorum sensing inhibitors (QSI) for treating oral biofilm-related infections (22). - Coumarin, for example, inhibits P. gingivalis biofilm formation by targeting its quorum sensing system (23) - Curcumin has demonstrated the ability to reduce the expression of biofilm formation and virulence-related genes in both single-species and mixed-species biofilms of S. mutans and C. albicans [27].	-
4.	Antimicrobial Peptides (AMPs)	- Antimicrobial Peptides (AMPs) are short oligopeptides, typically less than a hundred amino acids long, naturally produced by organisms ranging from bacteria to humans as a frontline defence. They can also be synthesised chemically . - AMPs possess broad-spectrum activity against bacteria, fungi, viruses, and parasites, and they also exhibit antioxidant and antitumor properties [24]. - These peptides employ multiple mechanisms simultaneously, effectively killing microorganisms while modulating the immune response, which hinders the development of microbial resistance [25].	-it is one of the most promising treatment modalities , but clinical relevance is yet to be established.

5.	Probiotics	- Probiotics are living microorganisms possess beneficial traits like non-pathogenicity, safety, genetic consistency, and the capability to endure processing and administration conditions. - Lactobacillus spp. probiotics have demonstrated enhancements in clinical indicators of periodontal health by decreasing species associated with periodontitis.(28)	-research shows that oral microbiome is much more robust than gut microbiome.(11) Hence, its applicability in terms of amr is questionable. -research is ongoing in this field.

Abbreviation

AMP	Antimicrobial Peptides
AMR	Antimicrobial Resistance
APDT	Antimicrobial Photodynamic Therapy
ARG	antibiotic resistance gene
AWaRe	Access, Watch, Reserve
BPPL	Bacteria Priority Pathogens List
CAP	Cold Atmospheric Plasma
DOTS	Directly observed therapy short course
EPS	Extracellular polymeric substance
ESBL	Extended-spectrum β-lactamase
FDC	fixed-dose combinations
GLASS	Global Antimicrobial Resistance and Use Surveillance System
ICHP	Informal health care providers
INSAR	Indian Network for Surveillance of Antimicrobial Resistance
MALDI-TOFMS	Matrix-assisted laser desorption ionisation-time of flight mass spectrometry
MRSA	Methicillin-resistant Staphylococcus aureus
NAP-AMR	National Action Plan on Antimicrobial Resistance
NDM-1	New Delhi metallo-β-lactamase 1
NHS	National Health Service
NLEM	National List of Essential Medicines
OECD	Organization for Economic Cooperation and Development
QSI	Quorum sensing inhibitors
UK	united kingdom
WHO	World Health Organization

8. Conclusion

AMR probably could be another devastating catastrophe like the recent pandemic world has faced , unless we take note of the prevailing red flags and act upon swiftly .Data world wide has undoubtedly proven the menace of AMR in grevious medical situations in clinical practice .Dentistry, an allied field of the same , is mutely playing a role in AMR. Without a proper curriculum in any undergraduate & speciality teaching & no guidelines for antibiotic usage we are heading towards this apocalypse.

Government policies highlight One Health concept, yet fail to address rampant antibiotic misuse. Moreover, inadequate awareness and the glaring lack of comprehensive research hampers our grasp of how dental practices contribute to antibiotic resistance, leaving us blind to the true gravity of this crisis.

It's time we take control in terms of our policies & concurrently update our knowledge to follow the protocol ,else AMR will soon become an intractable alien for us !

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] WHO/Sarah Pabst, Antimicrobial resistance [internet], WHO Newsroom,2023, November 21, factsheets section. Available from https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance

[2] Kim DW, Cha CJ. Antibiotic resistome from the One-Health perspective: understanding and controlling antimicrobial resistance transmission. Exp Mol Med. 2021 Mar;53(3):301-309. doi: 10.1038/s12276-021-00569-z. Epub 2021 Mar 1. PMID: 33642573; PMCID: PMC8080597.

[3] Carr V.R., Witherden E.A., Lee S., Shoaie S., Mullany P., Proctor G.B., Gomez-Cabrero D., Moyes D.L. Abundance and diversity of resistomes differ between healthy human oral cavities and gut. *Nat. Commun.* 2020;**11**:693. doi: 10.1038/s41467-020-14422-w.

[4] Bessa LJ, Botelho J, Machado V, Alves R, Mendes JJ. Managing Oral Health in the Context of Antimicrobial Resistance. Int J Environ Res Public Health. 2022 Dec 8;19(24):16448. doi: 10.3390/ijerph192416448. PMID: 36554332; PMCID: PMC9778414.

[5] Cornaglia G. Fighting infections due to multidrug-resistant Gram-positive pathogens. Clin Microbiol Infect. 2009 Mar;15(3):209-11. doi: 10.1111/j.1469-0691.2009.02737.x. PMID: 19335367.

[6] Abdul Ghafur K. An obituary--on the death of antibiotics! J Assoc Physicians India. 2010 Mar;58:143-4. PMID: 20848810.

[7] Shahid M, Malik A, Adil M, Jahan N, Malik R. Comparison of beta-lactamase genes in clinical and food bacterial isolates in India. *J Infect Dev Ctries.* 2009;**3**:593–598.

[8] Khare S., Purohit M., Sharma M., Tamhankar A.J., Lundborg C.S., Diwan V., Pathak A. Antibiotic Prescribing by Informal Healthcare Providers for Common Illnesses: A Repeated Cross-Sectional Study in Rural India. *Antibiotics.* 2019;8:139.

[9] Patrick A, Kandiah T. Resistance to change: how much longer will our antibiotics work? *Fac Dent J* 2018; 9: 103–111.

[10] Bhuvaraghan A, King R, Larvin H, Aggarwal VR. Antibiotic Use and Misuse in Dentistry in India-A Systematic Review. Antibiotics (Basel). 2021 Nov 26;10(12):1459. doi: 10.3390/antibiotics10121459. PMID: 34943671; PMCID: PMC8698453.

[11] Rosier BT, Marsh PD, Mira A. Resilience of the oral microbiota in health: mechanisms that prevent dysbiosis. *J Dent Res* 2018; 97: 371–380.

[12] Sukumar, S., Martin, F.E., Hughes, T.E., Adler, C.J. (2020) Think before you prescribe: how dentistry contributes to antibiotic resistance. *Australian Dental Journal* https://doi.org/10.1111/adj.12727

[13] Gajic I, Kabic J, Kekic D, Jovicevic M, Milenkovic M, Mitic Culafic D, Trudic A, Ranin L, Opavski N. Antimicrobial Susceptibility Testing: A Comprehensive Review of Currently Used Methods. Antibiotics (Basel). 2022 Mar 23;11(4):427. doi: 10.3390/antibiotics11040427. PMID: 35453179; PMCID: PMC9024665.

[14] Munita J.M., Arias C.A. Mechanisms of antibiotic resistance. *Microbiol. Spectr.* 2016;4:464–472. doi: 10.1128/microbiolspec.VMBF-0016-2015.

[15] Kumarasamy, Karthikeyan K., et al. "Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study." *The Lancet infectious diseases* 10.9 (2010): 597-602.

[16] Dantuluri KL, Bonnet KR, Schlundt DG, Schulte RJ, Griffith HG, Luu A, Charnogursky C, Perkins JM, Whitmore CC, Banerjee R, Howard LM, Grijalva CG. Antibiotic perceptions, adherence, and disposal practices among parents of pediatric patients. PLoS One. 2023 Feb 9;18(2):e0281660. doi: 10.1371/journal.pone.0281660. PMID: 36758043; PMCID: PMC9910628.

[17] WHO Access, Watch, Reserve (AWaRe) classification of antibiotics for evaluation and monitoring of use [internet], 2021. Geneva: World Health Organization; 2021, (WHO/MHP/HPS/EML/2021.04). Licence: CC BY-NC-SA 3DIGO

[18] National Action Plan on Antimicrobial Resistance (NAP-AMR)[internet]. Available on http://www.searo.who.int/india/topics/antimicrobial_resistance/nap_amr.pdf

[19] Ramburrun P., Pringle N.A., Dube A., Adam R.Z., D'Souza S., Aucamp M. Recent advances in the development of antimicrobial and antifouling biocompatible materials for dental applications. Materials. 2021;14:3167. doi: 10.3390/ma14123167.

[20] Jiao Y., Tay F.R., Niu L.N., Chen J.H. Advancing antimicrobial strategies for managing oral biofilm infections. *Int. J. Oral Sci.* 2019;**11**:28. doi: 10.1038/s41368-019-0062-1.

[21] Sivaramakrishnan G., Sridharan K. Photodynamic therapy for the treatment of peri-implant diseases: A network meta-analysis of randomized controlled trials. *Photodiagnosis Photodyn. Ther.* 2018;**21**:1–9. doi: 10.1016/j.pdpdt.2017.10.013.

[22] Asfour H. Anti-quorum sensing natural compounds. *J. Microsc. Ultrastruct.* 2018;**6**:1–10. doi: 10.4103/JMAU.JMAU_10_18.

[23] He Z., Jiang W., Jiang Y., Dong J., Song Z., Xu J., Zhou W. Anti-biofilm activities of coumarin as quorum sensing inhibitor for Porphyromonas gingivalis. *J. Oral Microbiol.* 2022;**14**:2055523. doi: 10.1080/20002297.2022.2055523.

[24] Griffith A., Mateen A., Markowitz K., Singer S.R., Cugini C., Shimizu E., Wiedman G.R., Kumar V. Alternative antibiotics in dentistry: Antimicrobial peptides. *Pharmaceutics.* 2022;**14**:1679. doi: 10.3390/pharmaceutics14081679.

[25] Dostert M., Trimble M.J., Hancock R.E.W. Antibiofilm peptides: Overcoming biofilm-related treatment failure. *RSC Adv.* 2021;**11**:2718–2728. doi: 10.1039/D0RA09739J.

[26] Galdiero E., Lombardi L., Falanga A., Libralato G., Guida M., Carotenuto R. Biofilms: Novel strategies based on antimicrobial peptides. *Pharmaceutics.* 2019;**11**:322. doi: 10.3390/pharmaceutics11070322.

[27] Li X., Yin L., Ramage G., Li B., Tao Y., Zhi Q., Lin H., Zhou Y. Assessing the impact of curcumin on dual-species biofilms formed by Streptococcus mutans and Candida albicans. *MicrobiologyOpen.* 2019;**8**:e937. doi: 10.1002/mbo3.937

[28] Pandey, D.; Sharon Lazarus; Shweta Sardhana; C.S. Baiju. Periodontal Microbiology: The Emergence. *Univ J Dent Sciences* 2024, *10*.

[29] WHO Bacterial Priority Pathogens List, 2024: bacterial pathogens of public health importance to guide research, development and strategies to prevent and control antimicrobial resistance. Geneva: World Health Organization; 2024. Licence: CC BY-NC-SA 3.0 IGO.

[30] A.Gafur, Rapid, diagnostic test for UTIs may help stem super bug crisis, The Hindu,2024, June13, sci-health section.Available from https://www.thehindu.com/sci-tech/health/rapid-diagnostic-test-from-india-may-help-stem-super-bug-crisis/article68284305.ece