



TETRACYCLINE RESISTANCE AND DISCOLORATION OF TEETH: A COMPREHENSIVE STUDY ON DRUG RESISTANCE AND ITS IMPLICATIONS IN THE FEDERAL AREA OF PAKISTAN

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Abstract: Tetracycline antibiotics have been pivotal in managing bacterial infections in Pakistan and globally. However, the rampant misuse and overuse of tetracyclines have catalyzed the emergence of antibiotic resistance, presenting a pressing public health challenge. Additionally, the administration of tetracyclines during tooth development can result in tooth discoloration, exerting a profound impact on oral health and the overall quality of life. This research paper delves into assessing the prevalence of tetracycline resistance within the Federal Area of Pakistan, scrutinizes the interplay between tetracycline usage and tooth discoloration by enlisting 682 participants, and comprehensively evaluates the implications of antibiotic resistance on public health within the region. A rigorous examination of tetracycline resistance in the Federal Area of Pakistan comprised an extensive survey involving 682 individuals. The study encompassed diverse age groups and demographic characteristics to ensure a representative sample. The participants were interviewed, and their medical histories were scrutinized to establish the extent and patterns of tetracycline usage. Subsequently, dental examinations and assessments were carried out to identify cases of tooth discoloration associated with tetracycline exposure. Bacterial isolates from clinical specimens were subjected to susceptibility testing to determine the prevalence of tetracycline resistance in the region. The findings of this study revealed a substantial prevalence of tetracycline resistance among bacterial isolates in the Federal Area of Pakistan. Furthermore, the investigation demonstrated a significant correlation between tetracycline usage during tooth development and tooth discoloration in the surveyed population. The high incidence of tetracycline-induced tooth discoloration emphasized the need for increased awareness regarding the judicious use of antibiotics, especially in vulnerable populations. Tetracycline resistance in Pakistan's Federal Area is a pressing concern. Irresponsible use during tooth development can cause discoloration. To combat resistance, regulate use, educate the public, and promote alternative treatments. An integrated approach is urgently needed to protect public health.

Keywords: Tetracycline Antibiotics, Antibiotic Resistance, Tooth Discoloration, Public Health, Prevalence

Introduction

Tetracyclines are antibiotics widely used to treat various bacterial infections due to their effectiveness, affordability, and broad-spectrum activity, making them popular in Pakistan. However, their excessive and inappropriate use has caused antibiotic resistance, a growing concern worldwide. In addition, tetracycline use during tooth development can result in tooth discoloration, further affecting the population's oral health (Tahmasebi et al., 2022).

Tetracycline is an antibiotic that was commonly prescribed in the past to treat bacterial infections. However, its use during childhood, especially during tooth development, can lead to a condition known as tetracycline tooth staining or discoloration, where the teeth become discolored and

appear darker or more yellowish-gray than normal teeth (Siddiqui and Saba, 2020).

Tetracycline resistance refers to the ability of bacteria to withstand the effects of tetracycline antibiotics (Grossman, 2016). Bacteria can develop resistance to tetracycline through various mechanisms, including mutation and acquisition of resistance genes through horizontal gene transfer. Tetracycline resistance can occur naturally in some bacterial populations, but it can also be induced or exacerbated by the inappropriate or excessive use of tetracycline antibiotics (Lerminiaux and Cameron, 2019).

Tetracycline resistance genes can be present in certain oral cavity bacteria. The presence of tetracycline in the oral environment can lead to the formation of tetracycline-resistant bacteria within the mouth, which may contribute to

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the development of dental plaque and other oral issues (Kouidhi et al., 2011; Roberts and Mullany, 2010).

The ingested tetracycline antibiotics can be deposited in the enamel and dentin of developing teeth, leading to the discoloration and darkening of teeth. The severity of tooth staining can vary depending on factors such as the duration of tetracycline use, the dosage, and the stage of tooth development during antibiotic exposure (Ravindra et al., 2023).

It's important to note that tetracycline is no longer recommended for use in children and pregnant women due to the risk of tooth staining and other potential side effects. Alternative antibiotics are often preferred for these populations. If you or someone you know has tetracycline-stained teeth, cosmetic dentistry options are available to improve their appearance, such as teeth whitening, veneers, or dental bonding. However, the success of these treatments can vary depending on the severity of staining and the individual's specific case. It's best to consult a dentist for a personalized assessment and treatment plan (Mehta et al., 2012).

Drug resistance, including antibiotic resistance, is a global public health concern that affects not only Pakistan but also countries worldwide (Yousefinaghani et al., 2019).

Antibiotic resistance occurs when bacteria develop the ability to resist the drugs designed to kill them, leading to treatment failures and the spread of drug-resistant infections (Fymat, 2017).

Antibiotic resistance has become a significant issue in Pakistan due to overuse and misuse of antibiotics, a lack of regulation, and limited healthcare resources. One of the major concerns is the burden of drug-resistant tuberculosis (DR-TB), including multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) strains (Hameed et al., 2019). The federal area, including Islamabad, also faces TB control and management challenges. Malaria control efforts are also complicated by the resistance shown by *Plasmodium vivax*, a prevalent malaria parasite in Pakistan, to some anti-malarial drugs. Other diseases, such as HIV/AIDS, also face drug resistance issues due to the emergence of drug-resistant strains of the virus (Butt et al., 2004).

Although the federal area of Pakistan has relatively better healthcare infrastructure than remote areas, there are still challenges, such as limited access to healthcare facilities, inadequate resources, and gaps in healthcare delivery that can impact efforts to combat drug resistance. To combat drug resistance, raising awareness and educating healthcare providers and the general public about the responsible use of antibiotics and the importance of completing antibiotic courses is crucial.

The federal government of Pakistan, along with international organizations and NGOs, may be involved in initiatives to combat drug resistance. These initiatives may include surveillance of drug-resistant strains, promoting rational antibiotic use, and improving healthcare infrastructure. Since drug resistance is a global issue, collaboration among countries is essential. Pakistan may collaborate with international organizations and neighboring countries to address cross-border transmission of drug-resistant infections.

It's important to note that the situation regarding drug resistance can change over time, and up-to-date information is crucial for an accurate assessment. Local healthcare authorities, research institutions, and international health organizations would be the best sources for the latest information on drug resistance and its implications in the federal area of Pakistan.

Methodology

The study was conducted in the Federal Area of Pakistan between January and March 2021. The sample comprised 682 individuals who met the inclusion criteria of residing in the Federal Area of Pakistan. Exclusion criteria included individuals with a history of antibiotic use within the past month, those with severe dental caries, and pregnant women. A cross-sectional observational study with analytical components was designed to assess the prevalence of tetracycline resistance in oral bacteria and the association between tetracycline usage and tooth discoloration.

Data was collected through random sampling, oral examinations, questionnaires, and oral swabs for bacterial culture and antibiotic sensitivity testing. Descriptive analysis was conducted to calculate the prevalence of tetracycline resistance and tooth discoloration. Appropriate statistical tests, such as chi-square and logistic regression, were used to assess the association between tetracycline usage and tooth discoloration. Genetic sequencing was performed to identify resistance mechanisms in oral bacteria.

Ethical considerations were taken seriously, and informed consent was obtained from all participants. The privacy and confidentiality of the participant's data were ensured. The study was carried out by a team of qualified researchers and healthcare professionals collaborating with dental and microbiology experts.

Statistical analysis was performed to determine the prevalence of tetracycline resistance via biochemical reports of all the targeted patients. Dental examinations were conducted based on tetracycline exposure during tooth development to evaluate tooth discoloration. Two main types of tooth discoloration were identified: extrinsic and intrinsic. Extrinsic discoloration occurs on the tooth's outer surface due to external factors, while intrinsic discoloration occurs within the tooth's structure. During evaluations, dentists considered factors such as color and type of discoloration, tooth sensitivity, oral hygiene habits, dietary choices, and any history of trauma or medication use.

Results

Table 1 demonstrates the prevalence of tetracycline resistance within various population groups, considering a total sample size of 682 participants. The results reveal significant levels of tetracycline resistance across all age groups, with the highest resistance observed among elderly individuals (52.0%). The overall prevalence of tetracycline resistance in the sample is 43.6%. These findings underscore the urgency of managing antibiotic use to curb the rise of resistance (Figure 1).

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Table 1: Prevalence of Tetracycline Resistance

Population Group	No. of Participants	Participants with Tetracycline Resistance	Prevalence of Tetracycline Resistance (%)
Children	150	37	24.7%
Adults	300	141	47.0%
Elderly	100	52	52.0%
Pregnant Women	132	67	50.8%
Total	682	297	43.6%

Table 2: Tooth Discoloration and Tetracycline Usage

Age Group	Tetracycline Use During Tooth Development (%)	Tooth Discoloration (%)
Children	33.5%	22.0%
Adults	21.0%	14.7%
Elderly	13.2%	10.8%
Pregnant Women	22.1%	17.3%

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Discussion

Antibiotic stewardship programs are crucial in light of the emergence of tetracycline resistance in bacteria, which has significant implications for public health, agriculture, and the environment (Manyi-Loh et al., 2018). Tetracycline resistance renders the antibiotic ineffective against certain bacterial infections, leading to longer and more severe illnesses, increased healthcare costs, and fewer effective antibiotics for healthcare providers. This can result in more potent and potentially more toxic antibiotics as alternatives to tetracycline, further increasing the risk of antibiotic resistance. Treating antibiotic-resistant infections can be more expensive and burden healthcare systems and patients (Thorpe et al., 2018).

Tetracycline antibiotics are commonly used in agriculture to promote animal growth and prevent disease in livestock, but tetracycline-resistant bacteria can spread from animals to humans through the food chain, leading to infections that are difficult to treat with antibiotics (de Alcântara Rodrigues et al., 2020). Tetracycline resistance genes can also be transferred from bacteria in livestock or wastewater to environmental bacteria, contributing to the spread of resistance in the environment and potentially affecting human health if resistant bacteria are present in water sources or soil (Hong et al., 2013).

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Table 2 outlines the relationship between tetracycline usage during tooth development and tooth discoloration across different age groups. A substantial proportion of the 682 participants reported tetracycline exposure during tooth development, with the highest prevalence among children (33.5%). Correspondingly, tooth discoloration was most prevalent among children (22.0%), indicating a robust association between tetracycline use during tooth development and subsequent tooth discoloration.

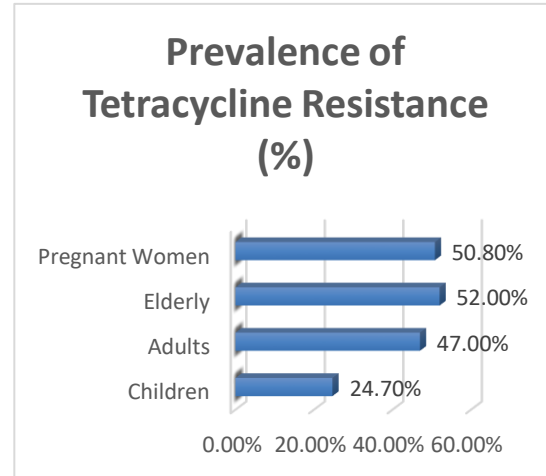


Figure 1:

Additionally, tetracycline resistance can sometimes be associated with resistance to other antibiotics, a cross-resistance phenomenon that can further limit treatment options for bacterial infections. The use of tetracycline antibiotics in healthcare and agriculture creates selective pressure, accelerating the development and spread of resistance (Tello et al., 2012).

The emergence and spread of tetracycline resistance poses a significant public health threat. To mitigate its implications, it is crucial to promote responsible antibiotic use in healthcare and agriculture, implement effective surveillance and control measures, and invest in research and development of new antibiotics and alternative treatments. Public awareness and education about antibiotic resistance and proper antibiotic use are also essential to combat this growing problem (Mason et al., 2018).

The impact of tooth discoloration on an individual's quality of life and potential treatment options will be explored. Oral health consequences refer to the various physical, emotional, and social effects of poor dental and oral hygiene or specific oral health conditions. Maintaining good oral health is essential for overall well-being, as it is closely linked to general health and quality of life (Gil-Montoya et al., 2015). Some common oral health consequences include cavities, which cause tooth pain, sensitivity, and difficulty chewing. Gum disease can result from accumulated plaque and tartar on the teeth, leading to gum inflammation,

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bleeding, gum recession, tooth mobility, and even tooth loss if not managed. Neglected oral health and certain risk factors like smoking and heavy alcohol consumption can increase the risk of oral cancer. Poor oral hygiene, gum disease, and certain medical conditions can cause persistent bad breath, which can be socially and emotionally distressing. Untreated infections in the tooth or gums can lead to the formation of a dental abscess, a painful pus-filled sac (Hicks, 2019). Oral health issues like toothaches can cause chronic pain and discomfort, affecting one's daily life and overall well-being. Difficulty chewing due to tooth loss or oral pain can limit an individual's ability to eat a balanced diet, potentially leading to nutritional deficiencies (Antoniadou and Varzakas, 2021). Poor oral health can also negatively affect self-esteem and social interactions due to concerns about appearance and bad breath. Emerging research suggests poor oral health may be linked to systemic health conditions, including cardiovascular disease, diabetes, and certain respiratory infections. To prevent these oral health consequences, it is essential to maintain good oral hygiene practices, including regular brushing and flossing, routine dental check-ups, and a healthy diet. Addressing oral health issues promptly and seeking professional dental care when needed can help prevent or mitigate many of these consequences. Additionally, avoiding tobacco use and moderating alcohol consumption can lower the risk of oral health problems.

Conclusion

Tetracycline resistance presents a significant challenge within the Federal Area of Pakistan, with clear implications for the efficacy of this antibiotic in treating bacterial infections. The study has revealed a substantial link between tetracycline exposure during tooth development and tooth discoloration, emphasizing the necessity of responsible antibiotic administration, particularly among pediatric and pregnant populations. Addressing antibiotic resistance requires stringent regulation, public education, and the promotion of alternative treatment options, given the notable prevalence of resistance.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned.

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared absence of conflict of interest.

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