*Original Research Article*

Detection of Plasmid-Mediated Extended-Spectrum β-Lactamase genes (*bla* CTX-M) in Enterobacteriaceae Isolated from the Oral Cavity of Patients in a Dental Clinic in Abidjan (Côte d’Ivoire)

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ABSTRACT

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| **Background:** The oral cavity represents one of the most complex and densely colonized environments of the human body, harboring a diverse microbiota including bacterial and fungal communities. Antimicrobial resistance has emerged as a pressing global health concern, with particularly severe implications for low-resource settings  **Aims:** . This study aimed to assess the antibiotic resistance profiles of extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae strains isolated from the oral cavity.  **Methodology:** samples were collected from patients presenting with dental disorders for the isolation and characterisation of ESBL-producing Enterobacteriaceae from the oral cavity. Plasmid DNA was extracted using the phenol-chloroform method, and conventional PCR was employed to detect the presence of plasmid-borne resistance genes *bla CTX-M-2* , *bla CTX-M-8* , and *bla CTX-M-9*  **Results:** Four Enterobacteriaceae strains were successfully isolated and characterized, corresponding to an isolation rate of 5.40% (4/74). Among these, 60% harbored the *bla CTX-M-2* and *bla CTX-M-8* resistance genes. The *bla CTX-M-9* gene was not detected in any of the isolates.  **Conclusion:** Although uncommon in the oral cavity, the emergence of Enterobacteriaceae in this niche may represent a potential public health concern. The presence of ESBL-producing strains could contribute to therapeutic failures or limited treatment options, particularly if antibiotic prescribing guidelines are not adequately followed by healthcare professionals. |

*Keywords: Antibiotic resistance, ESBL-producing Enterobacteriaceae,Oral cavity, Resistance genes*

1. INTRODUCTION

From birth, humans are exposed to a diverse array of microorganisms including bacteria, archaea, viruses, and fungi which colonize various anatomical sites such as the skin, gastrointestinal tract, respiratory system, oral cavity, and urogenital tract. This complex microbial community, known as the microbiota, establishes a symbiotic relationship with the host, contributing to a dynamic state of equilibrium referred to as homeostasis (Doré et al., 2017; Lepage, 2017). Studies have shown that this host–microbiota interaction plays a fundamental role in maintaining immune function, metabolic balance, and protection against pathogens (Burcelin, 2017; Candela et al., 2008; Lozupone et al., 2012).

The oral cavity, due to its anatomical position and physiological function, is one of the most septic sites in the human body. It harbours a dense and diverse microbial and fungal flora, with over 500 different species identified to date (Moore & Moore, 1994). Oral diseases, predominantly of infectious origin, primarily encompass dental caries and severe periodontal disorders. Among these, untreated dental caries represents the most widespread health condition worldwide, affecting approximately 2.5 billion individuals (Hamers et al., 2023).

Antibiotics are widely used for the treatment and prevention of bacterial infections. However, antibiotic resistance arises when bacteria evolve in response to exposure to these drugs, resulting in infections that are increasingly difficult to treat in both humans and animals. Antimicrobial resistance (AMR) poses a significant threat to global health, particularly in low-resource settings, where access to effective treatment options is limited (O’Neill, 2016; Ventola, 2015)

In many African countries, antimicrobial use is poorly regulated, with self-medication and over-the-counter antibiotic sales contributing significantly to the rise of resistant infections (Ayukekbong et al., 2017; Essack et al., 2017). In Côte d’Ivoire, a clinical study in maxillofacial surgery highlighted pain, swelling, and suppuration as the main symptoms among infected patients (ANZOUAN-KACOU et al., 2022), with socio-economic factors such as low purchasing power and access to informal pharmaceutical markets exacerbating the spread of resistance (Okeke et al., 2005).

Over the past two decades, infections caused by multidrug-resistant Gram-negative bacteria have emerged as a major public health concern in developing countries (Shakibaie et al., 2012). In Côte d’Ivoire, the rising resistance of bacteria to antibiotics particularly the emergence of extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae represents a significant healthcare challenge (Akoua-Koffi et al., 2004; Baguy et al., 2014; N. K. Guessennd et al., 2013)

Several studies have documented the presence and dissemination of ESBL-producing strains in human-derived Enterobacteriaceae (Ibrahim et al., 2023; Soma et al., 2024), as well as in isolates of animal and environmental origin. Enzymes of the TEM, SHV, and CTX-M families have notably been identified in human strains(N. Guessennd et al., 2008; Toty et al., 2016).

This study seeks to investigate whether Enterobacteriaceae isolated from the oral cavity harbour plasmid-encoded ESBL genes, to identify the types of ESBLs produced, and to characterise the genetic determinants involved.

2. material and methods

**2.1 Study Design and Setting**

This was a prospective, descriptive study conducted from August to October 2023 at the Private Catholic Hospital “Saints-Cœurs” in Abobo-Té, Abidjan. The investigation focused on the epidemiological, clinical, and bacteriological aspects of oral and dental infections. Patients were recruited from the dental surgery department of the hospital. All biological samples were processed at the Institut Pasteur of Côte d’Ivoire, specifically at the Clinical Bacteriology Unit in Cocody and the Molecular Biology Platform in Adiopodoumé.

**2.2 Sample Collection Procedures**

A total of 74 samples were collected from patients with clinically evident oral infections. Specimens were obtained either by syringe aspiration from closed purulent collections or using sterile swabs after wound cleansing with diluted antiseptic soap followed by rinsing with sterile water. All eligible cases identified during the study period were consecutively enrolled.

**2.3 Bacteriological Analyses**

**2.3.1 Isolation and Purification of Colonies**

Upon reception, samples were promptly cultured to prevent contamination. The swab was streaked over MacConkey agar, a selective medium for Enterobacteriaceae.

After 24 hours of incubation, colonies were subcultured on fresh MacConkey agar to obtain pure isolates.

**2.3.2 Strain Identification**

Identification was conducted using the API 20E system (bioMérieux), designed for Enterobacteriaceae.

**2.4 Plasmid DNA Extraction Using Phenol-Chloroform Method**

Genomic DNA was extracted using a modified phenol–chloroform protocol. Briefly, 500 µL of the biological sample was incubated at 95 °C for 10 minutes to initiate cell disruption. Lysis was performed by adding 1 mL of lysis buffer and 50 µL of proteinase K, followed by incubation at 55 °C for 1 hour and then 97 °C for 10 minutes. After centrifugation (14,000 rpm, 6 min), the supernatant was transferred to a new tube. To remove proteins, 250 µL of phenol: chloroform:isoamyl alcohol (25:24:1) was added. The aqueous phase was then recovered and extracted once more using 250 µL of chloroform: isoamyl alcohol (24:1). DNA was precipitated by mixing the aqueous phase with 200 µL of absolute ethanol and 15 µL of 3 M sodium acetate, followed by incubation at −80 °C for 10 minutes. The DNA pellet was washed with 70% ethanol, centrifuged, and air-dried before being resuspended in 100 µL of elution buffer and incubated at 37 °C for 2 hours. DNA integrity was verified by 1% agarose gel electrophoresis, while purity and concentration were assessed using a NanoDrop™ One spectrophotometer. A 260/280 ratio of ~1.8 was considered indicative of pure DNA, whereas lower or higher values suggested protein or RNA contamination, respectively (Green & Sambrook, 2017; Sambrook & Russell, 2001).

* 1. **PCR Amplification of ESBL-Encoding Genes**

Detection of extended-spectrum beta-lactamase (ESBL) genes (*bla*CTX-M) was performed using conventional PCR (Table.1). The reaction mix included: 4 µL of 5X FirePol Master Mix (Solis Biodyne), 7 µL of nuclease-free water, 2 µL of each primer, and 5 µL of extracted DNA, totalling 20 µL. Amplification was carried out in an Eppendorf thermocycler. The PCR programme was as follows: Initial denaturation at 94°C for 5 minutes, denaturation at 94°C for 30 seconds (×35 cycles), Annealing at 55°C for 60 seconds, extension at 72°C for 60 seconds and final extension: 72°C for 10 minutes. The total PCR run lasted 92 minutes. Amplified products were separated on 1.5% agarose gels for 40 minutes and visualised using a Gel Doc imaging system (BIO-RAD)

**Table 1. Sequence of ESBL genes primers**

| **Target gene** | **Primers** | **Sequence (5′–3′)** | **Amplicon**  **Size (bp)** | **References** |
| --- | --- | --- | --- | --- |
| *blaCTX-M-2* | CTX-M2-F / CTX-M2-R | F: ATGATGACTCAGAGCATTCG  R: TTATTGCATCAGAAACCGTG | 884 | (Bauernfeind et al., 1996) |
| *blaCTX-M-8* | CTX-M8-F / CTX-M8-R | F: ATGATGAGACATCGCGTTAAG  R:CGTGGACGATTTTTCCGCGGCAG | 864 | (Chmelnitsky et al., 2005) |
| *blaCTX-M-9* | CTX-M9-F / CTX-M9-R | F:ATGGTGACAAAGAGAGTGCA  R: CCCTTCGGCGATGATTCTC | 651 | (Eckert et al., 2004) |

* 1. Statistical Analysis

Patients’ sociodemographic and clinical characteristics were recorded using a structured questionnaire. The data were first entered into Microsoft Excel and then transferred to Epi Info version 7.2.3.1 for statistical analysis. Categorical data were presented as percentages.

3. results and discussion

**3.1 Results**

**3.1.1 Epidemiological and clinical profile of patients**

Among the 74 patients presenting with oral and dental infections included in the study, 30 were male and 44 were female, yielding a sex ratio of 0.68. Participants ranged in age from 4 to 48 years (Table 2). Pain was the most common reason for consultation (100%), followed by swelling (4.05%), suppuration (4.05%), and fever (1.35%).  
Periodontitis was the most frequently observed condition, accounting for 67.56% of cases.

**Table 2. Patients epidemiological and clinical characteristic**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Category** | **Frequency (n)** | **Percentage (%)** |
| Age | 0 -15 | 3 | 4,05 |
| 16-31 | 45 | 60,81 |
| 32-47 | 25 | 33,78 |
| >48 | 1 | 1,35 |
| Sex | Male | 30 | 40 ,54 |
| Female | 44 | 59,46 |
| Dental pathology | Cellulitis | 3 | 4,05 |
| Periodontal abscess | 50 | 67,56 |
| Gingivitis | 21 | 28,37 |

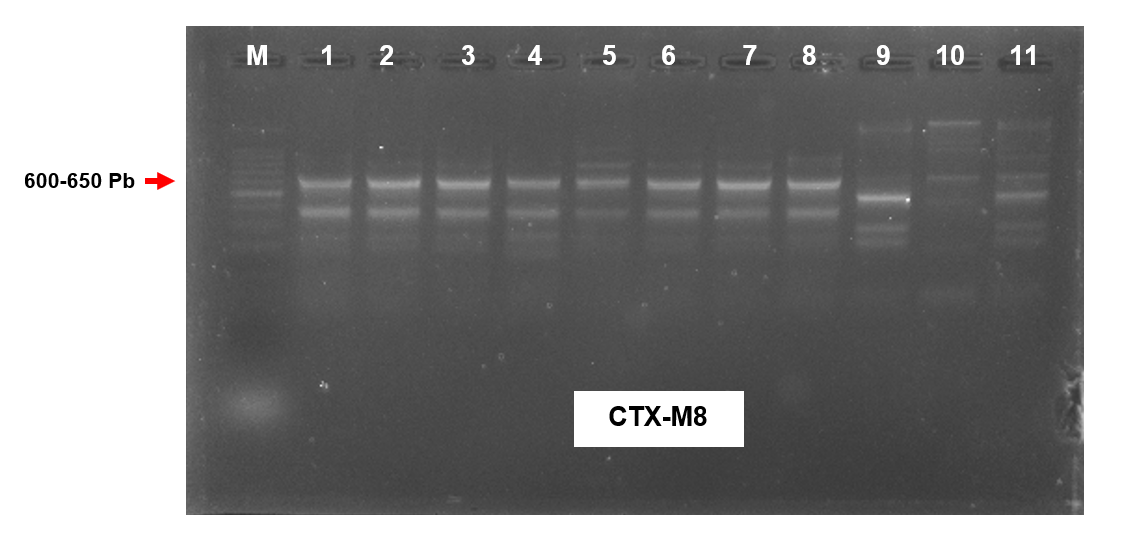
**3.1.2 Microbiological Data**

Four samples tested positive, corresponding to a positivity rate of 5.40% for Enterobacteriaceae specifically isolated from the oral cavity (Table VII). The main species identified were *Klebsiella oxytoca*, *Enterobacter aerogenes*, *Enterobacter cloacae*, and *Klebsiella pneumoniae*. These isolates were primarily associated with cellulitis (40%) and periodontal abscesses (40%). The most frequently affected teeth were the first mandibular molars.

**III.1.4 Molecular Data**

Following DNA extraction, optical density measurements using a spectrophotometer were recorded, revealing that 80% of the extracted DNA was of acceptable purity. Prior to PCR, electrophoresis confirmed the presence of extracted DNA.  
post-PCR agarose gel electrophoresis enabled the detection of resistance genes in Enterobacteriaceae isolates, and electrophoretic profiles were visualised (Figures 1 and 2).

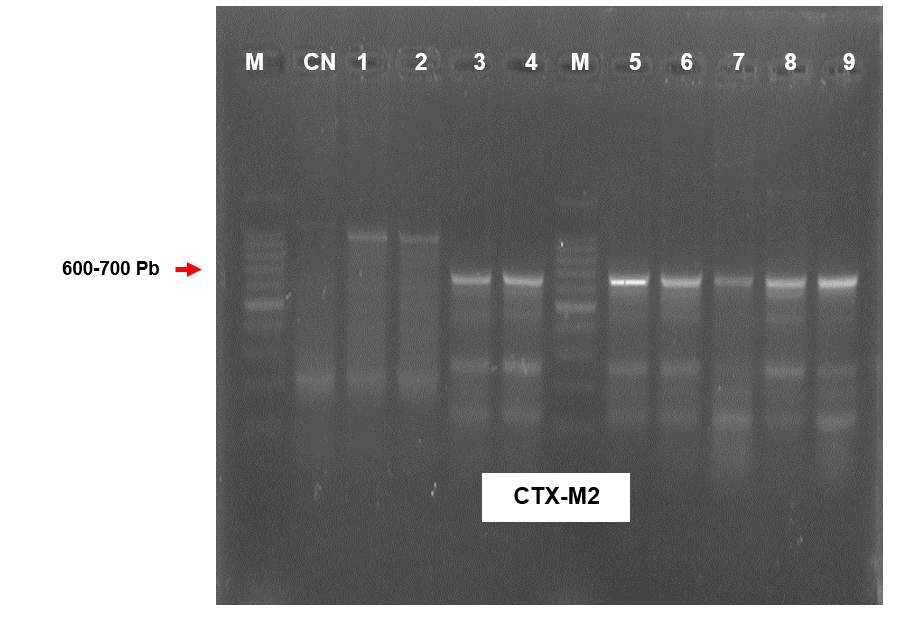
The genes (*Bla CTX-M-2 and Bla CTX-M-8*) were amplified in all the enterobacteria strains isolated; however, the *Bla CTX-M-9* gene was not amplified in any of the strains (Table 3).

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**Fig. 1. Electrophoretic profile of CTXM 8 genes**

*M: Molecular weight marker; Samples (1, 2): Klebsiella oxytoca; Samples (3,4,5): Enterobacter aerogenes ; Samples (6,7,8,) :Klebsiella pneumoniae, samples (9,10,11) Enterobacter cloacae*

**M 1 2 3 4 5 6 7 8 9 10 11**



**Fig. 2. Electrophoretic profile of CTXM 2 genes**

*M: Molecular weight marker; Samples (1, 2)* Pseudomonas *aeruginosa; Samples (3, 4, 5,6):* Klebsiella*. oxytoca; Samples 7:* Enterobacter *aerogenes; Samples (8, 9): Klebsiella pneumoniae; CN : Negative Control*

**Table 3. Enterobacterial strains amplified genes**

|  |  |  |  |
| --- | --- | --- | --- |
| **Enterobacteria strains (n=4)** | **gene *bla* CTX-M2** | **gene *bla* CTX-M8** | **gene *bla* CTX-M9** |
| *Klebsiella oxytoca (n=1)* | Positive | Positive | Negative |
| *Enterobacter aerogenes (n=1)* | Positive | Positive | Negative |
| *Klebsiella pneumoniae (n=1)* | Positive | Positive | Negative |
| *Enterobacter cloacae (n=1)* | Positive | Positive | Negative |

**3.2 Discussion**

This study presents several limitations that should be acknowledged. Firstly, the relatively small sample size and the low number of Enterobacteriaceae isolates may limit the generalisability of the findings and preclude robust statistical analysis. The low prevalence of ESBL-producing strains in the oral cavity restricts broader epidemiological conclusions regarding their dissemination in the population. Secondly, only three blaCTX-M gene groups (CTX-M-2, CTX-M-8, and CTX-M-9) were targeted by PCR, which may have led to an underestimation of the full diversity of ESBL genes present. Expanded molecular screening, whole-genome sequencing and the inclusion of a larger, more diverse sample population are needed to comprehensively assess the oral reservoir of antimicrobial resistance in Côte d'Ivoire.

Several epidemiological studies have highlighted a higher prevalence of dental infections among females, although findings across regions and studies remain variable. For example, (Ba et al., 2018) reported a female predominance in oral infections, whereas (Akpata, 2004) observed no significant gender disparity in stomatological infection rates. Similar trends have been reported across sub-Saharan Africa, where women often show a higher burden of dental disease (Kutesa et al., 2015). The increased susceptibility among women may be partially explained by hormonal fluctuations associated with menstruation, pregnancy, and menopause, which can modulate periodontal tissue vascularisation and inflammatory responses, increasing vulnerability to oral infections (Gürsoy et al., 2008; Tilakaratne et al., 2000). Furthermore, in many low-resource African settings, women often face socio-economic disadvantages that limit their access to preventive care, nutritious diets, and effective oral hygiene practices (Ayo-Yusuf, 2008).

Age has also been identified as a contributing factor in dental infection patterns. In our study, infection rates were higher among adults aged 35–60 years. This age group often accumulates risk due to prolonged exposure to cariogenic factors and limited access to regular dental care. Severe infections such as periapical abscesses, advanced periodontitis, or facial cellulitis frequently result from untreated carious lesions, a scenario commonly observed in adult populations (Kikwilu et al., 2008).

Additionally, self-medication and reliance on traditional remedies are widespread in African contexts, especially among young adults, contributing to delayed consultations and progression to advanced infectious complications(Kaboré et al., 2016). These patterns underscore the need for targeted public health strategies addressing both gender-specific vulnerabilities and age-related risk accumulations in the prevention and management of oral infections.

Limited financial means and unemployment may impede access to oral hygiene resources and dental care. (Sotunde et al., 2023) previously associated low socioeconomic status with increased incidence of oral infections, reinforcing our findings where 40.54% of patients were unemployed. Pain was the most commonly reported symptom (100%), followed by swelling and suppuration findings echoed in (Kikwilu et al., 2008) study on periondontal infections in Tanzania. Self-medication was reported in 75% of our patients, aligning with studies by(Jerez-Roig et al., 2014) , which documented high rates of non-prescribed drug use. By contrast, study in Burkina Faso (Kaboré et al., 2016) recorded lower frequencies (30.4), indicating geographic and cultural variation in self-care behaviours. Enterobacteriaceae were isolated in 5.4% of oral samples, a finding close to that of (Kaboré et al., 2016) in Burkina Faso (3.2%). While infrequent, the detection of these bacteria in the oral cavity supports the concept of microbial imbalance due to ecological and behavioural factors such as poor hygiene, reflux, or traditional medicine use (LEÃO-VASCONCELOS et al., 2015).

The presence of ESBL-producing Enterobacteriaceae in the oral cavity, as demonstrated by 60% of isolates harbouring either *blaCTX-M-2* or *blaCTX-M-8*, highlights the oral environment as a potential reservoir of antimicrobial resistance. Similar findings have been reported in several other regions (Kitamoto et al., 2020; LEÃO-VASCONCELOS et al., 2015). These genes, commonly located on plasmids, encode resistance to third-generation cephalosporins and are capable of horizontal transmission (Eckert et al., 2004; Rôças & Siqueira, 2013). While these resistant strains are typically investigated in urinary tract and other systemic infections (Helmy & Wasfi, 2014), their identification in the oral microbiome raises concerns about silent dissemination. In light of the growing global threat posed by ESBL- and carbapenemase-producing pathogens, the (Essack et al., 2017) recommends enhanced gene-level surveillance and the use of rapid diagnostic tools to support antimicrobial stewardship and containment strategies.

4. Conclusion

The primary objective of this study was to detect resistance genes in extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae isolated from the oral cavity. Through this investigation, the prevalence of such isolates within the oral microbiota was established. Although infrequent, these bacteria represent a significant public health concern due to their potential to cause serious oral infections and contribute to antimicrobial resistance. A notable observation was the widespread practice of self-medication among patients, including the use of unregulated ‘street medicines’, often driven by limited access to healthcare services and financial constraints. Furthermore, molecular characterisation of the isolates revealed the presence of plasmid-mediated resistance genes, particularly *blaCTX-M-2* and *blaCTX-M-8.*

Consent

All authors declare that ‘written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal

Ethical approval

The study received formal approval from the Pasteur Institute of Côte d'Ivoire. Patient anonymity and the confidentiality of all collected data were strictly maintained throughout the research process, in accordance with ethical standards for biomedical research involving human participants. Each participant was informed about the study's objectives, data collection procedures, potential benefits, and associated risks. Informed consent was obtained from all participants prior to inclusion in the study.

**Disclaimer (Artificial intelligence)**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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