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Review Article

Extended β-Lactamase Producing Bacteria in Pathogenic Oral Biofilms: An Overview

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Abstract

The antibiotic resistance exhibited by different bacterial genera in their biofilm mode has been reported to be thousands times higher than the resistance shown by their planktonic counterparts. To add to this menace, an alarming prevalence of Extended Spectrum Beta Lactamase (ESBL) producing bacterial species in the oral biofilms has further been a matter of concern that requires utmost attention. The present precise overview highlights the presence of ESBL producers in the oral cavity with special focus on current scenario and future perspectives. The effort could prompt our resolve to further understand the mechanistic approaches at physiological and molecular level for subsequent control of ESBL producing forms and curb dissemination of the drug resistance genes in the ecosystem.

Keywords: *Oral Cavity; Biofilms; ESBL; Extended Beta Lactamase*

Introduction

Bacterial pathogenic oral biofilms are a major healthcare threat. Their development and progression lead to hazardous infections and the failure of various dental care procedures. The mature biofilm is said to constitute of approximately 5 - 25% bacterial cells [1]. *Actinomyces* spp, *Streptococcus* spp, *Haemophilus* spp, *Capnocytophaga* spp, *Veillonella* spp, and *Neisseria* have been mentioned as the predominant pioneer bacterial genera which adhered to the surface of the tooth [2-4]. Besides these, different sub gingival bacterial species viz. *Actinomyces naeslundii, Actinomyces meyeri Bacteroides* species, *Bifidiobacterium* species, *Campylobacter* species, *Eubacterium* species, *Fusobacterium alocis, F. nucleatum, Faecalibacterium prausnitzii, Prevotella loescheii, Streptococcus intermedius, Streptococcus parasanguinis, Streptococcus sanguinis, Veillonella atypical* and *Veillonella parvula* have also been studied [5]. Majority of the above cited bacterial genera are potential biofilm formers and could act as focus to trigger pathogenesis and lead to oral cavity associated infections.

In the biofilm mode, the bacterial cells exhibit their unique architectural skills and strengthen the defensive mechanisms to create a safe niche for themselves. One such defensive mechanism is their ability to resist the detrimental effects of antimicrobial agents. Biofilm cells have been reported to display higher minimum inhibitory concentration (MIC) as compared to their relative planktonic cells [5]. It has been documented that the antibiotic resistance in the oral flora has increased over the years [6]. The reports have quoted 1,000 to 1,500 times higher antibiotic resistance in bacterial cells in biofilm mode as compared to that of their planktonic counterparts [7]. In another

study, *Actinomyces naeslundii, Campylobacter species, F. nucleatum, P. intermedia/nigrescens, P. loescheii, S. intermedius, S. parasanguinis, S. sanguinis, V. atypical* and *V. parvula* have been studied to demonstrate a significant increase, to an extent of 250 fold, in antibiotic resistance in biofilm mode as compared to their planktonic forms [5].

Over the years, the broad spectrum beta lactamase producing organisms have added to the worldwide problem and pose potential threat and a big challenge to the mankind [4]. As per NCCLS (Now Clinical and Laboratory Standards Institute) recommendations, the isolates resistant to any two of the following three Beta lactam antibiotics viz. cefpodoxime, ceftazidime, aztreonam, cefotaxime or ceftriaxone have been termed ESBL (Extended Spectrum Beta Lactamase) producers [8]. However, chromogenic cephalosporin (nitrocefin) disc method has been listed as the recommended method by CLSI for ESBL detection [9].

Extended spectrum beta-lactamases (ESBLs) have also been defined as beta-lactamases which could hydrolyze and cause resistance to 1st, 2nd and 3rd generation cephalosporins, penicillins and monobactams like aztreonam. However, ESBLs are said not cause resistance to cephamycins, namely, cefoxitin and cefotetan, carbapenems, namely, ertapenem, imipenem and meropenem and are inhibited by clavulanic acid [10]. In general, more than two hundred ESBLs have been reported to be characterized till 2005 [11]. The human oral cavity hosts a diverse microbiome. It might act as potential niche for hazardous infections within the oral cavity and their subsequent dissemination to other parts of the body. Thus, the present precise write up attempts to highlight the ESBL producers in the oral cavity with special focus on current scenario and future perspectives.

Extended β-lactamase producing bacteria in oral cavity: Present scenario

A large number of articles could be traced out on β-lactamase producers in the oral cavity, however, there seems to be dearth of reports concerning Extended β-Lactamase (ESBL) producers. Previously, the studies have discussed the presence of β-Lactamase producing bacteria in the oral cavity since childhood [12]. A research article has described that approximately one-fourth of the total bacterial isolates cultured from the cases of chronic periodontitis were found to be ESBL producers. Further, it was reported that amongst all those isolates, *Bacteroides fragilis* followed by *Fusobacterium spp.* were found to be the most common ESBL producers [13]. Supragingival plaque has also been found to harbor antibiotic resistant determinants. This site has been thought of as a poorly investigated site for ESBL carriage and its further transmission [14]. It was interesting to state here that reports were also available on the presence *Rahnella aquatilis* carrying class A ESBL gene (RAHN-1/2 gene) in the oral cavity [14]. Following table 1 enlists some of the important ESBL producing bacteria in the oral cavity.

S. No	Name	Source	Reference
1	*Bacteroides fragilis*	Chronic periodontitis patient	[13]
2	*Fusobacterium species*	Chronic periodontitis patient	[13]
3	Porphyromonas spp	Chronic periodontitis patient	[13]
3	*Prevotella spp*	Dentoalveolar infection	[15]
4	*Escherichia coli*	Oropharyngeal samples	[16]
5	*Pseudomonas*	Oropharyngeal samples	[16]
6	*Acinetobacter*	Oropharyngeal samples	[16]

Table 1: *Some important ESBL producers in oral cavity.*

Extended β-lactamase producing bacteria in oral cavity: Future challenges

The presence of Extended β-lactamase producing bacteria in the oral cavity and their ability to form biofilms have hardened the resolve to understand and tackle these drug resistant forms. The studies have explained that the plasmid mediated transfer of antibiotic resistance genes between bacterial cells within biofilm could result in a biofilm-wide resistance to the antibiotics [17]. Further, the studies have also documented that the possible acceleration of the genetic diversity and the rapid transmission of ESBL genes by the efficient mobile elements and plasmids might be a cause for genetic evolution of bacteria. Thus, the evolved bacteria with fewer effective drugs available on the table could be an emerging threat to the mankind [18].

Interestingly, the scientists have isolated bacteria from animals with matching phenotypic and genotypic profiles with that of isolates from human beings; while they studied the multiple drug resistance and ESBL producers among the members of Enterobacteriaceae which inhabited oral cavities of animals. The authors have suggested the possibility of direct or indirect transmission of resistant bacteria through animal human contact and the subsequent transmission to the environment. Moreover, researchers have also emphasized the need for gene coding to detect emerging resistance genes and their dissemination in the ecosystem so as to develop efficient tools to control menace of multi drug resistant bacterial strains [19].

In wake of the large impending threat, a larger part of the population needed to be consistently surveyed for oral ESBL carriage. It has already been quoted elsewhere that low prevalence of oral ESBL-carriage in healthy adults or carriage in selected groups of patients due to testing limited number of individuals could not be excluded [14].

Conclusion

In concluding paragraph, it would not be absurd to highlight that miniatures are skillful agents evolving every now and then. The oral microbiome being a complex habitat, the consistent surveillance mechanisms at the ecological and molecular levels could map out the possible mutations and gene transfers leading to evolution of newer Beta lactamases and call for timely efforts to generate plausible solutions.

Bibliography

1. Geesey GG., *et al*. "Biofouling and Biocorrosion in Industrial Water Systems". Ann Arbor, Lewis Publishers (1994).

2. Ritz HL. "Microbial population shifts in developing human dental plaque". *Archives of Oral Biology* 12 (1967): 1561-1568.

3. Foster JS and Kolenbrander PE. "Development of a multispecies oral bacterial community in a saliva-conditioned flow cell". *Applied and Environmental Microbiology* 70 (2004): 4340-4348.

4. Dige I., *et al*. "Application of stereological principles for quantification of bacteria in intact dental biofilms". *Oral Microbiology and Immunology* 24 (2009): 69-75.

5. Sedlacek MJ and Walker C. "Antibiotic resistance in an in vitro subgingival biofilm model". *Oral Microbiology and Immunology* 22 (2007): 333-339.

6. Hojo K., *et al*. "Bacterial interactions in dental biofilm development". *Journal of Dental Research* 88 (2009): 982-990.

7. Levy SB. "The challenge of antibiotic resistance". *Scientific American* 278 (1998): 46-53.

8. National Committee for Clinical Laboratory Standards (NCCLS),. Performance standards for antimicrobial susceptibility testing. Ninth Information supplement, National Committee for Clinical Laboratory Standards, Wayne PA. MS 100.S9 (1999).

9. Sixth Informational Supplement M11-A6. Wayne, USA: CSLI: Clinical and Laboratory Standards Institute Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard (2004).

10. Salahuddin P., *et al*. "Structure, function of serine and metallo-β-lactamases and their inhibitors". *Current Protein and Peptide Science* 19.2 (2017): 130-144.

11. Paterson D and Bonomo R. "Extended-spectrum beta-lactamases: a clinical update". *Clinical Microbiology Reviews* 18.4 (2005): 657-686.

12. Nyfors S., *et al*. "Beta-lactamase production by oral anaerobic gram-negative species in infants in relation to previous antimicrobial therapy". *Antimicrobial Agents and Chemotherapy* 43 (1999): 1591-1594.

13. Benachinmardi KK., *et al*. "Prevalence of extended spectrum beta-lactamase producing anaerobic bacteria in chronic periodontitis". *Journal of Indian Society of Periodontology* 18.5 (2014): 567-569.

14. Søraas A., *et al*. "Extended-spectrum beta-lactamase-producing bacteria are not detected in supragingival plaque samples from human fecal carriers of ESBL-producing Enterobacteriaceae". *Journal of Oral Microbiology* 6 (2014): 24026.

15. Iwahara K., *et al*. "Detection of cfxA and cfxA2, the beta-lactamase genes of Prevotella spp., in clinical samples from dento alveolar infection by real-time PCR". *Journal of Clinical Microbiology* 44 (2006): 172-176.

16. Le MNT., *et al*. "Oral colonisation by antimicrobial-resistant Gram-negative bacteria among long-term care facility residents: prevalence, risk factors, and molecular epidemiology". *Antimicrobial Resistance and Infection Control* 9 (2020): 45.

17. Erickson PR and Herzberg MC. "Emergence of antibiotic resistant *Streptococcus sanguis* in dental plaque of children after frequent antibiotic therapy". *Journal of Paediatric Dentistry* 21 (1999): 181-185.

18. Chong Y., *et al*. "Genetic evolution and clinical impact in extended-spectrum β-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae*". *Infection, Genetics and Evolution* 11.7 (2011): 1499-1504.

19. Oliveira PA., *et al*. "Detection of extended spectrum beta-lactamases and resistance in members of the Enterobacteriaceae family isolated from healthy sheep and dogs in Umuarama, Paraná, Brazil". *Semina: Ciências Agrárias* 37.2 (2016): 829-840.

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