Research Article

Serum levels of antimicrobial peptides (Cathelicidins and Beta Defensins-1) in patients with periodontitis

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Abstract: Background: periodontitis is a multifactorial oral inflammatory disease characterized by the gradual loss of bone and eventual tooth loss. It starts with microbes and is then influenced by the environment. A diverse family of host defense major compounds known as antimicrobial peptides react quickly to combat microbial invasion and challenge. These little cationic peptides are crucial for the development of innate immunity. The goal of this study was to evaluate the blood levels of healthy individuals and patients with periodontitis for cathelicidins and human beta-defensin-1. In this case-control study, 35 healthy volunteers (matched exactly by age and sex to the patients) and 50 periodontitis patients (aged 20 to 59) participated. In this investigation, periodontal parameters such as plaque index, gingival index bleeding on probing, probing pocket depth, and clinical attachment loss were employed. The levels of cathelicidins and human beta-defensin-1 in patients and controls were estimated using ELISA after blood samples from all individuals were taken. The current findings showed that the mean levels of cathelicidin and human beta defensin-1 were significantly higher ($P<0.01$) in the patient group compared to the control group, and that there was no significant correlation with all clinical periodontal parameters. These findings support the notion that antimicrobial peptides play a crucial role in periodontitis' inflammatory process.

Keywords: *periodontitis, antimicrobial peptides, cathelicidins, human beta defensins-1.*

Introduction

Periodontal disease is a significant public health issue due to its widespread prevalence across the world [(1)]. A more severe form of periodontal inflammation is periodontitis. It is a chronic inflammatory disease that destroys the periodontium and leads to tooth loss. Different factors, including dental biofilm accumulation, poor oral hygiene, and an immune response that is out of balance, can lead to periodontal destruction. Periodontitis is believed to have its beginnings in dysbiosis, a disturbance of the oral microbiota. An increase in the inflammatory infiltrate is caused by the buildup of bacterial biofilm [(2)]. Complex dynamic interactions among specific pathogenic bacteria, harmful host immune responses, and environmental variables like smoking are involved in the disease [(3)]. Gingival inflammation, clinical attachment loss, radiographic evidence of alveolar bone loss, sites with deep probing depths, mobility, bleeding on probing, and pathologic migration are all typical indicators of periodontitis [(4)].

Antimicrobial peptides (AMPs), also called host defense peptides, exerting a cationic nature, are part of the innate immune response. AMPs are thought of as naturally occurring antibiotics that fight microbial invasion early on [(5)]. Human saliva and GCF contain more than 45 different AMPs [(6)]. They form a continuous layer on the mucosal surfaces and are generated by the salivary glands and epithelial cells [(7)]. According to reports, these AMPs have different but complementary functions in preserving oral health and avoiding viral, bacterial, and fungal adhesion and infection [(8)]. The four main AMPs found in the oral cavity are defensins, cathelicidins (LL-37), calprotectins, and histatins [(9)]. In a preservative co-evolution

with the microbiome, AMPs take part and support a balanced microbiota. Additionally, in addition to their antimicrobial action, the AMPs have been shown to have a number of other significant roles in host tissues, including wound healing, cell proliferation, and chemotactic for immune cells [10].

Cathelicidins (LL-37) are AMPs from the family of a-helical peptides without cysteine and located at the carboxyl terminus of a 15–18 kDa highly conserved cathepsin-L-inhibitor (cathelin)-like domain [11]. Human cationic antimicrobial peptide (hCAP18), which is found in the oral cavity and respiratory tract, is the only delegate of cathelicidins in humans [12]. When needed, proteases divide them into a cathelin protein and an AMP after they are created and stored in cells as 2-domain proteins.

They comprise 37 amino acids and get their names from the first two residues at the N-terminus, leucine and leucine [13]. Monocytes, neutrophils, mast cells, and T-cells are all stimulated by LL-37/hCAP18. Numerous investigations have shown that LL-37/hCAP18 is an effective antibacterial against a wide range of Gram-positive and negative bacteria, fungi, viruses, and parasites [14]. By creating ionic channels in the bacterial cell membranes and having the capacity to bind lipopolysaccharide, LL-37/hCAP18 rapidly neutralizes bacteria [13].

Defensins peptides are small, cationic in nature, having two families: α defensins and β-defensins with high vital role in innate and adaptive immune system [15]. Classified as α-defensins, β-defensins, and θ-defensins by the disulfide bond in their molecular structure, β-defensins were found in the constitutively generated epithelial cells of the skin, oral cavity, trachea, stomach, and tonsils. According to reports, HBD-1 has chemotactic activity in a small number of cells, induces active immunity, modulates inflammation, breaks down low-density lipoprotein and lipoprotein (α), and improves wound healing [16]. HBD-1 is an important salivary component of the innate immune defense against an invasion by oral microbes. By adhering to chemokine receptors, it signals the adaptive immune system and plays a crucial part in attracting immature dendritic cells and T cells. By limiting bacterial colonization and viral infection, it also preserves the equilibrium of microbial pathogens.

Previous studies demonstrated elevated HBD-1 levels in people with a variety of oral disorders, including lichen planus, leukoplakia, glossitis, glossodynia, and oral discomfort [17]. The purpose of this study was to compare the serum levels of healthy individuals and patients with periodontitis for LL-37 and HBD-1.

Materials and Methods

Subjects: In this case-control study, 50 patients with periodontitis, ranging in age from 20 to 59, with a mean age of 38.98±9.88 years were included. While 35 healthy subjects matched with the case group were considered a control group, with ages ranging from 20 to 56, and a mean age of 35.088.24 years. This study was approved by ethical committee at the University of Baghdad, College of Dentistry (ID No. 378 in 21/11/2021).

Calculation of sample size: The sample size was calculated with G Power 3.1.9.7 (program written by Franz-Faul of the University of Kiel, Germany), with a study power of 95%, probability alpha error of 0.05 on both sides, statistical tests are two independent sample T tests, with the effect size assumed to be 0.8 (large) between two groups under all these conditions, the sample size is 84, so 85 subjects are calculated to be sufficient over G Power [18].

Criteria for inclusion and exclusion: The criteria for inclusion include good general health and no history of systemic disease, participants who have not received oral therapy over the past six months, and at least 20 natural teeth. The exclusion criteria were including; patients with systemic diseases, pregnant women, smoking or alcohol dirking, previous periodontal therapy for the last 6 months, antibiotics and/or anti-inflammatory medication in the last 3 months, intake of supplements and wearing orthodontic appliances or prosthodontics. According to the new classification of periodontal disease, a healthy periodontium should have BOP <10%, PPD ≤ 3mm and no probing attachment loss [19] . As well, a patient is a periodontitis case in the context of clinical care if interdental CAL is detectable at ≥2 non-adjacent teeth, or buccal or oral CAL ≥3 mm with pocketing >3 mm is detectable at ≥2 teeth [20].

Oral examination: A calibrated dentist conducted the clinical examination for each individuals involved in the study. Using a periodontal probe of William's graduation, the periodontal status of each tooth was evaluated. PLI, GI, BOP, PPD, and CAL are among the periodontal parameters [21,22].

Sample collection: Three ml of venous blood were taken as a sample from each patient using an aseptic approach. Serum was extracted from blood by centrifuging it at 3000 rpm for 10 minutes, and then it was divided into tiny aliquots and stored at -20 °C until it was utilized for LL-37 and HBD-1 analysis.

Measurement of LL-37 and HBD-1: Concentrations of LL-37 and HBD-1 in serum were measured by ELISA in accordance with the instructions in the kit's instruction manual (Shanghai, China).

Statistical analysis: The Pearson correlation coefficient test was used to determine correlations between biomarkers and clinical parameters. The T-test was employed to determine the statistical significance of differences between groups. Significant P-values have been defined as $P<0.05$.

Results

The results of the present study were based on a comparison of 50 patients with periodontitis to 35 healthy controls who were matched for age and sex . Figure (1) demonstrates that there was not statistically significant difference in age between the two groups ($P>0.05$).

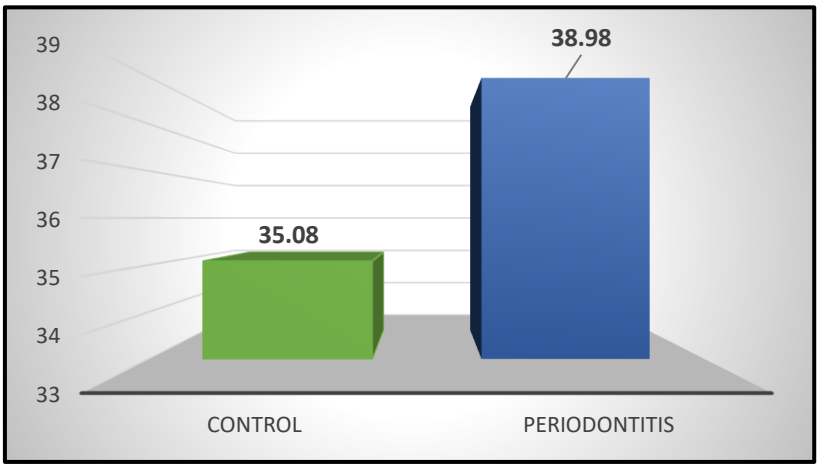

Figure 1: Case-Control Differences in Age

Figures (2) and (3) demonstrate that the values of clinical periodontal parameters in patients were significantly different from those in healthy controls.

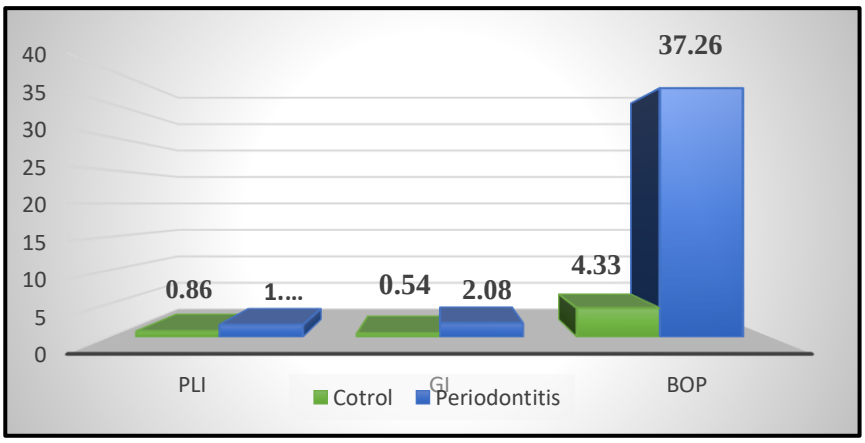

Figure 2: The mean values of PLI, GI, and BOP in patients and control groups

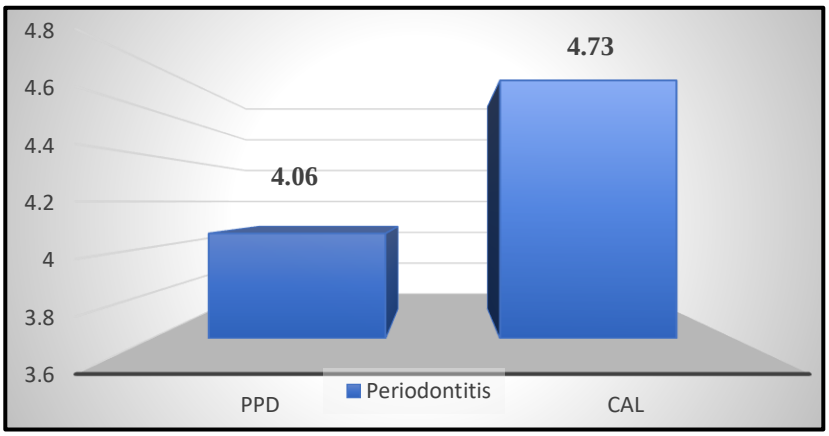

Figure 3: The Mean Values of PPD and CAL in Patients and Control Groups

As shown in table (1), the current study found a significant increase (P<0.01) in the mean value of LL-37 in the patient group (44.32±10.08 ng/ml) compared to the control group (27.71±7.81 ng/ml). Additionally, as it was shown in table (2), the findings revealed that there was no correlation between LL-37 and periodontal parameters in the patient group.

Table 1: Mean of LL-37 (ng/ml) Values in patients and Control Groups

LL-37(ng/ml)	Study groups		T- test (P-value)
	Patients N=50	Control N=35	
Minimum	28.74	8.82	
Maximum	89.34	44.96	
Mean	44.32	27.71	0.000**
SD	10.08	7.81	

Table 2: Correlation between LL-37 (ng/ml) and Periodontal Parameters in patients Group

Periodontal Parameters	LL-37	
	r	p value
PLI	-0.002	0.989
GI	0.031	0.832
BOP	0.161	0.264
PPD	-0.045	0.754
CAL	0.036	0.803

This study found highly significant elevation (P<0.01) in mean value of HBD-1 among patients group (589.18±205.38 pg/ml) in comparison to control group (300.02± 148.48 pg/ml), as shown in table (3) . Additionally, the findings below demonstrate that there is no significant correlation as most correlations are weak with either positive or negative between HBD-1 and periodontal parameters in patients group, table (4).

Table 3: Mean of HBD-1(pg/ml) Values in patients and Control Groups

HBD-1(pg/ml)	Study groups		T- test (P-value)
	Patients N=50	Control N=35	
Minimum	82.17	101.37	
Maximum	971.92	748.70	
Mean	589.18	300.02	0.000**
SD	205.38	148.48	

Table 4: Correlation Between HBD-1(pg/ml) and Periodontal Parameters in patients Group.

Periodontal Parameters	HBD-1	
	r	p-value
PLI	-0.177	0.220
GI	-0.150	0.299
BOP	-0.098	0.500
PPD	0.218	0.127
CAL	0.211	0.142

Discussion

A significant difference was found between the two study groups regarding the PLI. This result was consistent with the findings of Levin et al. (2018) [23] and Mahmood (2020) [,24]. The plaque index expresses the level of dental plaque, and can be used to determine whether or not an individual has poor oral hygiene. There is pronounced relationship between poor oral hygiene and increased accumulation of dental plaque, high prevalence and increased severity of periodontal disease [25]. Results revealed highly significant difference in GI between the two study groups, this finding agrees with other local previous results conducted by Abbas (2019) [26] and Ibrahim (2020) [,27].

These results could be explained by the effect of dental plaque on gingival condition, since the accumulation of microbial biofilm on teeth cause gingival inflammation with sign and symptom of inflammation [28]. Moreover, statistical significant difference in mean value of BOP was found between the two study groups, this finding agrees with other previous result of Glimvall et al. (2012)[29].

Absence of bleeding on probing indicates periodontal stability, but its presence shows low specificity as an indicator of disease progression [29]. Gingival bleeding provides an important objective sign of inflammation that has been used as a key parameter in the clinical evaluation of the periodotium. Besides, the value of BOP as predictor of future periodontal deterioration seems to significantly increase when associated with periodontal pocket depth greater than or equal to 6 mm [30,31]. In terms of PPD and CAL, this study found that periodontitis patients had high mean PPD and CAL values, whereas the control group had normal gingival sulcus and no attachment loss. These findings were consistent with previous research conducted by Sakalauskiene et al. (2014) [32] and Tarannum et al. (2017) [33]. Collagen fibers and connective tissue connection to the tooth are lost as periodontal disease advances, and junctional

epithelial cells proliferate apically along the root surface; these structural alterations manifest clinically as attachment loss and increased PPD [34].

In the current study, individuals with periodontitis showed significantly higher serum levels of LL-37 than the control group, the increase could be related to a response to pathogenic microbe stimulation and the existence of an inflammatory process in periodontitis. In parallel with other result findings reported by Cheah and colleagues also showed that serum LL-37 level was significantly higher in periodontitis group than periodontal health group, and recommended that those with high serum levels of LL-37 have complete periodontal treatment [35].

Moreover, Puklo et al. (2008) [36] have demonstrated that unprocessed LL-37 levels in patients with periodontitis were significantly higher compared to the healthy control. Increase of this AMPs may be due to the association of LL-37 with inflammation during periodontal disease. However, Eick et al. (2014) [37] failed to show any differences in level of LL-37 between periodontitis patients and healthy controls. In contrast to this finding other study by Turkoglu and colleagues (2017) [38] observed that patients with periodontitis had significantly low levels of serum LL-37 than healthy controls. This conflicting result might be caused by different techniques of the studies, in the present study analyzed LL-37 in serum was performed by ELISA.

This technique might detect not only the mature form but also immature forms of hCAP18/LL-37. This peptide is stored in secondary granules of neutrophils as an inactive precursor [39]. After neutrophils are stimulated, proteinase 3 releases mature hCAP18/LL-37 from hCAP18 [40]. Neutrophils that have been recruited and are releasing the hCAP18/LL-37 peptide are crucial to the non-oxidative killing process. It has been shown that mature hCAP18/LL-37 has a killing effect on *Aggregatibacter actinomycetemcomitans* [41], which is an important periodontopathogen for periodontitis. Growing evidence indicates that AMPs, including LL-37, take part in the pathomechanism of various diseases including, periodontitis. Furthermore, because LL-37 possesses a broad spectrum of antimicrobial activities and can directly kill a variety of Gram-positive and Gram-negative bacteria [42,43,44], it is probably to have a role in immune defense processes during infectious disorders. The present study showed no significant correlation between LL-37 and clinical periodontal parameters in patients, which was consistent with prior findings (Turkoglu et al., 2017) [38].

No correlation between LL-37 and periodontal parameters may be attributed to that periodontitis cases with a relatively fair oral hygiene were included in this study. This outcome, on the other hand, is incongruent with previous results [45,46] who found positive relationship between periodontal parameters and levels of LL-37.

In the present study, the HBD-1 level in patients with periodontitis group was found to be higher than control group. This result was consistent with the findings of Yilmaz et al., (2020) [47] who reported that patients with periodontitis had higher levels of salivary HBD-1 and HBD-3 in comparison to periodontally healthy controls. Similarly, Lu et al. (2004) [48] found that HBD-1 mRNA levels in the pocket epithelium of patients with severe periodontitis were higher than those in the healthy sulcus epithelium of the same patients. HBD-1 levels might increase due to the presence of pathogens or an inflammatory process.

During bacterial infection and subsequent inflammation, cytokines recruit plasma cells to the epithelium, enabling HBD-1 to be released into the tissues [49]. According to Mathews et al. (1999) [50] continuous contact of the oral mucosa with the commensal microflora can stimulate HBD-1 production even in the absence of periodontal disease.

On the contrary, Costa and colleagues (2018) [51] reported that periodontally healthy individuals had significantly higher levels of HBD-1 when compared to individuals with periodontitis and suggested a potential protective role of HBD-1 in periodontitis susceptibility . Dommisch et al. (2005) [52] found decreased human HBD-1 mRNA levels in the gingiva of patients with periodontitis compared with healthy controls; however, the difference was not statistically significant. This disparity in outcomes could be brought about by variations in gene copy numbers and responses to bacterial stimulation. In addition to methodological variations, another aspect of the study is the sample age and stage of periodontitis.

Another notable finding in this study is that there is no significant association between HBD-1 and clinical periodontal parameters. Although HBD-1 levels were high in this group, periodontal destruction in periodontitis could not be stopped, which may indicate that the other mechanisms are also important in the first line of host defense [53]. Likewise Costa et al. (2018) [51] discovered no significant correlations between HBD-1 and periodontal parameters. Overall, there is a non-significant correlation between AMPs and clinical periodontal parameters in this study, suggesting that this systemic increase in AMPs is not sufficient to protect patients from periodontal destruction. The limitations of the current study are; the sample size in this study was relatively small, as well study only two types of AMPs, as other types also has a role in the pathogenesis of periodontitis.

Conclusion

Elevated LL-37 and HBD-1 levels in patients may form the initial response against infection and thus could function as an early diagnostic marker of periodontitis. There is no significant correlation between AMPs and clinical periodontal parameters in patients, suggesting that this systemic increase of AMPs is insufficient to fully protect individuals against periodontal destruction.

Conflict of interest

The authors have no conflicts of interest to declare.

Author contributions

FZA., BH. and NA. contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript

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Ethical approval

All of the individuals were given thorough information about the study and the procedures involved, and their informed consent was acquired on a form approved by the ethics committee of the University Of Baghdad \ College Of Dentistry.

References

1. Petersen PE, Ogawa H: The global burden of periodontal disease: towards integration with chronic disease prevention and control. Periodontol. 2000 2012; 60:15-39. https://doi.org/10.1111/j.1600-0757.2011.00425.x

2. Rosier BT, De Jager M, Zaura E, Krom BP: Historical and contemporary hypotheses on the development of oral diseases: are we there yet? Front. Cell. Infect. Microbiol. 2014; 4:92. https://doi.org/10.3389/fcimb.2014.00092

3. Slots J. Periodontitis: facts, fallacies and the future. Periodontol 2000 2017;75:7-23. https://doi.org/10.1111/prd.12221

4. Papapanou PN, Sanz M, Buduneli N, Dietrich T, Feres M, Fine DH, et al. Periodontitis: consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Periodontol 2018;89(Suppl 1):S173-82.

5. Pasupuleti M, Schmidtchen A, Malmsten M. Antimicrobial peptides: Key components of the innate immune system. Crit. Rev. Biotechnol. 2012, 32, 143-171. https://doi.org/10.3109/07388551.2011.594423

6. Gorr S.-U, Abdolhosseini M. Antimicrobial peptides and periodontal disease. J. Clin. Periodontol. 2011, 38, 126-141. https://doi.org/10.1111/j.1600-051X.2010.01664.x

7. Khurshid Z, Naseem M, Sheikh Z, Najeeb S, Shahab S, Zafar MS. Oral antimicrobial peptides: Types and role in the oral cavity. Saudi Pharm. J. 2016, 24, 515-524. https://doi.org/10.1016/j.jsps.2015.02.015

8. Ouhara K, Komatsuzawa H, Yamada S, Shiba H, Fujiwara T, Ohara M, et al. Susceptibilities of periodontopathogenic and cariogenic bacteria to antibacterial peptides, β-defensins and LL37, produced by human epithelial cells. J. Antimicrob. Chemother. 2005, 55, 888-896. https://doi.org/10.1093/jac/dki103

9. Ji S, Choi Y. Innate immune response to oral bacteria and the immune evasive characteristics of periodontal pathogens. J. Periodontal Implant. Sci. 2013, 43, 3-11. https://doi.org/10.5051/jpis.2013.43.1.3

10. Hans M, Hans VM. Epithelial Antimicrobial Peptides: Guardian of the Oral Cavity. Int. J. Pept. 2014, 2014, 1-13. https://doi.org/10.1155/2014/370297

11. review. Molecular biology reports. 2012 Dec;39(12):10957-70. https://doi.org/10.1007/s11033-012-1997-x

12. Tecle T, Tripathi S, Hartshorn KL. Defensins and cathelicidins in lung immunity. Innate immunity. 2010 Jun;16(3):151-9. https://doi.org/10.1177/1753425910365734

13. Zanetti M, Gennaro R, Scocchi M, Skerlavaj B. Structure and biology of cathelicidins. The Biology and Pathology of Innate Immunity Mechanisms. 2002:203-18. https://doi.org/10.1007/0-306-46831-X_17

14. López-García B, Lee PH, Yamasaki K, Gallo RL. Anti-fungal activity of cathelicidins and their potential role in Candida albicans skin infection. Journal of Investigative Dermatology. 2005 Jul 1;125(1):108-15. https://doi.org/10.1111/j.0022-202X.2005.23713.x

15. Gorr SU. Antimicrobial peptides of the oral cavity. Periodontol 2000 2009; 51: 152-80. https://doi.org/10.1111/j.1600-0757.2009.00310.x

16. Wilson SS, Wiens ME, Smith JG. Antiviral mechanisms of human defensins. J Mol Biol 2013; 425(24): 4965-80. https://doi.org/10.1016/j.jmb.2013.09.038

17. Pierson T, Pierson SL, Pinto D, Hoek ML. Cigarette Smoke Extract Induces Differential Expression Levels of Beta-Defensin Peptides in Human Alveolar Epithelial. Tob Induc Dis 2013; 11(1):10. https://doi.org/10.1186/1617-9625-11-10

18. Cohen J. Statistical power analysis for the behavioral sciences Lawrence Earlbaum Associates. 20th-.

19. Chapple IL, Mealey BL, Van Dyke TE, Bartold PM, Dommisch H, Eickholz P, et al. Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. Journal of periodontology. 2018; 89: S74-84. https://doi.org/10.1002/JPER.17-0719

20. Tonetti MS, Greenwell H, Kornman KS. Staging and grading of periodontitis: Framwork and proposal of a new classification and case definition. Journal of periodontology. 2018; 89: S159-72. https://doi.org/10.1002/JPER.18-0006

21. Silness J, Loe H. Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. Acta Odont Scand. 1964;22:121-135. https://doi.org/10.3109/00016356408993968

22. Newbrun E. Indices to measure gingival bleeding. J Periodontol. 1996;67:555-561. Newbrun E. Indices to measure gingival bleeding. J Periodontol. 1996;67:555-561. https://doi.org/10.1902/jop.1996.67.6.555

23. Levin L, Zini A, Levine J, Weiss M, Lev R, Taub DC, et al. Demographic profile, Oral Health Impact Profile and Dental Anxiety Scale in patients with chronic periodontitis: a case-control study. International dental journal. 2018 Aug 1;68(4):269-78. https://doi.org/10.1111/idj.12381

24. Mahmood HK. Identification of Human Cytomegalovirus (HCMV) and it is Associated with Interleukin-6 and TumorNecrosis Factor-Alpha Production in Patients with Chronic Periodontitis. A Thesis submitted to the the College of Dentistry / University of Baghdad, for the MSc in Science of Oral Microbiology. 2020.

25. Albandar JM. Global risk factors and risk indicators for periodontal diseases. Periodontology 2000. 2002 Apr;29(1):177-206. https://doi.org/10.1034/j.1600-0757.2002.290109.x

26. Abbas RF. Analysis of Nuclear Factor Kappa and Toll-Like Receptor-4 Genes Polymorphisms and there Associations with Selected Immunological Biomarkers in Iraqi Population with severe Chronic Periodontitis. A Thesis submitted to the College of Dentistry / University of Baghdad, for the Degree of Doctorate of Philosophy in Periodontics.(2019).

27. Ibrahim SK. Analysis of Salivary MicroRNA-146a and IL-17 A in Chronic Periodontitis and Their Association with Disease Severity. A Thesis submitted to the the College of Dentistry / University of Baghdad, for the MSc in Science of Oral Microbiology.(2020). https://doi.org/10.36295/ASRO.2021.24420

28. Murakami S, Mealey BL, Mariotti A, Chapple IL. Dental plaque-induced gingival conditions. Journal of clinical periodontology. 2018 Jun;45:S17-27. https://doi.org/10.1111/jcpe.12937

29. research. 2012 Oct;47(5):655-60. https://doi.org/10.1111/j.1600-0765.2012.01479.x

30. Claffey N, Egelberg J. Clinical indicators of probing attachment loss following initial periodontal treatment in advanced periodontitis patients. Journal of clinical periodontology. 1995 Sep;22(9):690-6. https://doi.org/10.1111/j.1600-051X.1995.tb00828.x

31. Checchi L, Montevecchi M, Checchi V, Zappulla F. The relationship between bleeding on probing and subgingival deposits. An endoscopical evaluation. The Open Dentistry Journal. 2009;3:154. https://doi.org/10.2174/1874210600903010154

32. Sakalauskiene J, Giedrimiene D, Kubilius R, Gleiznys A, Vitkauskiene A, Ivanauskiene E, et al. Cytokine production by leukocytes in patients with periodontitis. Central European Journal of Medicine. 2014 Dec;9(6):821-9. https://doi.org/10.2478/s11536-014-0699-2

33. Tarannum F, Faizuddin M. Association between lipoxin A4 and interleukin-12 in gingival crevicular fluid: a preliminary investigation. Journal of Periodontal Research. 2017 Apr;52(2):210-7. https://doi.org/10.1111/jre.12383

34. Newman MG, Takei HH, Carranza FA. Carranza's clinical periodontology, St. Louis, Missouri, Elsevier Inc.(2018).

35. Cheah CW, Al-Maleki AR, Vadivelu J, Danaee M, Sockalingam S, Baharuddin NA, et al. Salivary and serum cathelicidin LL-37 levels in subjects with rheumatoid arthritis and chronic periodontitis. Int J Rheum Dis. 2020 Oct;23(10):1344-1352. https://doi.org/10.1111/1756-185X.13919

36. Puklo M, Guentsch A, Hiemstra PS, Eick S, Potempa J. Analysis of neutrophil-derived antimicrobial peptides in gingival crevicular fluid suggests importance of cathelicidin LL-37 in the innate immune response against periodontogenic bacteria. Oral microbiology and immunology. 2008 Aug;23(4):328-35. https://doi.org/10.1111/j.1399-302X.2008.00433.x

37. Eick S, Puklo M, Adamowicz K, Kantyka T, Hiemstra P, Stennicke H, et al. Lack of cathelicidin processing in Papillon-Lefevre syndrome patients reveals essential role of LL-37 in periodontal homeostasis. Orphanet journal of rare diseases. 2014 Dec;9(1):1 https://doi.org/10.1186/s13023-014-0148-y

38. Turkoglu O, Emingil G, Eren G, Atmaca H, Kutukculer N, Atilla G. Gingival crevicular fluid and serum hCAP18/LL-37 levels in generalized aggressive periodontitis. Clinical oral investigations. 2017 Apr;21(3):763-9. https://doi.org/10.1007/s00784-016-1834-z

39. Bals R, Wilson J. Cathelicidins-a family of multifunctional antimicrobial peptides. Cellular and Molecular Life Sciences CMLS. 2003 Apr;60(4):711-20. https://doi.org/10.1007/s00018-003-2186-9

40. Sørensen OE, Follin P, Johnsen AH, Calafat J, Tjabringa GS, Hiemstra PS, et al. Human cathelicidin, hCAP-18, is processed to the antimicrobial peptide LL-37 by extracellular cleavage with proteinase 3. Blood, The Journal of the American Society of Hematology. 2001 Jun 15;97(12):3951-9. https://doi.org/10.1182/blood.V97.12.3951

41. Bedran TB, Mayer MP, Spolidorio DP, Grenier D. Synergistic anti-inflammatory activity of the antimicrobial peptides human beta-defensin-3 (hBD-3) and cathelicidin (LL-37) in a three-dimensional co-culture model of gingival epithelial cells and fibroblasts. PLoS One. 2014 Sep 4;9(9):e106766. https://doi.org/10.1371/journal.pone.0106766

42. Vandamme D, Landuyt B, Luyten W, Schoofs L. A comprehensive summary of LL-37, the factotum human cathelicidin peptide. Cellular immunology. 2012 Nov 1;280(1):22-35. https://doi.org/10.1016/j.cellimm.2012.11.009

43. Al-Ali GM, Jafar ZJ, AL-Ghurabi BH. The relation of salivary cathelicidin and beta-defensin with dental caries of schoolchildren. J Res Med Dent Sci. 2021 Apr;9(4):30-5.

44. Al-Ghurabi BH, Adham ZS, Abbas AA. Level of β-defensin among Iraqi patients with COVID-19 in relation to oral health status. Journal of Emergency Medicine, Trauma and Acute Care. 2022 May 31;2022(3-The International and Scientific Conference of Alnahrain College of Medicine and Colleges of Medicine in Iraq confronting COVID-19 Pandemic (ISMC-2022)):2. https://doi.org/10.5339/jemtac.2022.ismc.2

45. Hosokawa I, Hosokawa Y, Komatsuzawa H, Goncalves RB, Karimbux N, Napimoga MH, et al. Innate immune peptide LL-37 displays distinct expression pattern from beta-defensins in inflamed gingival tissue. Clinical & Experimental Immunology. 2006 Nov;146(2):218-25. https://doi.org/10.1111/j.1365-2249.2006.03200.x

46. Türkoğlu O, Emingil G, Kütükçüler N, Atilla G. Gingival crevicular fluid levels of cathelicidin LL-37 and interleukin-18 in patients with chronic periodontitis. Journal of periodontology. 2009 Jun;80(6):969-76. https://doi.org/10.1902/jop.2009.080532

47. Yilmaz D, Topcu AO, Akcay EU, Altındis M, Gursoy UK. Salivary human beta-defensins and cathelicidin levels in relation to periodontitis and type 2 diabetes mellitus. Acta Odontologica Scandinavica. 2020 Jul 3;78(5):327-31. https://doi.org/10.1080/00016357.2020.1715471

48. Lu Q, Jin L, Darveau RP, Samaranayake LP. Expression of human beta-defensins-1 and -2 peptides in unresolved chronic periodontitis. J Periodont Res 2004;39: 221-227. https://doi.org/10.1111/j.1600-0765.2004.00727.x

49. Ganz T. Defensins: antimicrobial peptides of innate immunity. Nat Rev Immunol 2003;3:710-20. Doi.org/10.1038/nri1180 https://doi.org/10.1038/nri1180

50. Mathews M, Jia HP, Guthmiller JM, Losh G, Graham S, Johnson GK, et al. Production of beta-defensin antimicrobial peptides by the oral mucosa and salivary glands. Infect Immun. 1999;67(6):2740-2745. https://doi.org/10.1128/IAI.67.6.2740-2745.1999

51. Costa LC, Soldati KR, Fonseca DC, Costa JE, Abreu MH, Costa FO, et al. Gingival crevicular fluid levels of human beta-defensin 1 in individuals with and without chronic periodontitis. Journal of Periodontal Research. 2018 Oct;53(5):736-42. https://doi.org/10.1111/jre.12558

52. Dommisch H, Acil Y, Dunsche A, Winter J, Jepsen S. Differential gene expression of human β-defensins (hBD-1,-2,-3) in inflammatory gingival diseases. Oral microbiology and immunology. 2005 Jun;20(3):186-90. https://doi.org/10.1111/j.1399-302X.2005.00211.x

53. Vardar-Sengul S, Demirci T, Sen BH, Erkizan V, Kurulgan E, Baylas H. Human β defensin-1 and-2 expression in the gingiva of patients with specific periodontal diseases. Journal of periodontal research. 2007 Oct;42(5):429-37. https://doi.org/10.1111/j.1600-0765.2006.00964.x

مستويات الببتيدات المضادة للميكروبات (Cathelicidins and Human Beta Defensins-1) في مصل المرضى المصابين بألتهاب اللثة

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المستخلص:

المستخلص: الخلفية: التهاب اللثة هو مرض التهاب الفم متعدد العوامل يتميز بألتدمير التدريجي للعظام وفقدان الأسنان في نهاية المطاف. يبدأ عن طريق الكائنات الحية الدقيقة ويتأثر كذلك بالعوامل البيئية. الببتيدات المضادة للميكروبات هي فئة واسعة النطاق من جزيئات الدفاع للمضيف والتي تعمل في وقت مبكر لمواجهة الغزو الميكروبي, وتلعب هذه الببتيدات الموجبة الصغيرة دورًا مهمًا في تطوير المناعة الفطرية. أجريت هذه الدراسة لتقييم مستويات الببتيدات الفمويه المضادة للميكروبات **(cathelicidins and human beta defensins-1)** في مصل مرضى التهاب اللثة والأشخاص الاصحاء. شارك خمسون مريضًا تتراوح أعمارهم بين (20-59) عامًا ، و خمسة وثلاثون متطوعًا سليمًا تمت مطابقة أعمارهم و جنسهم مع المرضى في هذه الدراسه .

معلمات اللثة المستخدمة في هذه الدراسة هي (**PLI, GI, BOP, PPD and CAL**). تم جمع عينات الدم من جميع الأشخاص ، ثم تم تقدير مستويات تلك الببتيدات بواسطة تقنية الاليزا . أظهرت النتائج الحالية زيادة معنوية (**P <0.01**) في مستويات تلك الببتيدات في المرضى مقارنة بألأصحاء ، علاوة على ذلك ، لا توجد علاقة معنوية (**P>0.05**) مع جميع المتغيرات السريرية اللثوية. تقدم هذه النتائج دليلاً على الدور المهم للببتيدات المضادة للميكروبات في العملية الالتهابية في التهاب اللثة وان تلك الزياده ليست كافية لحماية المرضى من تدمير اللثه .