A study of IL-35 and IL-17 Levels for People with Periodontal Disease

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ABSTRACT

This research aims to evaluate the functions of IL-17 and IL-35 indicators in periodontal disease. This investigation involved forty-five patients with periodontal disease and forty-five healthy individuals as a control group. from November 2023 until April 2024. All indicators were quantified using enzyme-linked immunosorbent assay (ELISA). The findings of the present investigation indicated. The findings revealed that the majority of patients were male (66.7%) and smokers (57.8%), with a predominant age range of 51 to 60 years (35.6%). He also observed elevated levels of IL-17 and IL-35 in patients comparing to the healthy control group ($p<0.05$). The ROC curve analysis indicated that IL-17 exhibited superior sensitivity, specificity, odds ratio, and relative risk compared to IL-35, all demonstrating significant differences ($p<0.05$). A positive connection existed between IL-17 and IL-35 ($r=0.249$), although it was not statistically significant ($p>0.05$). This study indicated that IL-17 is more crucial for identifying periodontal disease due to its superior sensitivity and specificity in comparison to IL-35.

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1.Introduction

Periodontitis, recognized as the second most common dental condition worldwide, ranks just after dental caries in prevalence. This illness progressively deteriorates the tissues that sustain the teeth and is associated with other systemic ailments [1, 2]. Periodontitis affects roughly 10% to 15% of the global population and is more common in individuals from lower socioeconomic backgrounds, reflecting trends observed in other health conditions associated with restricted access to hygiene, medical oversight, and fundamental care [3]. Social and environmental factors, including age, sex, genetic predisposition, tobacco consumption, pregnancy, financial difficulties, and depression, influence periodontal diseases [4]. Moreover, diet and nutrition, obesity, and immunological weakness also influence periodontitis [5]. Systemic disorders, such as type 1 and type 2 diabetes mellitus, are risk factors for periodontal diseases [6]. Gram-negative and anaerobic microorganisms are primarily responsible for inducing periodontitis, an inflammatory condition affecting the tissues that protect the teeth [7]. The degeneration of periodontal ligaments, alveolar bone, and gingiva, leading to tooth loss, is a consequence of periodontal. Within gingival plaques, there exists a presence of live bacteria and the byproducts of biofilm bacteria, including lipopolysaccharides, which trigger inflammation. As a result, the inflamed tissues release inflammatory cytokines into the bloodstream, acting as signaling proteins [8]. The interactions between periodontal pathogens and the immune system are altered by multiple genetic and environmental components plus the presence of chronic diseases and behaviors like smoking [9]. The host's immune system's disproportionate reaction is what causes all of these harmful occurrences [10]. A redesigned system of grades (A-C) and stages (I-IV) for periodontitis has been introduced recently. While the grading is based on the rate of advancement, which is linked to a number of risk factors, the staging is based on the severity and breadth of the disease [11, 12] The pathophysiology of many inflammatory illnesses, including periodontitis, is caused by soluble protein molecules called cytokines. A particular type of CD4+ T cell is the main secretor of interleukin 17, 2a class of pro-inflammatory cysteine [13], IL-17 was directly act on osteoblasts through different mechanisms, promoting osteoclastogenesis [14]. The IL-17 cytokine is of significant importance as it plays a crucial role in both monitoring the health of the mucosal barrier and contributing to immunopathology. Numerous studies have identified elevated levels of IL-17 in individuals with chronic periodontitis [15]. Furthermore, there is a noteworthy association between heightened IL-17 expression and both the severity of the disease and the clinical indicators of periodontal damage [16, 17] produced by

various regulatory lymphocytes, interleukin 35 (IL-35) is an anti-inflammatory cytokine that functions in immune suppression. Its role includes inhibiting the growth of Th1 and Th17 cells through the restriction of early T cell proliferation [18]. The regulation of periodontitis pathogenesis, specifically the loss of alveolar bone, is achieved by IL-35/IL-37-producing plasma cells within chronic periodontitis lesions. These plasma cells directly inhibit the formation of osteoclasts, effectively preventing bone loss [19. Immunological and infectious diseases are closely linked to the IL-35, which plays a crucial role in maintaining the peripheral immune system, regulating the proliferation of T effector cells, and inhibiting the differentiation of Th17 cells and synthesis of IL-17 [20]. Periodontal is considered the second most common dental condition on Earth, following tooth decay. It causes the tissue supporting the tooth to progressively deteriorate, it's also associated with other systemic issues. Cytokines are involved in the cause of various diseases that have inflammatory symptoms, including periodontal, Therefore some cytokines IL-35, IL-17 were studied to determine their roles in patients with periodontal disease

2. Materials and methods

This study was conducted in Baghdad city for the period from November 2023 to April/2024 ,

It includes Forty- five blood samples were collected from periodontitis patients diagnosed by a specialist in health care centers and outpatient clinics, if 30 (68.2%) samples were collected from males and 14 (31.8%) samples were collected from females. Forty-five samples were collected from healthy individuals as a control group, if 13 (28.9%) were males and 32 (71.1%) were females. The age range in both study groups was 21-66 years.

2.2 Techniques

The collected blood in a gel tube was separated by a centrifuge machine (4000 rpm for 6 minutes) to have serum for detection levels of IL-17 and IL-35 by enzyme immunoassay (ELISA) (Cloud-Clone Group, China). By adding human interleukin to wells that have already been coated with interleukin monoclonal antibody and then incubating, the enzyme-linked immune sorbent assay (ELISA), which is based on biotin double antibody sandwich technology, was able to determine the concentration of immunological markers. Antibodies tagged with biotin should be added after incubation so they can combine with streptavidin-HRP to create the immunological complex. Substrates A and B are added after the unbound enzymes have been removed through incubation and washing. As a result of the acid,

the solution will turn blue and then yellow. Human interleukin concentration and solution colors have a favorable correlation [10].

2.3- Statistical Analysis:

IL-17 and IL-35 indicators were shown as Mean and SD. Student t-tests were utilized to detect variations in levels of the above markers within patients and healthy. Demographic characters were presented such as frequencies and percentages, and the differences in these characters measured by Pearson-Chi-square test. The receiver operating characteristic (ROC) curve was depended to calculate area under the curve (AUC), cut-off, specificity, sensitivity, odd ratio and relative risk of IL-17 and IL-35. Pearson coefficient was utilize to detect type and strong of relationship between IL-17 and IL-35. $P \leq 0.05$ was utilized to detect statistical differences. SPSS v. 22.0 and Prism v.10 statistical software programs were applied for analysis present results.

3. Results and discussion

3.1 Demographic features of periodontitis patients

Present findings showed that most periodontal patients were males (66.7%), smokers (57.8%), and within the age group 51-60 years (35.6%). The differences among percentages of gender were significant ($p<0.05$), while differences within age groups and smoking were not significant ($p>0.05$) (Table 1).

Table 1: Frequencies and percentages of personal features of periodontitis patients

		Count	Percent	P value
Age groups (years)	21-30	8	17.8%	p>0.05
	31-40	8	17.8%	
	41-50	7	15.6%	
	51-60	16	35.6%	
	>60	6	13.3%	
Gender	male	30	66.7%	p<0.05*
	female	15	33.3%	
Smoking	yes	26	57.8%	p>0.05
	no	19	42.2%	

3.2 Mean levels of IL-17 and IL-35 within study groups

The current findings showed increased amounts of IL-17 and IL-35 in patients (334.90±28.05 and 54.59±17.36) versus healthy (196.56±72.65 and 29.54±7.50) with significant differences ($p<0.05$) (table 2 and figure 1).

Table 2: Comparative concentrations of IL-35 and IL-17 between periodontitis patients versus healthy

Groups		N	Mean	Std. Deviation	P value
IL-35 (pg/ml)	Patients	45	54.59	17.36	p<0.001***
	Healthy	45	29.54	7.50	
IL-17 (pg/ml)	Patients	45	334.90	28.05	p<0.001***
	Healthy	45	196.56	72.65	

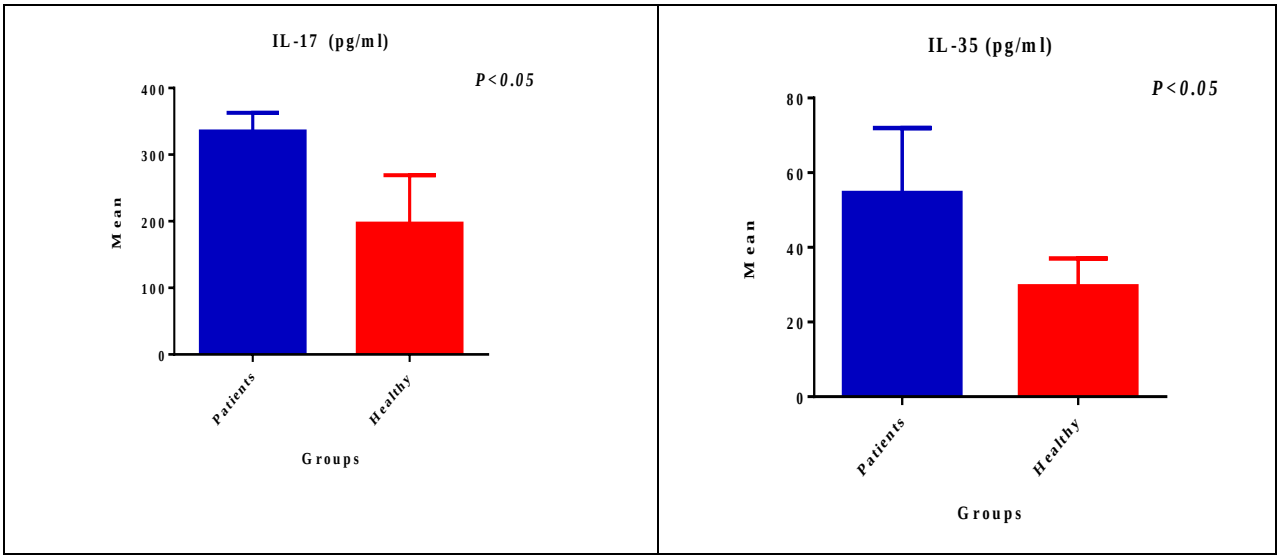

Figure 1: Comparative concentrations of IL-35 and IL-17 between study groups

3.3 ROC curve of IL-17 and IL-35

ROC curve outcomes showed the sensitivity, specificity, odd ratio, and relative risk of IL-17 (97%, 89%, 52, and 36.82) and IL-35 (84%, 87%, 35.29, and 5.67) at cut-off values (293.7 and 34.64) respectively in diagnosis periodontitis patients with significant differences ($p<0.05$) (table 3 and figure 2).

Table 3: ROC curve, sensitivity, specificity, odd ratio, relative risk and accuracy of immunological indicators in screening periodontitis diseases

Variables	AUC	Std. Error	P value	Cut off	Sn. %	Sp. %	odd ratio (C.I.)	relative risk (C.I.)
IL-35 (pg/ml)	0.925	0.029	P<0.001 ***	34.64	84	87	35.29 (10.86 - 89.7)	5.67 (2.84 - 11.34)
IL-17 (pg/ml)	0.943	0.026	P<0.001 ***	293.7	97	89	52 (39.40 – 98.78)	36.82 (5.29 - 92.12)

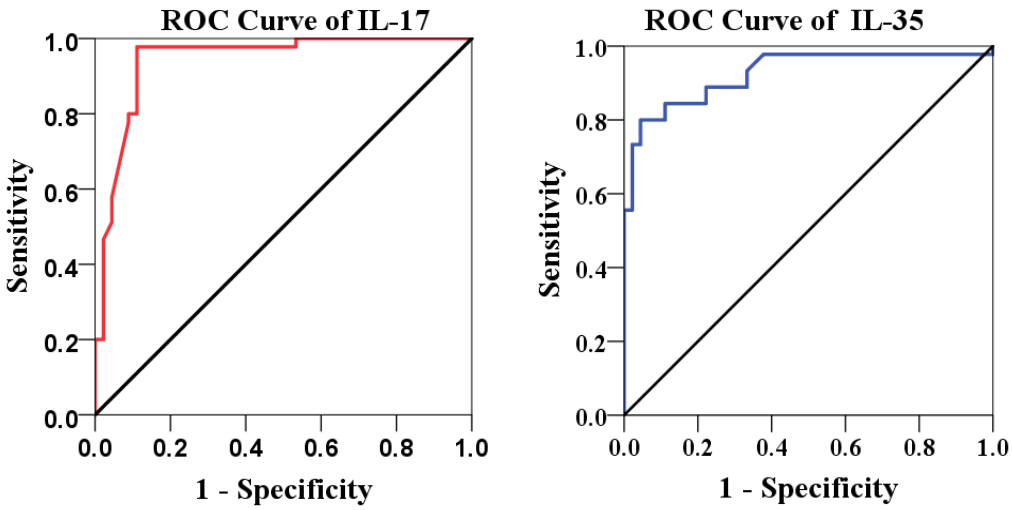

Figure 2: ROC curve of IL-17 and IL-35 indicators in screening periodontitis patients

3.4 Correlation relationship between 17 and IL-35

Pearson coefficient test showed there is a positive correlation between IL-17 and IL-35 (r=0.249) without significant differences (p>0.05) (table 4 and Figure 3).

Table 4: Correlation relationship between IL-17 and IL-35 indicators

		IL-17
IL-35	Pearson Correlation	0.249
	Sig. (2-tailed)	0.099

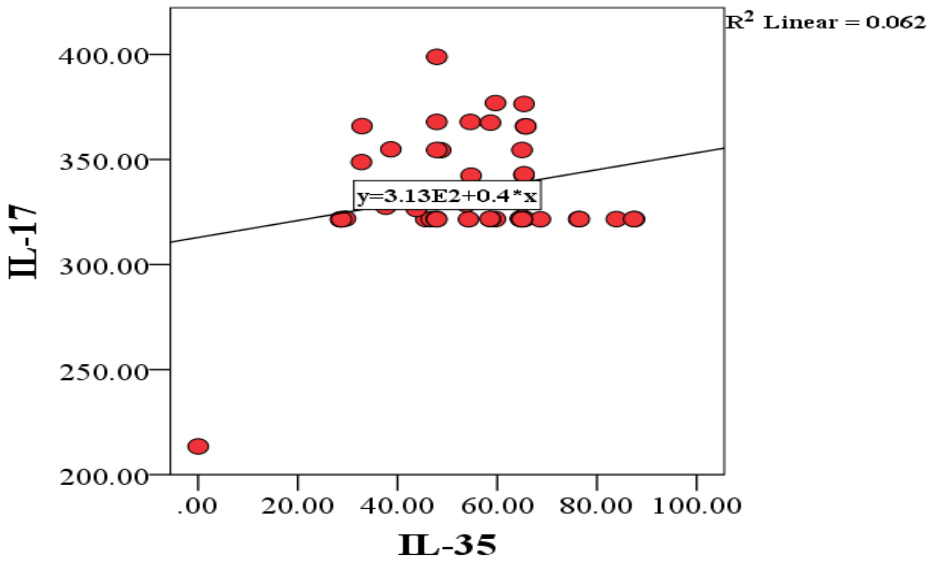

Figure 3: Correlation relationship between IL-17 and IL-35 indicators

3. Discussions

The objective of the current experiment was to identify IL-35 and IL-17 markers in persons with periodontitis. The findings of Levin et al. [21], which revealed that most individuals with periodontitis were nonsmokers aged 30–40, contrasted with current data showing that the majority of affected patients were male smokers over 50 years old. Conversely, Kim [22] discovered that most patients were men aged over 50. A major worldwide health problem, periodontitis is an ongoing inflammatory condition that is more common and severe in the elderly. In the elderly population, aging is a major risk factor for the occurrence of periodontitis, which exacerbates the

breakdown of alveolar bones and results in tooth decay [23]. According to Liu et al. [24], a prior study found that the rates of periodontitis and periodontal health were 3.41% and 13.64% in people aged 35–44, 1.71% and 53.14% in people aged 45–64, and 4.71% and 47.06% in people aged 55–64. In elderly persons, gum recessions are prevalent. At this point, the structure of the tooth's base, or root, becomes visible when the adjacent gum tissues separate from the exposed tooth. This facilitates the accumulation of germs that lead to inflammation and degradation [25]. Rapidly progressing periodontitis can occur as a result of inadequate immune response regulation. The growth of type 17 helper T cells, which are crucial to the immunological response against germs, is also linked to this process [26]. According to a previous investigation, Saudi women had more serious periodontitis compared to their male counterparts [27]. These results did not align with the current study, which found that men are more susceptible to periodontitis than women due to their propensity to disregard their dental health. Males are also more likely to develop heart disease, and the drugs used to treat it can lead to dry mouth or other oral health problems. Dentists are the first stage of defense because there is documentation linking gum disease to heart problems [28]. According to a US research that analyzed extensive data, cigarettes is an important risk factor for periodontitis and could be the cause of over 50% of adult cases of the disease [29]. This research was almost identical to the current one. Smoking impairs the body's immunological system, which fights infections. This makes preventing a gum infection more difficult. Smoking also hinders the healing process of gum injury [30] (Table 1). The findings of the present study aligned with those of Feng et al. [31], who indicated that individuals with periodontitis had elevated levels of IL-17 compared to healthy subjects. In the progression of chronic periodontal disease, IL-17 exhibits both a protective and a deleterious role. Neutrophils are among the first beneficial cells to arrive at the diseased location and have the ability to swiftly exit blood vessels when a periodontal disease infection begins. According to Mazurek-Mochol et al. [32], IL-17 has the ability to attract neutrophils to the afflicted site of periodontal ligaments and control their migration from the bone marrow into the bloodstream. Through both independent and oxygen-dependent processes, neutrophils eat germs and sterilize in order to activate the immune system and provide protection. Yet, neutrophils' primary bactericidal agents are the lysosomal enzymes and superoxide ions, whose overproduction can harm nearby tissue and cell types and intensify the immune system's reaction. Furthermore, the neutrophils' generation and expulsion of inflammatory compounds during the phagocytosis of bacteria will exacerbate inflammatory processes and encourage the regional inflammatory reaction of periodontal tissues, resulting in the destruction and damage of

those tissues [33]. In individuals with periodontitis, IL-17 can also cause osteoblasts to release RANKL, which aids in osteoclast differentiation and mediates alveolar bone absorption [34]. Although several studies have demonstrated that IL-17 is strongly linked to bone destruction in rheumatoid arthritis, researchers have demonstrated that IL-17 has a significant protective function in preventing the breakdown of bones in Porphyromonas gingivalis-induced periodontitis [35]. Moreover, IL-17 can work in concert with IL-1 an2d TNF-α to stimulate gingival fibroblasts to generate MMP-1 and MMP-3, which is crucial for the tissue degradation associated with periodontitis [36]. It is yet unknown if IL-17 contributes to the development of periodontitis, however, it can encourage keratinocytes to release peptides that are antimicrobial and perform defense functions. It is unknown whether IL-17 promotes M1 macrophage polarization and secretes inflammatory markers that trigger the degradation of tooth tissue, but it is implicated in the pathophysiology of obliterative bronchiolitis in the mouse animal model of unusual tracheal the transplantation by controlling M1 macrophage separation [31]. Our study was consistent with Schmidlin et al. [37] results that those with periodontitis had higher levels of IL-35 than controls. Th1 and Th17 cells and their inflammatory markers have been linked to periodontal disease in previous research [38]. According to the findings of several research, continual periodontitis causes aberrant immune cell function, and the emergence of periodontal disease may be concurrently linked to increased peripheral Th17 and Th1 cells. Interestingly, IL-35 could guard against periodontal disease by inhibiting Th17 and Th1 cells [39]. According to a recent study, IL-35 may be a useful biomarker for reducing inflammation and preventing periodontal disease. Consequently, periodontitis may benefit from IL-35 target treatment , and the investigators observed that IL-35 may suppress the synthesis of cytokines associated with inflammation including IL-6 and IL-8 and proposed an anti-inhibitory role for IL-35 in the pathophysiology of periodontitis [40]. Accordingly, the findings of an interventional animal investigation also took into account IL-35 inhibitory role in the pathophysiology of resorption of alveolar bones [41]. According to a different in vitro cell investigation, IL-35 and RANKL may work in concert to promote osteoclastogenesis , But according to their findings, bone marrow-derived macrophages comprise a variety of cell types, mostly lymphocytes, which can be impacted by IL-35 in different ways [42].

By controlling the immune system's response, IL-35, a Treg-specific suppression of cytokines associated with inflammation, may help persistent periodontal individuals avoid periodontal tissue harm brought on by an excessively stimulated immune response by balancing bacterial infection

with effector cells [43]. When compared to normally functioning tissue, sick tissue has greater amounts of IL-35 amino acids and subunit mRNA, suggesting that it may be a significant factor in the progression of persistent periodontitis (CP). Given the ease of sampling gingival crevicular fluids (GCFs) and the availability of straightforward, accurate, and sensitive IL-35 detection techniques, IL-35 may prove to be a significant clinical diagnostic tool [44]. Higher salivary IL-35 amounts are positively correlated with higher levels of clinical indicators such as the plaque index, gingival index, probing depth, and clinical connection, according to comparative and correlation studies. Although there isn't much research on IL-35, it has the potential to be a treatment for periodontitis-related alveolar bone resorption [45]. Thus, it would be interesting to look into how IL-35 inoculations affect the reduction of periodontitis in addition to helping to immunomodulate periodontal disease [46]. A possible link between serious periodontitis and IL-35 is suggested by a new study that found increased levels of IL-35 in people with stage III as well as stage IV periodontitis as well as a connection between IL-35 levels and periodontitis. By comparing various phases and grades of periodontitis, a more thorough investigation of this IL-35 may provide insightful information [47] (Table 2). Abdullameer and Abdulkareem [48] showed the sensitivity and specificity of saliva IL-17 in screening patients with periodontitis were (80% and 81%) at cut off 322.61 pg/ml, and these findings were lowest to our research that showed the sensitivity and specificity of serum IL-17 were (97% and 89%) at cut off 293.7 pg/ml. Therefore, measure of IL-17 in serum is most preferred in serum than saliva in screening periodontitis. Hassan et al., [40] showed the sensitivity and specificity of salivary IL-35 in periodontitis patients were 100% and 100%) at cut off <35 pg/ml, and these outcomes were highest compared to our study that mentioned the sensitivity and specificity of serum IL-35 were (84% and 87%) at cut off 34.64 pg/ml. Therefore, it is suggest calculate IL-35 in saliva for diagnosis periodontitis due to it has highest sensitivity and specificity (Table 3). Finally, person coefficient showed positive correlation between IL-17 and IL-35 indicators due to inflammation in periodontal region. IL-17 is pro-inflammatory cytokine and lead to increase inflammation in periodontal region (stimulate immune mediators), while IL-35 is anti-inflammatory which lead to inhibit immune mediators to prevent tissue damage. Therefore, both interleukins increase in periodontitis patients (table 4).

5. Conclusions

The current study concludes that patients exhibited an increase in anti-inflammatory IL-35 and pro-inflammatory IL-17 levels. IL-17 serves as a more significant biomarker for diagnosing periodontal disease compared to IL-35 because to its superior sensitivity and specificity. Additionally, the incidence rate among male smokers exceeds that of females. Periodontal disease is more prevalent in senior males aged 51-60 years, attributed to personal habits such as smoking and inadequate dental hygiene, resulting in the lifelong buildup of pathogenic components.

References

[1] D. Lin, K .Moss, J.D. Beck, A. Hefti, S . Offenbacher , Persistently high levels of periodontal pathogens associated with preterm pregnancy outcome, J. Periodontol , 78(2007) 833–41, https://doi.org/10.1902/jop.2007.060201

[2] M.M. Pinho, R. Faria-Almeida, E. Azevedo, M.C.Manso, L.Martins , Periodontitis and atherosclerosis an observational study, J. Periodontal Res, 48(2013) 452-7, DOI: 10.1111/jre.120268

[3] A.J. Gross, K.T. Paskett, V.J. Cheever, M.S. Lipsky , Periodontitis: a global disease and the primary care provider's role, Postgrad. Med. J., 93(2017) 560– 65, DOI: 10.1136/postgradmedj-2017-134801

[4] S. List, J.Galloway, P.A. Mossey, W. Marcenes , Global Economic Impact of Dental Diseases, J. Dental Res. , 94 (2015) 1355–61 , https://doi.org/10.1177/0022034515602879

[5] L.L .Pereira, S.A.Veiga, S.W. Brito, C.T. Almeida, P.C. Bispo, L.F. Barreto , Factors Associated with Periodontitis in Patients with and without HIV, Int . J . Dent . ,5(2023) 2-13, **https://doi.org/10.1155/2023/9929835**

[6] H. Qin, G. Li, X.Xu, C. Zhang, W. Zhong, S. Xu , The role of oral microbiome in periodontitis under diabetes mellitus, J. Oral Microbiol., 14(2022) 2078031, https://doi.org/10.1080/20002297.2022.2078031

[7] C. Pink , B . Holtfreter , H . Volzke , M. Nauck , M. Dorr , T. Kocher , Periodontitis and systemic inflammation as independent and interacting risk factors for mortality, evidence from a prospective cohort study, BMC. Med , 21(2023) 2-17 , https://doi.org/10.1186/s12916-023-03139-4

[8] M. Usui , S. Onizuka , T. Sato, S. Kokabu, W. Ariyoshi, N.Keisuke, Mechanism of alveolar bone destruction in periodontitis - Periodontal bacteria and inflammation, Jpn. Dent .Sci. Rev, 57(2021) 201–208, https://doi.org/10.1016/j.jdsr.2021.09.005

[9] B. G. Loos, T.E, Van Dyke,The role of inflammation and genetics in periodontal disease, Periodontol, 83(2020) 26-39, https://doi.org/10.1111/prd.12297

[10] D.H. Fine, A.G. Patil, B.G Loos, Classification and diagnosis of aggressive periodontitis, J. Clin. Periodontol, 45(2018) 95-111, https://doi.org/10.1111/jcpe.12942

[11] G. Hajishengallis,The inflammophilic character of the periodontitis-associated microbiota, Mol. Oral. Microbiol, 29(2014) 248–57, https://doi.org/10.1111/omi.12065

[12] M.S. Tonetti , H. Greenwell, K. S. Kornman, Staging and grading of periodontitis Framework and proposal of a new classification and case definition, J. Clin. Periodontol, 45(2018) 149-161, https://doi.org/10.1002/JPER.18-0006

[13] D.D. Patel, V.K. Kuchroo, Th17 Cell Pathway in Human Immunity Lessons from Genetics and Therapeutic Interventions, Immunity., 43 (2015) 1040–51, http://dx.doi.org/10.1016/j.immuni.2015.12.003

[14] P.Miossec, J.K. Kolls , Targeting IL-17 and TH17 cells in chronic inflammation, Nat, Rev. Drug. Discov. , 11(2012) 763-76, DOI: 10.1038/nrd3794

[15] C.Zenobia, G. Hajishengallis, Basic biology and role of interleukin-17 in immunity and inflammation, Periodontol , 69(2015) 142-59, https://doi.org/10.1111/prd.12083

[16] O.G. Shaker, N.A.Ghallab , IL-17 and IL-11 GCF levels in aggressive and chronic periodontitis patients relation to PCR bacterial detection , Med. Inflamm., (2012) 174764, DOI: 10.1155/2012/174764

[17] N. Dutzan , R. Vernal, J.P . Vaque, J.Garcia-Sesnich, M. Hernandez, L. Abusleme, Interleukin-21 expression and its association with proinflammatory cytokines in untreated chronic periodontitis patients, J. Periodontol., 83(2012) 948–954, https://doi.org/10.1902/jop.2011.110482

[18] P. Behzadi, E.Behzadi, R.Ranjbar , IL-12 Family Cytokines General Characteristics Pathogenic Microorganisms Receptors and Signalling Pathways, Act. Micro. Immun. Hun. , 63 (2016) 1–25, https://doi.org/10.1556/030.63.2016.1.1

[19] L. Jing, S. Kim, L.Sun, L.Wang, E. Mildner, K. Divaris, Y.Jiao , S.Offenbacher,

IL-37- and IL-35/IL-Producing Plasma Cells in Chronic Periodontitis, J. Dent. Res., 98(2019) 813-821, https://doi.org/10.1177/0022034519847443

[20] Y. Hu, C. Dong, Y.Yue, S.Xiong , In vivo delivery of interleukin-35 relieves coxsackievirus-B3-induced viral myocarditis by inhibiting Th17 cells, Arch. Virol., 159(2014) 2411-2419, DOI https://doi.org/10.1007/s00705-014-2098-z

[21] L.Levin , A. Zini , J. Levine, M. Weiss, R. Lev, D. C. Taub, G. Almoznino , Demographic profile, oral Health Impact Profile and Dental anxiety scale in patients with chronic periodontitis: a case–control study, Inter. Dental. J, 68(2018) 269-278,DOI: 10.1111/idj.12381

[22] B.R. Kim, Impact of Periodontal Treatment and Demographic and Socioeconomic Factors on Tooth Loss in Persons with Disabilities: An Analysis of Korean National Health Insurance Claims Data, J . Dental Hyg Sci., 23(2023) 225-235,DOI:10.17135/jdhs.2023.23.3.225

[23] Z.Zhu, X.Qi , Y. Zheng,Y. Pei, B. Wu, Age differences in the effects of multi-component periodontal treatments on oral and metabolic health among people with diabetes mellitus: A meta-epidemiological study, J. Dent , 135,(2023) 2-18, DOI: 10.1016/j.jdent.2023.104594

[24] Y. Liu, S. Xu, Q. Cai, Y.Chen, P. Zhu, M. Du, A. Li, Does periodontitis affect the association of biological aging with mortality, J. Dental . Res., 102(2023) 909-918, https://doi.org/10.1177/00220345231179117

[25] F.H. Al-Bayaty, A.A Kamaruddin, M.A. Ismail, M.M. Al-Obaidi, Evaluation of Clinical Efficacy of Biodegradable Chip Containing Salvadora persica (miswak) Extract in Chitosan Base as an Adjunct to Scaling and Root Planing in the Management of Periodontitis, Sul. Qab. Univ. Med. J, 24(2024) 360-366, https://doi.org/10.18295/squmj.6.2024.030

[26] Q. Wu , W. Zhang, Y. Lu, H. Li, Y. Yang, F. Geng, C. Li, (2024). Association between periodontitis and inflammatory comorbidities: The common role of innate immune cells, underlying mechanisms and therapeutic targets, Inter. Imm , 128(2024) 111558, https://doi.org/10.1016/j.intimp.2024.111558

[27]H.M.Alqahtani, M.K. Alshehri, Demographic insights into the periodontology workforce in Saudi Arabia: A descriptive study. Sau. Dent. J., 36(2024) 718-721, https://doi.org/10.1016/j.sdentj.2024.02.020

[28] A.Angjelova, E. Jovanova, A. Polizzi, L. Laganà ,S. Santonocito, R.Ragusa, G.Isola , Impact of periodontitis on endothelial risk dysfunction and oxidative stress improvement in patients with cardiovascular disease, J. Clin. Med., 13(2024) 2-17, https://doi.org/10.3390/jcm13133781

[29]K.Y.Sim, Y.S. Jang, Y.S Jang, N. Nerobkova , E.C. Park, Association between smoking and periodontal disease in South Korean adults, Inter.J. envir. Res. Pub. Heal., 20(2023) 2-11, https://doi.org/10.3390/ijerph20054423

[30] L.V. Knie, K.N. Leknes, Y. Xue, S.8A.Lie, D.F. Bunæs, Serum biomarker levels in smokers and non-smokers following periodontal therapy A prospective cohort study. BMC. Ora. Heal., 24(2024) 2-13 , https://doi.org/10.1186/s12903-024-04196-8

[31]Y.Feng, Z. Chen, S.Q. Tu, J.M.Wei, Y.L. Hou, Z.L. Kuang, & H.Ai, Role of interleukin-17A in the pathomechanisms of periodontitis and related systemic chronic inflammatorydiseases, Fro. Imm., 13,(2022)116,https://doi.org/10.3389/fimmu.2022.86245

[32]M. Mazurek-Mochol, K. Serwin, T. Bonsmann, M. Kozak, K. Piotrowska, M. Czerewaty, & A.Pawlik, Expression of Interleukin 17A and 17B in Gingival Tissue in Patientswith Periodontitis. J. Clin. Med., 12(2023) 2-9 ,https://doi.org/10.3390/jcm12144614

[33] S .Liu, Y. Chen, Y. Jiang, J. Du, L. Guo, J. Xu, & Y.Liu, The bidirectional effect of neutrophils on periodontitis model in mice: A systematic review, J.Or. Dis., 30(2024)2865-2875. https://doi.org/10.1111/odi.14803

[34] M.Relvas, R. Silvestre, M. Gonçalves, C .Cabral, A. Mendes-Frias, L. Monteiro, A.Viana da Costa, Analysis of Salivary Levels of IL-1β, IL17A, OPG and RANK-L in Periodontitis Using the 2017 Classification of Periodontal Diseases—An Exploratory Observational Study, J. clin. Med., 12(2023) 2-14, https://doi.org/10.3390/jcm12031003

[35] L.Jia, R. Wu, N. Han, J. Fu, Z. Luo, L. Guo, Y.Liu, Porphyromonas gingivalis and Lactobacillus rhamnosus GG regulate the Th17/Treg balance in colitis via TLR4 and TLR2, Clin. Transl. Imm., *9*(2020) 1-22 https://doi.org/10.1002/cti2.1213

[36]B. Lin, Y. Fan, X. Yang, J.L. Pathak, M. Zhong, MMP-12 and Periodontitis: Unraveling the Molecular Pathways of Periodontal Tissue Destruction, J. Inflamm.Res.,9(2024) 7793-7806, https://doi.org/10.2147/JIR.S480466

[37] P.R.Schmidlin, M. Dehghannejad, O. Fakheran , Interleukin-35 pathobiology in periodontal disease: a systematic scoping review, BMC. Oral. Heal., 21(2021) 2-9, https://doi.org/10.1186/s12903-021-01515-1

[38] Y.Kou, Y.Jiang, S.Liu, P. Yang, Y. Lu, H. Liu, M. Li, Regulatory T cells showed characteristics of T helper-17 (Th17) cells in mice periodontitis model, Ora. Disea., 29(2023) 1149-1162, https://doi.org/10.1111/odi.14072

[39] E.S.Taskaldiran, G. Tuter, A.A. Yucel, M. Yaman, Effects of smoking on the salivary and GCF levels of IL-17 and IL-35 in periodontitis, J.Odon ., 112(2024) 616-623, https://doi.org/10.1007/s10266-023-00843-8

[40] S.S.Hassan, M. Abdelkawy, O.G. Shaker, N.A.F. Tarrad, IL-39 and IL-35 gingival crevicular fluid levels in diabetic patients with generalized periodontitis, Clin. Oral Inves., *28*(2024) 2-11 , https://doi.org/10.1007/s00784-023-05484-3

[41] S.Li, L. Su, Q. Luan, G. Liu, W. Zeng, X. Yu, Regulatory B cells induced by interleukin-35 inhibit inflammation and alveolar bone resorption in ligature-induced periodontitis, J. Period., 94(2023) 1376-1388, https://doi.org/10.1002/JPER.23-0038

[42] Y.Kamiya, T. Kikuchi, H. Goto, I.Okabe, Y. Takayanagi, Y. Suzuki, A. Mitani , IL-35 and RANKL synergistically induce osteoclastogenesis in RAW8264 mouse monocytic cells, Int. J. Mol. Sci., 21(2020) 2-12, https://doi.org/10.3390/ijms21062069

[43] Y.Jin, D. Liu, X. Lin, IL-35 may maintain homeostasis of the immune microenvironment in periodontitis, Exp. Thera. Med., 14(2017) 5605-5610, https://doi.org/10.3892/etm.2017.5255

[44] A. Jadhav, S.R. Rathod, A.P. Kolte, P. Kasliwal , Effect of nonsurgical periodontal therapy on interleukin-35 level in gingival crevicular fluid, SRM. J. Res. Dent. Sci., 14(2023) 194-198, https://doi.org/10.4103/srmjrds.srmjrds_150_23

[45] E.A. Cafferata, C. Terraza-Aguirre, R. Barrera, N. Faúndez, N. González, C. Rojas , R.Vernal, Interleukin-35 inhibits alveolar bone resorption by modulating the Th17/Treg imbalance during periodontitis, J. Clin. Period., 47(2020) 676-688, https://doi.org/10.1111/jcpe.13282

[46] P.Yuvashri, R.R. Devi, H.E. Nalini, P.A.K. Prasad, Estimating the salivary levels of IL-35 in smokers with periodontitis: A cross sectional study, Sau. Den.J., 36(2024) 168-172, https://doi.org/10.1016/j.sdentj.2023.09.006

[47] M.Altaca, E.I. Cebesoy, N.A. Kocak-Oztug, I. Bingül, E. Cifcibasi, Interleukin-6-17, and-35 levels in association with clinical status in stage III and stage IV periodontitis: a cross-sectional study, BMC. Oral . Heal., 24(2024) 2-11, https://doi.org/10.1186/s12903-024-04751-3

[48] M.A. Abdullameer, A.A. Abdulkareem , Diagnostic potential of salivary interleukin-17RANKL and OPG to differentiate between periodontal health and disease and discriminate stable and unstable periodontitis: A case-control study, Heal. Sci. Rep., 6(2023) 1-8, https://doi.org/10.1002/hsr2.1103

دراسة مستويات الحركيات الخلوية IL-17 , IL-35 في المرضى المصابين بأمراض اللثة

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المستخلص

يهدف هذا البحث إلى تقييم أدوار المؤشرات المناعية IL-17 و IL-35 في أمراض اللثة. شمل هذا البحث خمسة وأربعون مريضًا مصابًا بأمراض اللثة وخمسة وأربعون من الاصحاء (كمجموعة سيطرة). تم جمع العينات من نوفمبر 2023 إلى أبريل 2024. تم قياس جميع العلامات باستخدام اختبار الممتز المناعي المرتبط بالإنزيم (ELISA) أظهرت نتائج البحث الحالي أن معظم المرضى كانوا من الذكور (66.7٪) المدخنين (57.8٪) الذين تتراوح أعمارهم بين 51 إلى 60 عامًا (35.6٪). كما وجد زيادة في مستويات IL-17 و IL-35 في المرضى مقارنة بمجموعة التحكم الصحية ($p < 0.05$)أظهر تحليل منحنى ROC أن IL-17 لديه حساسية وخصوصية ونسبة احتمالات ومخاطر نسبية أعلى من IL-35، مع وجود فروق معنوية ($p < 0.05$) كان هناك ارتباط إيجابي بين IL-17 و IL-35؛ ($r = 0.249$) ومع ذلك، لم يظهر فروق معنوية ذا دلالة إحصائية ($p > 0.05$) وجدت هذه الدراسة أن IL-17 أكثر أهمية للكشف عن أمراض اللثة بسبب حساسيته العالية وخصوصيته مقارنة بـ IL-35.