Brazilian Dental Science

unesp
UNIVERSIDADE ESTADUAL PAULISTA
"JÚLIO DE MESQUITA FILHO"
Instituto de Ciência e Tecnologia
Campus de São José dos Campos

ORIGINAL ARTICLE

DOI: https://doi.org/10.4322/bds.2024.e3960

Molecular detection of IL-10 level to determine severity of periodontitis in type 2 Diabetes Mellitus patients

Detecção molecular do nível de IL-10 para determinar a gravidade da periodontite em pacientes com Diabetes Mellitus tipo 2

Titiek BERNIYANTI[1], Retno PALUPI[1], Baleegh Abdulraoof ALKADASI[2], Riski Rossa APRILIANI[3], Naufal Ikbar YAASIR[3]

1 - Universitas Airlangga, Faculty of Dental Medicine, Department of Dental Public Health, Surabaya City, Indonesia
2 - Ibb University, Faculty of Dentistry, Department of Periodontology and Oral Medicine, Ibb City, Yemen
3 - Universitas Airlangga, Faculty of Dental Medicine, Surabaya City, Indonesia

How to cite: Berniyanti T, Palupi R, Alkadasi BA, Apriliani RR, Yaasir NI. Molecular detection of IL-10 level to determine severity of periodontitis in type 2 Diabetes Mellitus patients. Braz Dent Sci. 2024;27(1):e3960. https://doi.org/10.4322/bds.2024.e3960

ABSTRACT

Objective: The prevalence of periodontal disease is increasing in most countries including developing and developed countries. It affects 20-50-% of the global population. Patients with type 2 Diabetes Mellitus (DM) with severe periodontal disease had a 3.2 times higher risk of death than individuals without periodontitis. Periodontitis contributes to small-scale systemic inflammation. The objective of this study was to determine the severity of periodontitis using IL-10 (Interleukin-10) level in type 2 diabetes mellitus. **Materials and Methods:** This study was cross-sectional. All methods were performed following the guidelines and regulations of the Ethics Committee, Faculty of Dental Medicine, Universitas Airlangga. The samples were 90 subjects. The instruments used were questionnaires, periodontal status measurements based on Community Periodontal Index (CPI), and random blood glucose measurements. Data on the IL-10 level was obtained using Gingival Crevicular Fluid (GCF). **Results:** There was a significant difference in lifestyle in each group. The highest IL-10 level was found in the periodontitis group, followed by the periodontitis with the type 2 DM group. **Conclusion:** The level of IL-10 can be used to determine periodontitis severity in type 2 DM. Most respondents with the highest level of IL-10 were found in periodontitis followed by periodontitis with type 2 DM group. High levels of IL-10 will decrease the synthesis of Tumor Necrosis Factor Alpha (TNF-α), Interleukin-1 (IL-1), Interleukin-6 (IL-6), activation of macrophages, and Polymorphonuclear neutrophil (PMN).

KEYWORDS

IL-10; Periodontitis; Diabetes Mellitus; Medicine; Health risk.

RESUMO

Objetivo: A prevalência da doença periodontal tem aumentado na maioria dos países, incluindo países em desenvolvimento e desenvolvidos, Afetando 20-50% da população global. Pacientes com Diabetes Mellitus tipo 2 (DM) com doença periodontal grave apresentaram risco 3,2 vezes maior de morte do que indivíduos sem periodontite. O objetivo deste estudo foi determinar a gravidade da periodontite utilizando o nível de IL-10 (Interleucina-10) no diabetes mellitus tipo 2. **Materiais e Métodos:** Este estudo transversalfoi realizadoseguindo as orientações e regulamentos do Comitê de Ética da Faculdade de Medicina Dentária da Universitas Airlangga. Noventa participantes,responderam um questionário e foram examinados , para o estado periodontal, baseadas no Índice Periodontal Comunitário (IPC) e medidas aleatórias de glicemia. Os dados do nível de IL-10 foram obtidos utilizando Fluido Crevicular Gengival (GCF). **Resultados:** Houve uma diferença significativa no estilo de vida em cada grupo. O nível mais alto de IL-10 foi encontrado no grupo com periodontite, seguido pela periodontite com o grupo DM tipo 2. **Conclusão:** O nível de IL-10 pode ser utilizado para determinar a gravidade da periodontite no DM tipo 2. A maioria dos participantes com maior nível de IL-10 estava no grupo periodontite seguida de periodontite com DM tipo 2. Altos níveis de IL-10 diminuiem a síntese do Fator de Necrose Tumoral Alfa (TNF-α), Interleucina-1 (IL-1), Interleucina-6 (IL-6), ativação de macrófagos e neutrófilos polimorfonucleares (PMN).

PALAVRAS-CHAVE

IL-10; Periodontite; Diabetes Mellitus; Medicina; Fatores de risco.

INTRODUCTION

Periodontitis is a disease that includes the chronic inflammatory process and is initiated and exacerbated by a weak host immune response to bacterial biofilms on teeth. Periodontitis affects the vitality of the periodontal tissue because the inflammatory process can cause progressive tissue damage and lead to tooth loss. According to its pathophysiology, periodontitis is an inflammatory response to an imbalance of microbes in the oral cavity. The severity of periodontitis occurs in 10-15%, and the prevalence is twice as high in individuals over 50 years of age [1,2]. The main features of periodontitis are loss of periodontal tissue manifested by loss of attachment (LOA) and bone resorption detected by radiographic examination, periodontal pockets, and bleeding on the probing of gingival tissue [3].

Periodontal disease can affect 50% of the global population, it is the most common oral disease and has serious damage such as tooth loss. The prevalence of periodontal disease is increasing in most countries including developing and developed countries. It affects 20-50-% of the global population. Patients with type 2 diabetes mellitus (Type 2 DM) with severe periodontal disease had a 3.2 times higher risk of death than individuals without periodontitis. Previous studies have also shown that there is a close association between lifestyle and diabetes mellitus. Lifestyle can determine the severity of Type 2 DM and it is also a risk factor in Type 2 DM. Good management of lifestyle can lead to a healthy lifestyle which can prevent the severity of DM and also delay the complications of this disease [4]. This association can also lead to further infection and also delay the wound healing process. According to the WHO, 80% of non-communicable diseases including Type 2 DM can be prevented by changes in lifestyle [4,5].

Periodontitis contributes to small-scale systemic inflammation. The cause of this systemic inflammation is related to the release of bacterial and virulence factors and/or inflammatory mediators from the periodontal tissues into the bloodstream. These factors allow the circulation of cytokines that lead to increased risk factors for heart disease, insulin resistance, complications of diabetes mellitus, and other systemic diseases [6]. Periodontitis is considered a complication of diabetes mellitus because it is very closely related to diabetes mellitus, especially uncontrolled diabetes mellitus. Individuals with systemic disorders of uncontrolled diabetes mellitus are more susceptible to infection and impaired wound healing [1].

Periodontitis has an association with the imbalances between protein inflammation such as pro-inflammatory cytokines and anti-inflammatory cytokines that affect systemic manifestations [6]. Pro-inflammatory cytokines have an important role in inflammatory reactions and show an increased risk of diabetes mellitus because they can increase the resistance of insulin in several cells of the body such as adipocyte cells, muscle cells, and hepatic cells directly, and will result in the systemic disturbances of insulin sensitivity and the damage in glucose homeostasis [7]. The previous study that was conducted in 2014 showed that 8.5% of adults aged 18 years and over had diabetes. Meanwhile, in 2016 diabetes was one of the causes of death with 1.6 million deaths, and high blood glucose levels were another cause of 2.2 million deaths [8].

The previous report that was obtained from 12,254 participants in the Third National Health and Nutrition Examination Survey (NHANES III) showed that all the participants of those study who had severe periodontitis also had an increase in both fasting glucose ($\geq$ 100 but $<$ 126 mg/dl) and were diagnosed with diabetes mellitus ($\geq$ 126 mg/dl). Studies showed that pro-inflammatory cytokines have an important role in inflammatory reactions and could increase the risk of diabetes mellitus [7]. Several studies have shown that inflammatory mediators such as fibrinogen, C-reactive protein (CRP), and pro-inflammatory cytokines (IL-6 and TNF-α) are associated with metabolic syndromes such as diabetes mellitus and dyslipidemia [9]. IL-10 is one of the anti-inflammatory cytokines that have a role in the response of anti-inflammatory in metabolic syndrome and diabetes mellitus. There is low production of IL-10 in response to proinflammatory cytokine activity on IL-10 which is associated with high levels of HbA1c and can be a predictor of hyperglycemia [9,10].

IL-10 deficiency can result in an accelerated bone resorption process and inhibition of the bone formation process. IL-10 stimulates the production of osteoprotegerin (OPG) which can inhibit bone resorption by preventing the attachment of the Receptor activator of

nuclear factor kappa-B ligand (RANK/RANKL). In addition, IL-10 is also considered to be an important regulator of bone homeostasis under both inflammatory and homeostatic conditions. Some studies have shown that the decrease in IL-10 levels is considered insufficient to inhibit the synthesis of pro-inflammatory cytokines and collagenases that impact the development of osteoporosis [11,12]. The increased levels of IL-10 can reduce the severity of periodontitis and diabetes mellitus certainly. This condition occurs due to the reduction of synthesis of pro-inflammatory cytokines such as IL-6 and TNF-α because TNF-α can downregulate the tyrosine kinase activity of the insulin receptor and can cause insulin resistance [9,13]. The findings from Toker *et al* in 2017 which stated that the levels of IL-10 GCF in periodontitis patients were higher than in the control group without periodontitis. In his research, Toker suggested that the polymorphism of the IL-10 gene that affects the amount of IL-10 depends on several factors such as cell type, stimulation time, type of stimulus, and the presence of other cytokines. Another study by Miranda et al in 2018 also conducted a similar study and found that the highest levels of IL-10 were found in the control group without periodontitis and diabetes mellitus and lower levels were found in the group with chronic periodontitis, while lower levels were found in the control group and a group with periodontitis and diabetes mellitus [6,14]. Based on the background, this study has an objective to determine the role of IL-10 in the severity of periodontitis in patients with diabetes mellitus.

MATERIALS AND METHODS

This study was an observational analytic with a cross-sectional approach. The instruments used were questionnaires, periodontal status measurements based on CPI, and random blood glucose measurements. Data on the IL-10 level was obtained using GCF. The population of this study was divided into four groups; 1) periodontitis patients with clinical examination of periodontal pockets 4 mm without diabetes mellitus, 2) patients with diabetes mellitus only without periodontitis, 3) patients with both periodontitis and diabetes mellitus, 4) while the control group samples were normal patients without periodontitis and diabetes mellitus. This study used a cluster random sampling technique to obtain the sample. The total sample that was used in this study was 156.

Data collection procedure

Blood glucose examination was carried out on the population of patients with diabetes mellitus and periodontitis at the Surabaya Public Health Center. Informed consent was given to the respondent as an agreement to become a research subject. Examination of blood glucose levels was carried out using Point of Care Testing (POCT) and glucose strips to determine random blood glucose values.

Performing an intra-oral examination using a WHO periodontal probe to determine the pocket depth, bleeding on probing (BOP), loss of attachment, and a dental mirror to assess the severity of the respondent's periodontitis, then recorded on the periodontal status sheet. The examinations carried out were the presence or absence of pockets and bleeding on probing. The criteria to determine pocket depth was ≥ 4 mm.

Conducting interviews with respondents to fill out questionnaires related to the respondent's history of diabetes mellitus

The patients declared that they did not have other systemic diseases other than type 2 diabetes mellitus and not use any drugs that affected on IL10 during the last 6 months.

GCF was obtained using paper points in the deepest periodontal pocket for 30 seconds. First, done the isolation and used paper points. Paper points were immersed in an Eppendorf tube containing 100μL of PBS solution, stored at -30^{0}C, and mixed using a vortex mixer for 1 minute. The solution was added to each well. The solution then was incubated for 90 minutes at 37^{0}C. After incubation, the solution then was transferred and was added 100μL of Biotinylated Detection Ab/Ag then was incubated again for 1 hour at 37^{0}C. The solution was then aspirated and washed 3 times. The solution was added by 100μL HRP Conjugate and was incubated for 30 minutes at 37^{0}C. The solution was then aspirated and washed 5 times. 90μL of substrate reagent was added and incubated for 15 minutes at 37^{0}C. 50μL of Stop Solution was added and the OD value was determined at a wavelength of 450 nm. All the procedures had to be done sequentially.

Data analysis

The results were calculated. The data that was obtained then was tested using a statistical analysis program SPSS 25 software.

RESULTS

Random blood glucose levels were divided into 3 categories (Figure 1), namely 69-140 mg/dl, 141-199 mg/dl, and ≥ 200 mg/dl. The distribution of health status based on random blood glucose levels resulted in 4 groups of respondents (Figure 1). Most random blood glucose levels of respondents were in the 69-140 mg/dl category. At 69-140 mg/dl category, the highest number was in the Periodontitis group without type 2 DM, and the least was in the type 2 DM group without periodontitis. In the category of random blood glucose levels of 141-199 mg/dl the most was in the Periodontitis group without type 2 DM and the least in the Normal and Type 2 Diabetes Mellitus groups. In the category of random blood glucose levels ≥ 200 mg/dl, the most common was the Periodontitis with Type 2 Diabetes Mellitus group.

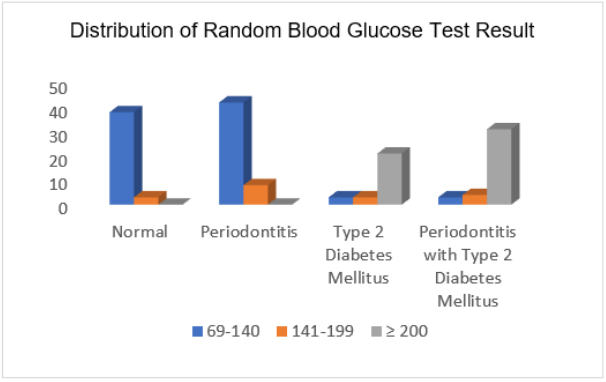

Figure 1 - Result of Random Blood Glucose Test.

Table I - Comparison of Distribution in Each Group

Group	N	Percentage (%)
Normal	42	26.9%
Periodontitis	50	32%
Type 2 Diabetes Mellitus	27	17.3%
Periodontitis with Type 2 Diabetes Mellitus	37	23.8%
Total	156	100%

Most respondents in this study had periodontitis with type 2 diabetes mellitus (Table I) and the least respondents were normal respondents without periodontitis or type 2 diabetes mellitus or both. The comparison test results in clinical examination between groups (Table II) showed significant results. It means that there were differences in clinical examination results (Pocket, LOA, and BOP) between groups. In and BOP results showed that the mean of the periodontitis group was the highest pocket 4.00 ±1.285, and 1.34 ± 0.48 respectively. Meanwhile, in the result of LOA, the highest mean was in periodontitis with type 2 diabetes mellitus group (1.13 ± 0.619). Periodontitis remained the main consistent occurrence. A comparative test of these variables in periodontitis showed significant results in all groups.

There are 14 subjects who have suffered from Type 2 DM for 0-3 years by 46.7% and as many as 16 other subjects for 3-7 years by 53.3% (Table III).

Table II - Comparison of pocket, loss of attachment, and bleeding on probing between all group

Variable	Group	Mean ± SD	p-value
Pocket	Normal	1.84 ± 0.765	0.000*
	Periodontitis	4.00 ±1.285	
	Type 2 Diabetes Mellitus	2.50 ±0.760	
	Periodontitis with Type 2 Diabetes Mellitus	2.31 ± 0.704	
LOA	Normal	0.00 ± 0.00	0.000*
	Periodontitis	0.83 ± 0.803	
	Type 2 Diabetes Mellitus	0.00 ± 0.00	
	Periodontitis with Type 2 Diabetes Mellitus	1.13 ± 0.619	
BOP	Normal	1.00 ± 0.00	0.001*
	Periodontitis	1.34 ± 0.48	
	Type 2 Diabetes Mellitus	1.00 ± 0.00	
	Periodontitis with Type 2 Diabetes Mellitus	1.06 ± 0.25	

*p < 0.05 represents a significant statistical difference.

According to Table IV, most of the respondents that had a bad life style were on periodontitis with type 2 diabetes mellitus group. P-value showed that there was significant difference of life style in each groups (p-value < 0.05).

Lifestyle of respondents showed that bad lifestyle was highest in the periodontitis group and followed by periodontitis and type 2 diabetes mellitus group (Table IV). According to Table V, IL-10 levels were divided into 3 groups mean±SD 3.44 ± 13.19, 13.20 ± 21.00, and 21.01 ± 96.36 pg/ml. In all categories, the mean of periodontitis category had the highest IL-10 level. It means that at all levels, people with periodontitis can produce IL-10 levels actively and progressively. The type 2 DM category had the least levels of IL-10 in the mean ± SD group of 13.20 ± 21.00. Overall based on Table V, the highest IL-10 level was found in the periodontitis without type 2 DM group, followed by Periodontitis with type 2 DM group was the same as the normal group, while in the type 2 DM group was the least.

DISCUSSION

Chronic diseases such as Type 2 Diabetes Mellitus showed insulin resistance. However, not all parents and elderly who have type 2 diabetes mellitus as a disease history also reduce insulin resistance. This condition occurs due to several factors that induce the occurrence of type 2 diabetes mellitus such as diet, lifestyle, and physical activity [15,16]. The highest level of IL-10 was found in the periodontitis group. According to Passoja, the host-pathogen interaction is complex. Its effect depends on the strength and nature of the immune response and the nature of the microbial pathogen that causes it [16]. The downregulation of IL-10 can be influenced by an increased concentration of TNF- α [16,17]. Meanwhile, a previous studies found that there was a higher concentration of IL-10 in the Periodontitis group [13,14]. In the previous study equalized age, and gender in each group of subjects and limited the subject's BMI to <30 kg/m2. Excessive BMI or obesity can affect inflammation. In obesity, there is an overexpression of pro-inflammatory cytokines. Adipose tissue responds to additional nutritional stimulation through adipocyte hyperplasia and hypertrophy. Due to the morphological structure of adipose tissue which is composed of immune cells, endothelium cells, and adipocyte cells that can easily lead to progressive adipocyte enlargement, the blood supply to adipocytes will be reduced

Table III - Distribution based on the history of diabetes mellitus

History of diabetes mellitus	N	Percentage	Total N (Percentage of Respondents with type 2 DM)
0-3 years	14	46.7%	30 (100% / 30%)
3-7 years	16	53.3%	

Table IV - Differences of the lifestyle in each group

Life style	Normal		Periodontitis		Diabetes Mellitus		Periodontitis-Diabetes Mellitus		p-value
	N (%)	(Mean±SD)	N (%)	(Mean±SD)	N (%)	(Mean±SD)	N (%)	(Mean±SD)	
Good	7 (19.4%)	50.05±13.24	25 (69.4%)	41.45±16.17	2 (5.6%)	49.52±11.92	2 (5.6%)	45.59±12.45	0.000*
Bad	12 (22.2%)		16 (29.6%)		12 (22.2%)		14 (25.9%)		

*p < 0.05 represents a significant statistical difference

Table V - Distribution of IL-10

IL-10 Mean±SD	Group (N)			
	Normal	Periodontitis	Type 2 Diabetes Mellitus	Periodontitis with Type 2 Diabetes Mellitus
3.44-13.19	9	25	6	5
13.20-21.00	4	8	6	5
21.01-96.36	6	8	2	6

resulting in hypoxia. Hypoxia is an etiology that triggers necrosis and infiltration of macrophages into adipose tissue, which can then lead to pro-inflammatory mediator overproduction. This will lead to local inflammation in the adipose tissue area, and it progressively spreads and results in systemic inflammation along the body that has an association with the comorbidities obesity-related [13,18,19].

In this study, the second higher results of IL-10 were found in the periodontitis-diabetes Mellitus group and normal group. This result is possible because of the consumption of drugs by patients with diabetes mellitus in this group and the influence of inflammation from the periodontal tissue in this group. This condition occurred due to the anti-inflammatory effect of the antidiabetic drugs consumed by most of our subjects. It is known that several types of antidiabetic medications such as insulin, metformin, sulfonylureas, and others, besides functioning to lower blood glucose also have anti-inflammatory mechanisms [13]. One of the drugs often given by doctors is metformin. Metformin inhibits Nuclear Factor Kappa B (NFkB) activation through blockade of the phosphoinositide 3-kinase (PI3K)-Akt pathway in human blood vessel wall cells, the study then continued that in macrophage-activated lipopolysaccharide, metformin can inhibit the production of the IL-1β precursor molecule. and other pro-inflammatory cytokines meanwhile enhance the induction of the anti-inflammatory cytokine IL-10. Meanwhile, the normal group can be influenced due to local factors such as oral hygiene that leads to tissue inflammation [17-19].

Another result that can be found in this study is the higher mean IL-10 in the group with chronic periodontitis compared to the diabetes mellitus group. IL-10 is a protein that has an important role as an anti-inflammatory cytokine, it represents part of the anti-inflammatory response in several diseases including metabolic syndrome and diabetes mellitus. There is low production of IL-10 in response to proinflammatory cytokine activity on IL-10 which has a correlation with high levels of HbA1c and can be a predictor of hyperglycemia [9,10]. Most patients with a high level of IL-10 were diagnosed with periodontitis and also periodontitis in the type 2 diabetes mellitus group. The severity of periodontitis that can be detected by IL-10 level can be decreased with control of lifestyle and also maintenance of oral health which can decrease the inflammation of periodontal tissue and lower the IL-10 level in periodontal tissue. High levels of IL-10 will decrease the synthesis of TNF-α, IL-1, and IL-6, activation of macrophages, and PMN. Lifestyles such as drinking alcohol, smoking, lower physical activity, bad diet habits, and insufficient sleep had a close correlation with periodontal inflammation, especially in diabetes mellitus patients. Several cells contribute in the severity of inflammation in patients with type 2 DM. Macrophages as cells that are very important in wound healing have the function of bacterial phagocytosis and dead tissue will turn into efferocytotic macrophages (M2) which secrete anti-inflammatory cytokines such as IL-10. IL-10 in patients with diabetes mellitus is less responsive so it is possible to cause the concentration of IL-10 in the diabetes mellitus group to be lower than in the healthy state (without metabolic and inflammatory disorders) and the effect of antidiabetic drugs in the diabetes mellitus group is less dominating, unlike in the periodontitis-diabetes Mellitus group. It should also be noticed that the results obtained also depend on the host-pathogen interaction which is complex and its effect depends on the strength and nature of the immune response and the nature of the microbial pathogen that causes it [7].

Most of the respondents in the Periodontitis group have a bad lifestyle, its score was the highest. It showed that lifestyle is also a risk factor in periodontitis [12]. This result also showed that respondents with bad lifestyles were found high in periodontitis with type 2 DM group which indicated that the lifestyle of patients with periodontitis and diabetes mellitus was worse. Lifestyle has an association with type 2 DM. Lifestyle can worsen the condition of diabetes mellitus and also suppress the immune which can lead to periodontal inflammation and tooth loss [4,5,10]. It was in line with the theory stating that lifestyle is the main risk factor for diabetes mellitus [12].

CONCLUSION

The level of IL-10 can be used to determine the periodontitis severity in patients with type 2 diabetes mellitus. Respondents with the highest level of IL-10 were found in periodontitis followed by periodontitis with type 2 DM group. High levels of IL-10 will decrease the synthesis of Tumor Necrosis Factor Alpha (TNF-α), Interleukin-1 (IL-1), Interleukin-6 (IL-6), activation of macrophages, and Polymorphonuclear neutrophil (PMN).

The higher level of IL-10 showed the more severe of inflammation in periodontal tissue in patients with type 2 DM.

Acknowledgements

All the authors would like to express their gratitude towards all the parties who supported this research including the Rector, the Director of the Research and Innovation Center, the Dean, and the Department of Dental Public Health, Faculty of Dental Medicine, Universitas Airlangga.

Author's Contributions

TB, RP: Conceptualization. TB, RP Data Curation. TB: Formal Analysis. TB, RP: Supervision. RP, NIY: Methodology. RP: Visualization. TB, RP, BAA: Writing – Review & Editing. RP, BAA: Validation. RRA, NIY: Resources. RRA, NIY: Writing – Original Draft Preparation. RRA: Project Administration. NIY: Investigation. NIY: Funding Acquisition.

Conflict of Interest

The authors declare that they do not have to compete with interests.

Funding

This study was supported by a grant from the Ministry of Higher Education, with grant number (No. 428/UN3/2020); Jakarta, Indonesia. The funder of this study did not have any role in the study design, data collection, data analysis, and interpretation, preparation of the manuscript, and the decision to submit the paper for publication.

Regulatory Statement

This study has been approved ethically by Ethics Committee, Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia (Number: 172/HRECC.FODM/IV/2019).

REFERENCES

1. Teeuw WJ, Kosho MXF, Poland DCW, Gerdes VEA, Loos BG. Periodontitis as a possible early sign of diabetes mellitus. BMJ Open Diabetes Res Care. 2017;5(1):e000326. http://doi.org/10.1136/bmjdrc-2016-000326. PMid:28316794.
2. Llanos AH, Silva CGB, Ichimura KT, Rebeis ES, Giudicissi M, Romano MM, et al. Impact of aggressive periodontitis and chronic periodontitis on oral health-related quality of life. Braz Oral Res. 2018;32(0):e006. http://doi.org/10.1590/1807-3107bor-2018.vol32.0006. PMid:29451591.
3. 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 Clin Periodontol. 2018;45(Suppl 20):162-70. PMid:29926490.
4. Samudera WS, Efendi F, Indarwati R. Effect of community and peer support based healthy lifestyle program (CP-HELP) on self care behavior and fasting blood glucose in patient with type 2 Diabetes Mellitus. J Diabetes Metab Disord. 2021;20(1):193-9. http://doi.org/10.1007/s40200-021-00729-y. PMid:34178831.
5. World Health Organization (WHO). 2013. Available from: https://www.who.int/publications/i/item/WHO-NMH-MND-13.2
6. Miranda TS, Haleuy SL, Cruz DF, da Silva HDP, Feres M, Figueiredo LC, et al. The ratios of pro-inflammatory to anti-inflammatory cytokines in the serum of chronic periodontitis patients with and without type 2 diabetes and/or smoking habit. Clin Oral Investig. 2018. http://doi.org/10.1007/s00784-018-2471-5. PMid:29737428.
7. Al-Shukaili A, Al-Ghafri S, Al-Marhoobi S, Al-Abri S, Al-Lawati J, Al-Maskari M. Analysis of inflammatory mediators in type 2 diabetes patients. Int J Endocrinol. 2013;2013:976810. http://doi.org/10.1155/2013/976810. PMid:23762057.
8. World Health Organization. Global Report On Diabetes. Geneve: WHO Press; 2014.
9. van Exel E, Gussekloo J, de Craen AJ, Frolich M, Bootsma-Van Der Wiel A, Westendorp RG. Low production capacity of interleukin-10 associates with the metabolic syndrome and type 2 diabetes: the Leiden 85-Plus Study. Diabetes. 2002;51(4):1088-92. http://doi.org/10.2337/diabetes.51.4.1088. PMid:11916930.
10. Wang X, Bao W, Liu J, Ouyang YY, Wang D, Rong S, et al. Inflammatory markers and risk of type 2 diabetes: a systematic review and meta-analysis. Diabetes Care. 2013;36(1):166-75. http://doi.org/10.2337/dc12-0702. PMid:23264288.
11. Fenol A, Sasidharan RK, Krishnan S. Levels of interleukin -10 in gingival crevicular fluid and its role in the initiation and progression of gingivitis to periodontitis. J Oral Hyg Health. 2014;2(3):3. http://doi.org/10.4172/2332-0702.1000135.
12. Zhang Q, Chen B, Yan F, Guo J, Zhu X, Ma S, et al. Interleukin-10 inhibits bone resorption: a potential therapeutic strategy in periodontitis and other bone loss diseases. BioMed Res Int. 2014;2014:284836. http://doi.org/10.1155/2014/284836. PMid:24696846.
13. Acharya AB, Thakur S, Muddapur MV. Evaluation of serum interleukin-10 levels as a predictor of glycemic alteration in chronic periodontitis and type 2 diabetes mellitus. J Indian Soc Periodontol. 2015;19(4):388. http://doi.org/10.4103/0972-124X.150876. PMid:26392685.
14. Toker H, Gorgun EP, Korkmaz EM, Yüce HB, Poyraz O. The effects of IL-10 gene polymorphism on serum, and gingival crevicular fluid levels of IL-6 and IL-10 in chronic periodontitis. J Appl Oral Sci. 2018;26(0):e20170232. http://doi.org/10.1590/1678-7757-2017-0232. PMid:29489938.
15. Bokhari SAH, Suhail AM, Malik AR, Imran MF. Periodontal disease status and associated risk factors in patients attending a dental teaching Hospital in Rawalpindi, Pakistan. J Indian Soc Periodontol. 2015;19(6):678-82. http://doi.org/10.4103/0972-124X.156882. PMid:26941520.
16. Holt R, Cockram C, Flyvbjerg A, Goldstein B. Textbook of diabetes (5th ed.). Chichester: John Wiley& Sons Ltd; 2017. http://doi.org/10.1002/9781118924853.

17. Passoja A, Puijola I, Knuuttila M, Niemela¨ O, Karttunen R, Raunio T, et al. Serum levels of interleukin-10 and tumour necrosis factor-a in chronic periodontitis. J Clin Periodontol. 2010;37(10):881-7. http://doi.org/10.1111/j.1600-051X.2010.01602.x. PMid:20718895.

18. Xourgia E, Tzouganatou E-M, Papazafeiropoulou A, Melidonis A. Anti-inflammatory properties of antidiabetic agents. World J Metaanal. 2019;7(4):129-41. http://doi.org/10.13105/wjma.v7.i4.129.

19. Mohammed SE, Patimah I, Khaza'ai H, Rahmat A, Abed Y. Obesity and inflammation: the linking mechanism and the complications. Arch Med Sci. 2017;13(4):851-63. http://doi.org/10.5114/aoms.2016.58928. PMid:28721154.

Titiek Berniyanti
(Corresponding address)
Universitas Airlangga, Faculty of Dental Medicine, Department of Dental Public Health, Surabaya, Indonesia
Email: titiek-b@fkg.unair.ac.id

Date submitted: 2023 July 13
Accept submission: 2024 Mar 27