Dental Journal
Majalah Kedokteran Gigi

Dental Journal
(Majalah Kedokteran Gigi)
2025 September; 58(3): 314–324

Review article

Understanding the role of salivary proteomic markers in detecting chronic periodontitis in adults with obesity—A systematic review

V. Ramya[1], Amaldas Julius[2], V. Aarthi Nisha[3], J. Bhuvaneswarri[1], Karthikeyan Pandiyambakkam Rajendran[4], Rakesh Anbazhagan[4]
[1]Department of Periodontics, Sree Balaji Dental College and Hospital, Bharath University, Chennai, Tamil Nadu, India
[2]Department of Biochemistry, Sree Balaji Dental College and Hospital, Bharath University, Chennai, Tamil Nadu, India
[3]Department of Oral Medicine and Radiology, Tamil Nadu Government Dental College and Hospital Chennai, Tamil Nadu, India
[4]Department of Epidemiology, The Tamil Nadu Dr. M.G.R Medical University, Chennai, Tamil Nadu, India

ABSTRACT

Background: *This manuscript investigated the intricate relationships among obesity, chronic periodontitis (CP), and salivary proteomics.* ***Purpose:*** *Aiming to provide a comprehensive understanding of the molecular mechanisms underlying these interconnected health conditions.* ***Methods:*** *A systematic literature review was conducted in compliance with the registered PROSPERO protocol (vide number CRD42023422848). Out of 361 screened records, four articles were chosen and analyzed to examine the potential connections between obesity-related systemic inflammation, oral health decline, and changes in salivary protein profiles.* ***Results:*** *The major biomarkers identified were interleukin-1 beta, interleukin-6, tumor necrosis factor-alpha, matrix metalloproteinases, and alpha defensins.* ***Conclusion:*** *The results shared here could aid in crafting specific diagnostic and treatment approaches for those suffering from obesity and CP.*

Keywords: *biomarkers; defensins; interleukins; periodontitis; proteomics; saliva*
Article history: *Received 3 February 2024; Revised 26 June 2024; Accepted 2 July 2024; Online 1 June 2025*

Correspondence: V. Ramya, Department of Periodontics, Sree Balaji Dental College and Hospital, Bharath University, Chennai, Tamil Nadu, India. Email: dr.ramya@yahoo.co.in

INTRODUCTION

Periodontitis is a chronic inflammatory condition affecting the supporting tissues of teeth, typically caused by dental plaque buildup. Dental plaque is a biofilm of bacterial colonies, saliva, and food debris. Studies indicate that several bacterial species, such as *Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, Tannerella forsythia, and Treponema denticola*, are linked to the onset of periodontitis.[1] Untreated periodontitis often leads to tooth loss and other serious health complications, including cardiovascular disease, diabetes, and respiratory disease.[2]

Obesity, recognized as a major public health issue worldwide, is often defined by an excessive accumulation of body fat, impacting millions of individuals globally. The prevalence of obesity has steadily risen over the past few decades, with more than 800 million adults classified as obese in 2020.[3] This condition is strongly linked to various health risks, ranging from debilitating illnesses to severe diseases such as cardiovascular disease, diabetes, and certain forms of cancer.[4] However, obesity typically arises from complex genetic, environmental, and behavioral interactions.[5]

Obesity and periodontitis are interconnected and show a strong correlation. Numerous studies have indicated that obesity is a significant risk factor for the development and progression of periodontitis.[2,6,7] Chronic systemic inflammation associated with excess adipose tissue is a well-established pathway common in obesity and chronic periodontitis (CP), leading to tissue destruction. Adipose tissue is a primary source of proinflammatory cytokines, contributing to the low-grade systemic inflammation seen in individuals with obesity.[8] This inflammation undermines immune function and intensifies the inflammatory response to bacterial infections in the gums, ultimately promoting the progression of periodontitis.[9]

DOI: 10.20473/j.djmkg.v58.i3.p314–324

Other probable mechanisms proposed to explain the connection between obesity and periodontitis include changes in the oral microbiome caused by obesity, which elevates harmful bacteria related to periodontitis.[10] Moreover, obesity leads to insulin resistance and heightens the risk of type 2 diabetes, both recognized as independent risk factors for periodontitis.[11]

The connection between obesity and periodontitis is complex and influenced by multiple factors. Grasping the fundamental mechanisms that underpin this relationship is essential for creating effective prevention and treatment methods for both conditions. Salivary proteomics, which involves analyzing proteins in saliva, has become a promising approach for examining the relationship between obesity and periodontitis.[12] This review seeks to pinpoint specific salivary protein biomarkers linked to both conditions while exploring shared molecular pathways to enhance the diagnosis and management of these widespread health concerns.

METHODS

This systematic review and meta-analysis was conducted in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[13] guidelines and registered the protocol at PROSPERO (vide number CRD42023422848).

Review question

What salivary proteomic markers help detect periodontitis severity in obese individuals, and what is their diagnostic accuracy?

Search terms

The search terms were constructed based on population, intervention, comparator, and outcome (PICO) domains. They were integrated using the Boolean operator "OR" within the same domains, and the operator "AND" was applied between the PICO domains, as detailed in Table 1.

Information sources

An initial search occurred on 1st April 2023, followed by an updated search on 31st July 2021. We systematically reviewed studies indexed in PubMed-Medline, Scopus, OVID, Web of Science, Embase, and EBSCOhost (see Table 2). All relevant studies available in these databases were included, with no restrictions on publication year; thus, every accessible study was considered.

Eligibility criteria

The population consisted of obese individuals (P) diagnosed with CP (E). The comparator was a nonobese individual without CP (C). Since the studies could feature various comparator groups (C), the inclusion criteria did not dictate the number of articles, marking this as a significant exclusion criterion in our full-text screening process. The study's outcome of interest (O) was the reliable salivary proteomics or other pertinent biomarkers associated with CP and obesity. The studies included were randomized controlled trials, nonrandomized trials, observational studies, reviews, and studies published in English. Studies published in other languages for which a translation could not be obtained and those excluded for their PICO characteristics that are not of the study's interest were omitted.

Selection process

The extracted studies were exported to Rayyan for collation and checked for duplicates. Once the duplication check was complete, the studies were evaluated for eligibility according to the selection criteria.

Two independent reviewer sets, each led by one reviewer (R) and another reviewer (PRK), meticulously screened the titles and abstracts of the studies from the electronic database search using the Rayyan web application. Following this screening, the reviewers independently assessed and selected studies based on the agreed-upon inclusion and exclusion criteria.

Data extraction and management

All pertinent information was gathered from the included studies via a designated data extraction form. The extracted data encompassed study features (study design and study location), participant information (age, gender, obesity metrics, and periodontal indices), biomarker sample sources, and outcomes of interest (salivary proteomics and other biomarkers). All aggregated data were taken as reported in the original studies. For quality assurance, data extraction was conducted by R and verified by PRK. Any differences between authors were addressed through discussion and, if necessary, consultation with a third reviewer (guide). Once their consistency was confirmed, the extracted data were validated and used for subsequent analysis.

Table 1. Search terms grouped under PICO components

P	I/E	C*	O
Obesity			Biomarker*
Overweight	Periodontitis		biological marker*
Fat	Periodontal Disease	Nonobese	salivary proteomes
Obese	Chronic Periodontitis		salivary biomarkers
Unhealthy weight	Severe Periodontitis		Diagnostic Biomarkers
High BMI			Salivary Proteomics

* The comparator, Nonobese, was avoided to fetch more volume of articles, to enable screening

DOI: 10.20473/j.djmkg.v58.i3.p314–324

Assessment of risk of bias

The risk of bias was evaluated using the Quality of Diagnostic Accuracy Studies-2 (QUADAS-2) tool.[14] This tool examines patient selection (including recruitment and inclusion criteria), index tests and reference standards (covering the methods of conducting and interpreting the tests), and the flow and timing (the flow of participants through the study and the time intervals between tests).

The judgment regarding the risk of bias was determined using signaling questions with responses such as "yes," "probably yes," "probably no," "no," and "no information." Two authors (MH and KVJ) independently assessed the risk of bias, after which a consensus was reached regarding disagreements. Furthermore, a third reviewer's opinion (BSB) was sought whenever necessary. The overall risk of bias was determined to be high, with some concerns or low for each study.

Data synthesis and analysis

This review aims to pinpoint distinct salivary proteomes prevalent in individuals with obesity and CP. These identified salivary proteomes are anticipated to act as diagnostic biomarkers. Initially, the goal was to aggregate the specificity and sensitivity values reported in the study. However, the identified reports are cross-sectional trials where only the gold standard measures of obesity and periodontitis were reported. Additionally, nine-factor synthesis without meta-analysis guidelines, complementing the PRISMA guidelines, was employed to summarize and synthesize the results.

RESULTS

An extensive search of the previously mentioned databases resulted in 361 records. After eliminating duplicates, around 332 records were left. Upon preliminary screening of the titles and abstracts, approximately 28 studies were chosen, with 25 reports identified for further assessment. A full-text review of these reports resulted in the selection of four records for detailed analysis. The process of selecting studies, including the number of records found, the studies excluded along with their exclusion reasons, and the number of studies included, is depicted in the PRISMA flow diagram (Figure 1). The fundamental characteristics

Table 2. Search strategy

PubMed	("periodontal"[All Fields] OR "periodontally"[All Fields] OR "periodontically"[All Fields] OR "periodontics"[MeSH Terms] OR "periodontics"[All Fields] OR "periodontic"[All Fields] OR "periodontitis"[MeSH Terms] OR "periodontitis"[All Fields] OR "periodontitides"[All Fields] OR ("chronic periodontitis"[MeSH Terms] OR ("chronic"[All Fields] AND "periodontitis"[All Fields]) OR "chronic periodontitis"[All Fields]) OR (("sever"[All Fields] OR "severe"[All Fields] OR "severed"[All Fields] OR "severely"[All Fields] OR "severer"[All Fields] OR "severes"[All Fields] OR "severing"[All Fields] OR "severities"[All Fields] OR "severity"[All Fields] OR "severs"[All Fields]) AND ("periodontal"[All Fields] OR "periodontally"[All Fields] OR "periodontically"[All Fields] OR "periodontics"[MeSH Terms] OR "periodontics"[All Fields] OR "periodontic"[All Fields] OR "periodontitis"[MeSH Terms] OR "periodontitis"[All Fields] OR "periodontitides"[All Fields]))) AND (("Salivary"[All Fields] AND ("proteom"[All Fields] OR "proteome"[MeSH Terms] OR "proteome"[All Fields] OR "proteomes"[All Fields] OR "proteomical"[All Fields] OR "proteomically"[All Fields] OR "proteomics"[MeSH Terms] OR "proteomics"[All Fields] OR "proteomic"[All Fields])) OR ("Salivary"[All Fields] AND ("biomarker s"[All Fields] OR "biomarkers"[MeSH Terms] OR "biomarkers"[All Fields] OR "biomarker"[All Fields])) OR (("diagnosis"[MeSH Terms] OR "diagnosis"[All Fields] OR "diagnostic"[All Fields] OR "diagnostical"[All Fields] OR "diagnostically"[All Fields] OR "diagnostics"[All Fields]) AND ("biomarker s"[All Fields] OR "biomarkers"[MeSH Terms] OR "biomarkers"[All Fields] OR "biomarker"[All Fields])) OR ("Salivary"[All Fields] AND ("diagnosis"[MeSH Terms] OR "diagnosis"[All Fields] OR "diagnostic"[All Fields] OR "diagnostical"[All Fields] OR "diagnostically"[All Fields] OR "diagnostics"[All Fields]) AND ("biomarker s"[All Fields] OR "biomarkers"[MeSH Terms] OR "biomarkers"[All Fields] OR "biomarker"[All Fields]))) AND ("obeses"[All Fields] OR "obesity"[MeSH Terms] OR "obesity"[All Fields] OR "obese"[All Fields] OR "obesities"[All Fields] OR "obesity s"[All Fields]
EBSCO Host	(obesity or overweight or fat or obese or unhealthy weight or high bmi) AND (periodontitis or periodontal disease) AND (biomarkers or biological markers or biomarker or biological marker) OR salivary proteomes OR salivary biomarkers
Web of Science	(/(TS=(Salivary proteomics)) AND TS=(Salivary Biomarkers)) AND TS=(Obesity)) AND TS=(Chronic Periodontitis))
OVID	(Obesity.mp. [mp=title, abstract, full text, caption text]) AND (Salivary proteomics.mp. [mp=title, abstract, full text, caption text] OR Salivary Biomarkers.mp. [mp=title, abstract, full text, caption text]) AND (Periodontitis.mp. [mp=title, abstract, full text, caption text] OR Chronic Periodontitis.mp. [mp=title, abstract, full text, caption text])

DOI: 10.20473/j.djmkg.v58.i3.p314–324

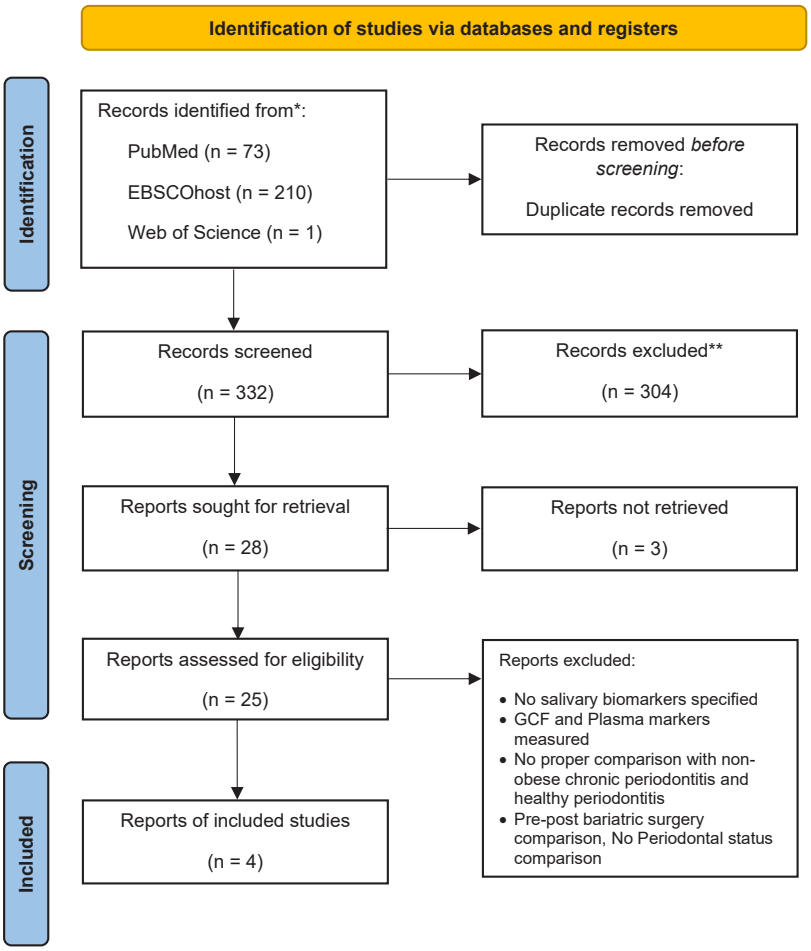

Figure 1. PRISMA Flow chart illustrating the screening and selection process of articles.

Table 3. Study characteristics included in the review and the study design

Study ID	Country	Year	Study Design
Rangé et al.[16]	Paris, France	2012	Observational
Dede et al.[17]	Turkey	2015	Observational
Al-Hamoudi et al.[18]	Saudi Arabia	2018	Clinico-laboratory study
Syrjäläinen et al.[19]	Finland	2019	cross-sectional study

Table 4. Sample characteristics, sample size and grouping

Study ID	Sample size	Study sample group	Sample distribution	Gender		Mean/ Median*	SD/ (Min-Max)
				Male	Female		
Rangé et al.[16]	57	Obese without Periodontitis	25	6	19	44.1	8
		Obese with periodontitis	13	2	11	46.9	5.6
		Obese	38	8	30	45.1	7.3
		normal weight no periodontitis	19	8	30	44.2	6.4
Dede et al.[17]	90	Obese-chronic periodontitis (O-CP)	15	8	7	47.13	7.17
		O-G	15	8	7	35.73	7.23
		(O-CTRL)	15	7	8	41.33	6.47
		Normal-weight chronic periodontitis (CP)	15	8	7	38.47	7.5
		G-gingivitis	15	7	8	31.53	6.8
		periodontally healthy controls (CTRL)	15	8	7	29.6	2.3
Al-Hamoudi et al.[18]	50	Obese Chronic Periodontitis	35	35		39.5*	(32-40)
		Non-Obese Chronic Periodontitis	35	35		36.3*	(33-44)
		Obese Control	34	32	2	37.5*	(31-42)
		Non-Obese Control	33	33		36.2*	(33-42)
Syrjäläinen et al.[19]	580	obese individuals	287	98	189	55	11.9
		Normal individuals	293	98	198	55.5	12

DOI: 10.20473/j.djmkg.v58.i3.p314–324

of the included studies are displayed in Table 3, which lists the study designs reported in these studies.

Sample size and composition

The studies feature varying sample sizes: Rangé et al.[16] had 57 participants, Dede et al. had 90[17], Al-Hamoudi et al.[18] had 50, while Syrjäläinen et al.[19] had a significantly larger group of 580 participants. These studies focused on different sample populations, including obese and normal-weight individuals with and without periodontitis, as well as various control groups (Table 4). Additionally, Al-Hamoudi et al.[18] made a distinction between obese and non-obese participants within the CP and control categories.

Age-gender distribution

Across the studies, the minimum age was around 31 years, while the maximum age reported was 55. Although there is variability in age distribution among the studies, the distribution remains consistent within each study. In contrast, there is greater variability in gender distribution among the sample groups. For instance, Rangé et al.[16] provided specific distributions for male and female participants across various obesity and periodontitis categories. Dede et al.[17] reported that the sex distribution in each subgroup, including obese CP, obese gingivitis, obese control, normal-weight CP, gingivitis, and periodontally healthy controls, was normal. Al-Hamoudi et al.[18] included both male and female participants in the obese CP, non-obese CP, obese control, and non-obese control groups. Additionally, in 2019, Syrjäläinen et al.[19] documented the sex distribution among obese and normal individuals.

Body mass index (BMI) is a standard measure of obesity utilized across various studies. The average values used to categorize patients as obese (35) and nonobese (21) were similar. However, the BMI measure reported by Rangé et al.[16] for obese individuals (48.5) was notably higher, as these individuals were admitted for bariatric surgery. Periodontitis metrics such as periodontal index, gingival index (GI), pocket depth, clinical attachment loss, and alveolar bone structure were consistently used in all studies, except for Syrjäläinen et al.[19] In that study, the cumulative risk score was calculated by multiplying the tertile values of salivary concentrations of *Porphyromonas gingivalis*, interleukin-6 (IL-6), and matrix metalloproteinase-8 (MMP-8).

Table 5 presents various biomarkers and their measurements. As shown in Table 5, the salivary biomarkers varied across the selected studies. While IL-6 was identified in two of these studies, the population characteristics, specifically the obesity and periodontitis sample groupings, differed. Furthermore, due to the lack of standardization in periodontitis measurements, pooling data for a comprehensive evidence synthesis was not feasible.

Data synthesis

Data synthesis is impossible as planned a priori because the studies identified here are highly heterogeneous regarding population characteristics. However, Al-Hamoudi et al.[18] and Syrjäläinen et al.[19] reported the biomarker IL-6. The population characteristics of individuals with obesity and periodontitis are highly heterogeneous, and the reported outcome of interest is not clearly defined according to the population characteristics. Therefore, pooling data for further meta-analyses, as initially planned, is impossible. Hence, a narrative synthesis of the findings is conducted according to the guidelines.

Summarizing the findings from the selected studies

Rangé et al.[16] reported alterations in the salivary protein/peptide profiles of obese individuals, both with and without periodontitis. Notably, alpha-defensins, a part of the salivary proteome, were found at lower levels in obese patients suffering from periodontitis than their counterparts without the condition. This observation implied that alpha-defensins could be linked to gingival inflammation and might contribute to the heightened risk of periodontal diseases in obese patients. The study also indicated that other potential markers, such as albumin and hemoglobin,

Table 5. Measures of obesity, periodontitis and salivary biomarkers

Study ID	Obesity	Measures for Periodontitis	Salivary Biomarkers
Rangé et al.[16]	BMI	PI GI PD CAL ABS	Alpha-defensins 1, 2 & 3
Dede et al.[17]	BMI	PI GI BOP PD CAL	8-OHdG/mg from DNA isolates
Al-Hamoudi et al.[18]	BMI	BOP PD PD	Salivary resistin Interleukin (IL-6)
Syrjäläinen et al.[19]	BMI	Cumulative Risk Score = Multiplying Tertile values of (Salivary concentrations of *P. gingivalis*, IL-6, MMP-8)	IL-B, IL-1Receptor antagonist IL-6 Il-8 IL-10 TNF-a MMP-8

DOI: 10.20473/j.djmkg.v58.i3.p314–324

Table 6. Study measures, various parameters

Study ID	n	Sampling Group	Obesity Measure	Periodontal Measures					Salivary Proteomics / Biomarkers									
			BMI	PI	GI	PD	CAL	ABS	Alpha-defensins									
Rangé et al.[16]	57	Obese without Periodontitis	48.5 ± 9.6	1.04 ± 0.58	1.87 ± 0.39	2.54 ± 0.36	2.60 ± 0.36	0.79 ± 0.18	36.47 (+19.84)									
		Obese with periodontitis	50.9 ± 7.8	1.58 ± 0.60	2.10 ± 0.48	2.93 ± 0.75	3.58 ± 1.17	1.38 ± 0.35	43.44 (+30.34)									
		Obese	49.3+9	1.23 ± 0.63	1.95 ± 0.43	2.68 ± 0.55	2.94 ± 0.87	0.99 ± 0.38	40.99 ± 26.66									
		normal weight no periodontitis	21.5 ± 2.1	0.39 ± 0.28	0.51 ± 0.44	1.95 ± 0.32	2.00 ± 0.31	0.49 ± 0.21	27.10 ± 23.98									
			BMI	PI	GI	PD	CAL	BOP	8-OHdG/mg									
Dede et al.[17]	90	Obese-chronic periodontitis (O-CP)	35.80 (± 3.89)	2.40 (± 0.40)	2.39 (± 0.41)	4.34 (±1.08)	5.02 (± 1.16)	90.26 (±7.23)	927.94 (±116.66)									
		O-G	38.63 (± 6.22)	1.68 (± 0.58)	1.69 (± 0.58)	1.54 (± 0.23)	1.54 (± 0.23)	69.26 (±11.28)	824.32 (± 115.65									
		(O-CTRL)	36.95 (± 5.18)	0.68 (± 0.20)	0	1.46 (± 0.16)	1.46 (± 0.16)	0	630.76 (± 74.89)									
		Normal-weight chronic periodontitis (CP)	22.87 (±1.03)	2.44 (± 0.30)	2.12 (± 0.21)	3.82 (± 1.23)	4.65 (± 1.33)	90.84 (± 6.62)	1023.48 (± 87.35)									
		G-gingivitis	22.55 (± 1.62)	1.66 (± 0.32)	1.83 (± 0.32)	1.69 (± 0.25)	1.69 (± 0.25)	65.39 (±18.51)	864.06 (± 139.60)									
		periodontally healthy controls (CTRL)	22.26 (± 1.67)	0.20 (+ 0.19)	0	1.48 (± 0.14)	1.48 (± 0.14)	0	4.61 (+ 50.40)									
			BMI	PD	BOP				Resistin		IL-6							
Al-Hamoudi et al.[18]	50	Obese Chronic Periodontitis	35.2 (31-38.5)	39.3 (30.5-44.1)	46.3 (38.4-66.5				18.4 ± 3.2		14.3 ± 3.6							
		Non-Obese Chronic Periodontitis	21.6 (20.5-23.2)	32.4 (30.5-36.2)	52.5 (39.3-58.1)				20.5 ± 5.1		15.1 ± 0.6							
		Obese Control	33.6 (30.4-38.5)	5.5 (0-10.5)	11.5 (5.7-15.2)				2.2 ± 0.2		2.1 ± 0.4							
		Non-Obese Control	22.4 (21.8-22.6)		8.5 (6.3-12.5)				2.1 ± 0.3		2.3 ± 0.6							
			BMI	CRS-I	CRS-II	CRS-III			IL-1Ra	p	IL-6	p	IL-8	p	IL-10	p	TNF-Alp	p
Syrjäläinen et al.[19]	580	Obese individuals	39.0 (4.1)	58(20.2)	82(28.6)	147(51.2)			7979(8712)	0.097	3.6(5.2)	0.095	378(472)	0.033	1.5(3.0)	0.022	10.4(17.4)	0.103
		Normal individuals	22.9 (1.6)	80 (27.3)	97(33.1)	116(39.6)			7782(8962)		3.3(4.2)		300(365)		2.0(3.7)		12.6(18.8)	
		Obese CRS-I							4419(2829)	0.064	3.6(4.3)	0.341	169(127)	0.44	3.5(5.8)	0.043	14.4(23.9)	0.035
		Normal Weight CRS-I							3727(3497)		4.5(4.7)		168(125)		5.7(8.1)		26.4(26.4)	
		Obese CRS-II							6582(5478)	0.666	2.9(3.3)	0.993	274(292)	0.682	1.5(2.8)	0.078	9.8(14.5)	0.46
		Normal Weight CRS-II							7224(5402)		3.0(3.0)		284(242)		2.0(3.0)		12.4(13.9)	
		Obese CRS-III							12136(9387)	0.212	4.8(6.8)	0.011	573(443)	0.784	1.3(2.2)	0.698	8.9(15.8)	0.841
		Normal Weight CRS-III							13045(1024)		3.0(5.5)		566(464)		1.2(1.9)		10.3(10.9)	

DOI: 10.20473/j.djmkg.v58.i3.p314–324

Table 7. QUADAS 2 assessment tools for risk of bias

Study ID	Risk of bias				Concerns regarding applicability		
	Participant selection	Index test	reference standard	Flow and timing	Participant selection	Index test	reference standard
Rangé et al.[16]	Low	Low	Unclear	Low	Low	High	Low
Dede et al.[17]	Unclear	Low	Unclear	Low	Low	Low	Low
Syrjäläinen et al.[19]	Unclear	High	Low	Low	Low	Low	Low
Al-Hamoudi et al.[18]	Low	Low	Low	Low	Low	Low	Low

were elevated in obese patients relative to controls, yet no significant differences were found in these markers when comparing those with and without periodontitis within the obese group. In conclusion, this research suggested that alpha-defensins might be promising biomarkers for periodontal disease in obese individuals.

Dede et al.[17] examined the parameters in obese individuals with CP compared to those with normal weight who also had CP, focusing particularly on how initial periodontal treatment affected levels of 8-hydroxy-deoxyguanosine (8-OHdG) in plasma, gingival crevicular fluid (GCF), and saliva among the obese patients with periodontal disease. The study involved 45 obese and 45 normal-weight participants, further divided into three subgroups based on their periodontal conditions. Clinical measurements and samples were collected at the baseline and after the initial periodontal treatment. Results indicated that the baseline levels of 8-OHdG in plasma, GCF, and saliva were higher in obese patients with periodontal disease compared to their normal-weight counterparts. Nevertheless, significant changes in 8-OHdG levels were observed only in plasma, not GCF or saliva. Additionally, there were statistically significant positive correlations detected between salivary, plasma, and GCF 8-OHdG levels and the GI, as well as between BMI across all groups, implying that 8-OHdG serves as a marker of oxidative stress that is particularly associated with both obesity and periodontitis.

Al-Hamoudi et al.[18] examined how obesity correlates with CP in relation to whole salivary resistin and IL-6 levels, by investigating both obese and nonobese individuals with or without periodontitis. Initially, whole salivary resistin and IL-6 levels were similar for obese and nonobese participants across the periodontitis and non-periodontitis categories. However, after six months of follow-up, post-scaling and root planning (SRP) therapy, these biomarkers exhibited significantly reduced levels among both obese and nonobese individuals in both the periodontitis and nonperiodontitis groups. This indicates that CP is likely the main factor affecting periodontal health and the expression of resistin and IL-6 levels in both obese and nonobese patients, with obesity playing a secondary role.

Syrjäläinen et al.[19] examined the connection between obesity and periodontitis by looking at cumulative risk scores (CRS): CRS-I, CRS-II, and CRS-III. They analyzed inflammatory markers including interleukin-1 receptor antagonist (IL-1Ra), IL-6, interleukin-8 (IL-8), interleukin-10 (IL-10), and tumor necrosis factor-alpha (TNF-α). These studies provide valuable insights into how obesity relates to periodontal health and systemic inflammation, highlighting the need to consider various factors to understand these intricate relationships (Table 6). The key finding of this study is that while individuals with obesity (BMI of 35 kg/m2) have worse periodontal health than normal-weight individuals (BMI of 18.5–25 kg/m2), this was not consistently reflected in their salivary cytokine levels. Thus, although obesity may increase the likelihood of periodontal disease, it does not necessarily alter salivary cytokine concentrations; rather, those concentrations are influenced more by periodontal health than obesity itself.

Risk of bias statement (QUADAS-2)

The risk of bias assessment was performed using QUADAS-2 (Table 7), assessing patient selection (recruitment and inclusion criteria), index tests and reference standards (how tests were conducted and interpreted), and the flow and timing (flow of participants through the study and time interval between tests).

Quantitative synthesis – Meta-analysis

At the protocol stage, it was envisioned that evidence synthesis could be conducted through quantitative data pooling via a meta-analysis. However, there were not enough studies on a specific biomarker, and the included studies comprised only four, which were too heterogeneous to combine meaningfully; hence, conducting a meta-analysis may not be feasible. Pooling their results in a meta-analysis could be inappropriate due to the risk of bias and potentially invalid conclusions.

DISCUSSION

Saliva is a noninvasive, affordable, and easily accessible biological fluid, making it a valuable diagnostic tool in dentistry. Due to its unique composition and the insights it offers regarding oral and systemic health, saliva is a valuable diagnostic tool.[20,21] Moreover, saliva may be an important biomarker for detecting, diagnosing, and monitoring periodontitis.[22]

DOI: 10.20473/j.djmkg.v58.i3.p314–324

In the case of periodontitis, saliva contains numerous components that serve as biomarkers, indicating the disease's presence, severity, and progression. Previously mentioned, obesity and periodontitis are two health issues linked to inflammatory processes in the body. This review aims to gather and analyze data from peer-reviewed studies related to salivary proteomics associated with obesity and periodontitis. Research indicates that obese individuals often exhibit changes in their salivary protein profiles, suggesting a higher risk of developing periodontal disease. Key biomarkers identified in saliva associated with periodontitis include: (i) cytokines and chemokines, such as interleukin-1 beta (IL-1β), IL-6, and TNF-α; (ii) enzymes such as matrix metalloproteinases (MMPs); (iii) proteins such as C-reactive protein; (iv) host-derived proteins such as defensins and cathelicidins; (v) bacterial markers including RNA and DNA; (vi) glycated proteins; and (vii) oxidative stress markers. This review discusses studies that examined 668 salivary biomarkers linked to periodontitis, detailing these biomarkers' levels in obese individuals and those with periodontitis.

The analysis of 8-OHdG in saliva DNA reflects the quantity of DNA extracted from saliva samples, typically quantified in milligrams. DNA isolation involves extracting genomic DNA from cells in the saliva.[23] Dede et al.[17] specifically explored 8-OHdG and found that its levels are notably higher in obese individuals compared to their nonobese counterparts. Furthermore, 8-OHdG levels are also significantly elevated in both obese individuals with CP and those with gingivitis when compared to healthy obese controls. These levels show consistency across samples, including saliva, GCF, and plasma. Additionally, in patients with both conditions, SRP therapy significantly diminished levels, underscoring the relevance of 8-OHdG in the context of periodontitis rather than obesity.

Resistin was initially identified in adipose tissue and is believed to contribute to insulin resistance.[24] Some studies suggest that resistin might be involved in inflammation linked to obesity. Elevated resistin levels in serum (blood) have been recorded in obese individuals, suggesting a potential connection to obesity.[25] Studies have also examined resistin levels in the saliva of obese people, indicating that salivary resistin may correlate with systemic inflammation and could act as a non-invasive biomarker for metabolic assessment. Resistin, known for its association with inflammation, has been extensively investigated in relation to periodontal disease. Research shows a positive relationship between salivary resistin levels and the severity of periodontal disease.[26] Considering the link between obesity and periodontitis, resistin's role in both areas suggests it could bridge the gap between obesity-related and periodontal inflammation. Furthermore, studies have demonstrated that obese patients have higher levels of salivary resistin and periodontal pathogens compared to non-obese individuals,[27] indicating a possible connection between obesity, periodontitis, and specific salivary proteins and pathogens. In particular, altered protein levels have been observed in the saliva of individuals[28] with generalized aggressive periodontitis compared to those without the condition.[29] Additionally, identifying haptoglobin as a potential biomarker for tracking disease activity in periodontitis underscores the importance of salivary proteomics in understanding and diagnosing periodontal diseases.[30]

IL-6 is a cytokine that is crucial in managing immune responses and inflammation.[31] Research has investigated the presence and levels of IL-6 in saliva, focusing on its potential implications for obesity and periodontitis.[32] The inflammatory environment in obesity, marked by heightened levels of cytokines such as IL-1β, may exacerbate inflammatory processes in periodontal tissues.[33] IL-1Ra is a natural inhibitor of interleukin-1 (IL-1), a proinflammatory cytokine. It competes with IL-1 for the IL-1 receptor, thus blocking the inflammatory effects linked to IL-1.[34]

The balance between IL-1 and IL-1Ra is crucial for regulating inflammation.[35] In individuals with obesity, alterations in the balance between IL-1 and IL-1Ra may occur. Some studies suggest that changes in IL-1Ra levels could be linked to insulin sensitivity in those with obesity.[36] Research has explored the role of IL-1Ra in modulating the inflammatory response in periodontal tissues. Altered levels of IL-1Ra have been noted in individuals with periodontitis, and an association may exist between IL-1Ra levels and disease severity.[37]

IL-8 is a pro-inflammatory cytokine that significantly contributes to the recruitment and activation of neutrophils, white blood cells integral to the inflammatory process.[38] Notably, adipose tissue, especially in obese individuals, is known to produce and secrete proinflammatory cytokines, including IL-8. Individuals with obesity often exhibit elevated systemic levels of IL-8.[39] This condition is linked to chronic low-grade inflammation, with IL-8 being a key player in the inflammatory cascade.[40] Furthermore, increased IL-8 levels are found in the gingival tissues of those with periodontal disease, highlighting its role in the local inflammatory response.[41]

IL-8 is a strong chemoattractant for neutrophils and is released as part of the body's defense mechanism against microbial threats in periodontal tissues.[42] Tracking salivary IL-8 levels may provide insights into the inflammatory conditions in individuals suffering from obesity and periodontitis. As a proinflammatory chemokine primarily produced by macrophages, IL-8 attracts neutrophils.[43] Research indicates that adipose tissue, especially visceral adipose tissue, releases greater levels of IL-8 in obese individuals, contributing to the chronic, low-grade systemic inflammation linked to obesity. Studies have found elevated IL-8 levels in the GCF and saliva of obese patients with periodontitis when compared to those who are not obese. This suggests that IL-8 might worsen the local inflammatory response within periodontal tissues. The heightened recruitment and activation of neutrophils due to increased IL-8 could amplify the tissue-destructive functions of these

DOI: 10.20473/j.djmkg.v58.i3.p314–324

cells by releasing proteases such as MMP-8. This may help to clarify the more pronounced periodontal damage and bone loss seen in obese individuals.[44]

IL-1β is another important cytokine that significantly influences the inflammatory response, particularly in studies related to obesity and periodontitis. This cytokine is found in saliva, and its concentration can be assessed through several laboratory methods, such as enzyme-linked immunosorbent assay (ELISA).[33] Salivary IL-1β levels are being examined as possible biomarkers for various inflammatory disorders due to the convenience of saliva collection.[45] In individuals with obesity, adipose tissue releases pro-inflammatory cytokines, including IL-1β. Increased IL-1β levels are responsible for the chronic low-grade inflammation linked to obesity. Additionally, IL-1β has been associated with the onset of insulin resistance, which is commonly observed in obesity and type 2 diabetes. IL-1β also plays a key role in the inflammatory process related to periodontitis, with elevated concentrations noted in the gingival tissues of those suffering from periodontal disease. Together with other cytokines, IL-1β contributes to the degradation of periodontal tissues in the advanced stages of periodontitis.[46] Researchers are looking into salivary IL-1β levels as potential diagnostic and prognostic indicators for periodontitis.

IL-10 is an anti-inflammatory cytokine essential for regulating immune responses and reducing inflammation. Studies have examined the presence and concentrations of IL-10 in the saliva of those with obesity and periodontitis.[47]

In periodontitis, there can be an imbalance between proinflammatory cytokines such as IL-1β and IL-8 and anti-inflammatory cytokines such as IL-10. Higher levels of IL-10 are generally seen as advantageous since they aid in resolving inflammation and facilitating tissue repair. Research has explored the link between salivary IL-10 levels and the severity of periodontal disease. Obesity is recognized as a potential risk factor for both the development and exacerbation of periodontitis. The ratio of proinflammatory to anti-inflammatory cytokines, including IL-10, may affect inflammatory processes in periodontal tissues. Assessing salivary IL-10 levels could provide insights into the inflammatory status of individuals with obesity and periodontitis.

TNF-α is a proinflammatory cytokine that plays a central role in the immune response and inflammation. TNF-α is present in saliva, and its levels can be measured using various laboratory techniques, including ELISA. TNF-α is part of the inflammatory cascade and is involved in regulating immune responses.

Adipose tissue, particularly in obese individuals, can produce and release TNF-α. Elevated systemic levels of TNF-α are linked to chronic low-grade inflammation in people with obesity. TNF-α is implicated in developing insulin resistance, which often accompanies obesity. It is one of the key cytokines involved in the inflammatory response in periodontal tissues. Increased levels of TNF-α are found in the gingival tissues of individuals with periodontal disease. TNF-α and other cytokines contribute to the destruction of periodontal tissues in advanced stages of periodontitis. Research has explored the relationship between salivary TNF-α levels and the severity of periodontal disease. Obesity is recognized as a potential risk factor for the onset and progression of periodontitis. The inflammatory environment in obesity, including elevated TNF-α levels, may facilitate inflammatory processes in periodontal tissues.[48] Monitoring salivary TNF-α levels may provide insights into assessing inflammatory status in individuals with both obesity and periodontitis. TNF-α is a crucial proinflammatory cytokine involved in the destruction of periodontal tissue by stimulating other inflammatory mediators, such as IL-1β. Elevated TNF-α levels have been detected both systemically and locally in the GCF of obese individuals with periodontitis.[48] Increased TNF-α production in obesity may enhance the inflammatory cascade in periodontal tissues by upregulating other cytokines such as IL-1β and IL-6.

MMP-8, also called collagenase-2, is an enzyme that breaks down extracellular matrix components, including collagen. Research has investigated the levels of MMP-8 in the saliva of individuals with obesity and periodontitis. This enzyme may play a role in the inflammatory processes occurring in adipose tissues.[49] MMP-8 is produced and released in larger quantities during periodontal inflammation. Increased salivary MMP-8 levels have been noted in individuals suffering from periodontitis.[50] Together with other MMPs, MMP-8 contributes to the degradation of periodontal tissues, which aids in advancing periodontal disease. Monitoring the levels of salivary MMP-8 might provide insights into the inflammatory status of individuals with both obesity and periodontitis. The heightened MMP-8 levels seen in obese individuals could lead to increased periodontal adhesion and bone loss due to the enhanced collagen breakdown at inflammation sites.

This manuscript examines the complex relationship between obesity, CP, and salivary proteomics, with the goal of enhancing understanding of the molecular mechanisms linking these health issues. By employing a comprehensive approach, we investigated potential connections among obesity-related systemic inflammation, declining oral health, and shifts in salivary protein profiles. The results presented here may aid in developing targeted diagnostic and therapeutic methods for people suffering from both obesity and CP. Studies on salivary proteomics have shown that variations in salivary protein profiles can signal periodontal disease. Although the field of periodontitis research is still advancing, it offers promising insights into the mechanisms, diagnosis, and treatment of these conditions.

In conclusion, salivary proteomics studies on salivary proteomics indicate a link between periodontitis and obesity. These investigations highlight the promise of salivary proteomics as a diagnostic resource for detecting individuals at risk of periodontal disease and tracking disease progression in obese patients. Salivary proteomics

DOI: 10.20473/j.djmkg.v58.i3.p314–324

has yielded important insights into the relationship between these two conditions. Examining biomarkers in saliva presents multiple benefits, such as noninvasiveness, easy collection, and suitability for chairside testing. Salivary biomarkers can assist in the early detection and risk assessment of periodontitis, enable effective monitoring, and facilitate timely interventions and personalized treatment strategies. Nevertheless, it is crucial to recognize that research in this area is ongoing, and the validation of certain salivary biomarkers for standard clinical application needs further exploration. Incorporating salivary diagnostics into periodontal treatment may improve both the accuracy and effectiveness of disease management.

While the review identified some relationships, the evidence presented limitations that deserve attention. The studies varied significantly in design, definitions, and had small sample sizes. Additionally, important confounding factors were not consistently controlled. Due to the mainly cross-sectional nature of the evidence, causal claims cannot be established, leaving room for potential bias. There is still a demand for larger and more robust studies to clearly define the relationships among obesity, periodontitis, and salivary biomarkers.

The evidence connecting obesity, periodontitis, and health risks is still inconclusive due to the shortcomings of current research. In particular, existing studies often feature small sample sizes and heterogeneous methodologies. There is a need for diagnostic accuracy studies or longitudinal cohort studies that apply consistent definitions and common proteomic analyses while controlling for confounders. Such rigorous research designs could yield definitive insights into these associations and their implications.

REFERENCES

1. Amalia NR, Budhy TI, Ridwan RD, Rianti D, Bramantoro T, Luthfi M, Ramadhani NF, Pramusita A, Putranti NAR, Nugraha AP, Situmorang PC, Shariff KA, Nugraha AP. Propolis nanoemulsion extract from celebes stingless bee (Tetragonula biroi) phytochemistry and antibacterial analysis to periodontopathogen bacteria. J Oral Biol Craniofacial Res. 2025; 15(3): 576–84.
2. Savitri IJ, Wijaksana IKE, Arief O, Falah MN, Tedjosasongko U, Siswanto OB, Ouhara K, Kurihara H, Mizuno N. Aesthetic consideration in patient management of severe periodontitis aggravated by oral dexamethasone. Dent J. 2023; 56(2): 73–9.
3. Lobstein T, Jackson-Leach R, Powis J, Brinsden H, Gray M. World obesity atlas 2023. London: World Obesity Federation; 2023. p. 232.
4. The Nutrition Source. Preventing obesity. Obesity. 2024. Available from: https://nutritionsource.hsph.harvard.edu/obesity/preventing-obesity/. Accessed 2024 Dec 22.
5. Thaker V V. Genetic and epigenetic causes of obesity. Adolesc Med State Art Rev. 2017; 28(2): 379–405.
6. Maulani C, Auerkari EI, C. Masulili SL, Kusdhany LS, Prahasanti C, Soedarsono N. Effect of obesity on risk and severity of periodontitis: a cross-sectional study. F1000Research. 2021; 10: 643.
7. Abu-Shawish G, Betsy J, Anil S. Is obesity a risk factor for periodontal disease in adults? A systematic review. Int J Environ Res Public Health. 2022; 19(19): 12684.
8. Chait A, den Hartigh LJ. Adipose tissue distribution, inflammation and its metabolic consequences, including diabetes and cardiovascular disease. Front Cardiovasc Med. 2020; 7: 22.
9. Cekici A, Kantarci A, Hasturk H, Van Dyke TE. Inflammatory and immune pathways in the pathogenesis of periodontal disease. Periodontol 2000. 2014; 64(1): 57–80.
10. Rahman B, Al-Marzooq F, Saad H, Benzina D, Al Kawas S. Dysbiosis of the subgingival microbiome and relation to periodontal disease in association with obesity and overweight. Nutrients. 2023; 15(4): 826.
11. Berniyanti T, Palupi R, Setiyowati D, Rahmadhani A, Novia D, Afanda NM, Khairani NI, Nurlaili AZ, Kartikasari F. Lifestyle as a risk factor of high periodontitis prevalence with and without type 2 diabetes mellitus in Surabaya. J Int Dent Med Res. 2021; 14(4): 1503–8.
12. 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. Brazilian Dent Sci. 2024; 27(1): e3960.
13. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021; 372: n71.
14. Whiting PF, Rutjes AWS, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, Leeflang MMG, Sterne JAC, Bossuyt PMM, QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011; 155(8): 529–36.
15. Campbell M, McKenzie JE, Sowden A, Katikireddi SV, Brennan SE, Ellis S, Hartmann-Boyce J, Ryan R, Shepperd S, Thomas J, Welch V, Thomson H. Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline. BMJ. 2020; 368: l6890.
16. Rangé H, Léger T, Huchon C, Ciangura C, Diallo D, Poitou C, Meilhac O, Bouchard P, Chaussain C. Salivary proteome modifications associated with periodontitis in obese patients. J Clin Periodontol. 2012; 39(9): 799–806.
17. Dede FÖ, Doğan ŞB, Ballı U, Avcı B, Durmuşlar MC. The effect of initial periodontal treatment on plasma, gingival crevicular fluid and salivary levels of 8-hydroxy-deoxyguanosine in obesity. Arch Oral Biol. 2016; 62: 80–5.
18. Al-Hamoudi N, Abduljabbar T, Mirza S, Al-Sowygh ZH, Vohra F, Javed F, Akram Z. Non-surgical periodontal therapy reduces salivary adipocytokines in chronic periodontitis patients with and without obesity. J Investig Clin Dent. 2018; 9(2): e12314.
19. Syrjäläinen S, Gursoy UK, Gursoy M, Pussinen P, Pietiäinen M, Jula A, Salomaa V, Jousilahti P, Könönen E. Salivary cytokine biomarker concentrations in relation to obesity and periodontitis. J Clin Med. 2019; 8(12): 2152.
20. Javaid MA, Ahmed AS, Durand R, Tran SD. Saliva as a diagnostic tool for oral and systemic diseases. J Oral Biol Craniofacial Res. 2016; 6(1): 67–76.
21. Patil P, Patil B. Saliva: A diagnostic biomarker of periodontal diseases. J Indian Soc Periodontol. 2011; 15(4): 310–7.
22. Ramadhani NF, Nugraha AP, Gofur NRP, Permatasari RI, Ridwan RD. Increased levels of malondialdehyde and cathepsin C by aggregatibacter actinomycetemcomitans in Saliva as aggressive periodontitis biomarkers: A review. Biochem Cell Arch. 2020; 20: 2895–901.
23. Nandakumar A, Nataraj P, James A, Krishnan R, K M M. Estimation of salivary 8-hydroxydeoxyguanosine (8-OHdG) as a potential biomarker in assessing progression towards malignancy: a case-control study. Asian Pacific J Cancer Prev. 2020; 21(8): 2325–9.
24. Berger A. Resistin: a new hormone that links obesity with type 2 diabetes. BMJ. 2001; 322(7280): 193.
25. Jamaluddin MS, Weakley SM, Yao Q, Chen C. Resistin: functional roles and therapeutic considerations for cardiovascular disease. Br J Pharmacol. 2012; 165(3): 622–32.
26. Akram Z, Baharuddin NA, Vaithilingam RD, Rahim ZHA, Chinna K, Krishna VG, Saub R, Safii SH. Effect of nonsurgical periodontal treatment on clinical periodontal variables and salivary resistin levels in obese Asians. J Oral Sci. 2017; 59(1): 93–102.

DOI: 10.20473/j.djmkg.v58.i3.p314–324

27. Kim E-H, Joo J-Y, Lee YJ, Koh J-K, Choi J-H, Shin Y, Cho J, Park E, Kang J, Lee K, Bhak J, Kim BC, Lee J-Y. Grading system for periodontitis by analyzing levels of periodontal pathogens in saliva. Passi AG, editor. PLoS One. 2018; 13(11): e0200900.
28. Orti V, Mertens B, Vialaret J, Gibert P, Relaño-Ginés A, Lehmann S, Deville de Périère D, Hirtz C. Data from a targeted proteomics approach to discover biomarkers in saliva for the clinical diagnosis of periodontitis. Data Br. 2018; 18: 294–9.
29. Hora S, Pandey AK, Jha S. Biomarker-based targeted therapeutics. In: Neoplasm. InTech; 2018.
30. Haigh BJ, Stewart KW, Whelan JRK, Barnett MPG, Smolenski GA, Wheeler TT. Alterations in the salivary proteome associated with periodontitis. J Clin Periodontol. 2010; 37(3): 241–7.
31. Kristanti RA, Bramantoro T, Soesilawati P, Hariyani N, Suryadinata A, Purwanto B, Nugraha AP, Tengku Ahmad Noor TNE binti. Inflammatory cytokines affecting cardiovascular function: a scoping review. F1000Research. 2022; 11: 1078.
32. Yakar N, Bostanci N, Özdemir G, Atmaca H, Türedi A, Şahin Ç, Köse T, Emingil G. Salivary inflammatory burden in pre- and postmenopausal women: Associations with body mass index, patient-reported health, serum cytokines, and periodontal parameters. J Periodontol. 2024; 95(3): 209–18.
33. Cheng R, Wu Z, Li M, Shao M, Hu T. Interleukin-1β is a potential therapeutic target for periodontitis: a narrative review. Int J Oral Sci. 2020; 12(1): 2.
34. Volarevic V, Al-Qahtani A, Arsenijevic N, Pajovic S, Lukic ML. Interleukin-1 receptor antagonist (IL-1Ra) and IL-1Ra producing mesenchymal stem cells as modulators of diabetogenesis. Autoimmunity. 2010; 43(4): 255–63.
35. Budhiparama NC, Lumban-Gaol I, Sudoyo H, Magetsari R, Wibawa T. The role of genetic polymorphisms of interleukin-1 (IL-1R1 and IL-1RN) in primary knee osteoarthritis in Indonesia. Sci Rep. 2023; 13(1): 7967.
36. Frühbeck G, Catalán V, Ramírez B, Valentí V, Becerril S, Rodríguez A, Moncada R, Baixauli J, Silva C, Escalada J, Gómez-Ambrosi J. Serum levels of IL-1 Ra increase with obesity and type 2 diabetes in relation to adipose tissue dysfunction and are reduced after bariatric surgery in parallel to adiposity. J Inflamm Res. 2022; 15: 1331–45.
37. Tazawa K, Azuma Presse MM, Furusho H, Stashenko P, Sasaki H. Revisiting the role of IL-1 signaling in the development of apical periodontitis. Front Dent Med. 2022; 3: 985558.
38. Bickel M. The role of interleukin-8 in inflammation and mechanisms of regulation. J Periodontol. 1993; 64(5 Suppl): 456–60.
39. Makki K, Froguel P, Wolowczuk I. Adipose tissue in obesity-related inflammation and insulin resistance: cells, cytokines, and chemokines. ISRN Inflamm. 2013; 2013: 139239.
40. Ellulu MS, Patimah I, Khaza'ai H, Rahmat A, Abed Y. Obesity and inflammation: the linking mechanism and the complications. Arch Med Sci. 2017; 4(4): 851–63.
41. Martínez-García M, Hernández-Lemus E. Periodontal inflammation and systemic diseases: an overview. Front Physiol. 2021; 12: 709438.
42. Silva N, Abusleme L, Bravo D, Dutzan N, Garcia-Sesnich J, Vernal R, Hernández M, Gamonal J. Host response mechanisms in periodontal diseases. J Appl Oral Sci. 2015; 23(3): 329–55.
43. Tecchio C, Micheletti A, Cassatella MA. Neutrophil-derived cytokines: facts beyond expression. Front Immunol. 2014; 5: 508.
44. Suvan J, D'Aiuto F, Moles DR, Petrie A, Donos N. Association between overweight/obesity and periodontitis in adults. A systematic review. Obes Rev. 2011; 12(5): e381-404.
45. Szabo YZ, Slavish DC. Measuring salivary markers of inflammation in health research: A review of methodological considerations and best practices. Psychoneuroendocrinology. 2021; 124: 105069.
46. Alfadul H, Sabico S, Al-Daghri NM. The role of interleukin-1β in type 2 diabetes mellitus: A systematic review and meta-analysis. Front Endocrinol (Lausanne). 2022; 13: 901616.
47. Iyer SS, Cheng G. Role of interleukin 10 transcriptional regulation in inflammation and autoimmune disease. Crit Rev Immunol. 2012; 32(1): 23–63.
48. Graves DT, Cochran D. The contribution of interleukin-1 and tumor necrosis factor to periodontal tissue destruction. J Periodontol. 2003; 74(3): 391–401.
49. Janovits PM, Leiguez E, Portas V, Teixeira C. A metalloproteinase induces an inflammatory response in preadipocytes with the activation of COX signalling pathways and participation of endogenous phospholipases A2. Biomolecules. 2021; 11(7): 921.
50. Balogun AO, Taiwo JO, Opeodu OI, Adeyemi BF, Kolude BM. Diagnostic utility of salivary matrix metalloproteinase-8 (MMP-8) in chronic periodontitis: a novel approach. Open J Stomatol. 2020; 10(4): 41–9.

DOI: 10.20473/j.djmkg.v58.i3.p314–324