Academia Open
Vol. 10 No. 2 (2025): December
DOI: 10.21070/acopen.10.2025.12088

Periodontal Pathogens and Their Association with Cardiovascular Diseases: Patogen Periodontal dan Hubungannya dengan Penyakit Kardiovaskular

Hussam Hashim Mohammed — Middle Technical University, Baqubah Technical Institute, Diyala
Zina Lafta Hassan — Department of pathological analysis, College of Applied Sciences, University of Samarra
Zahraa Khudhair Dawood — College of Science,University of Diyala,Diyala
Osama A. Mohsein — Main Laboratory Unit, Al Habbobi Teaching Hospital, Thi-Qar Health Directorate, Thi-Qar

Background: Cardiovascular diseases (CVDs) remain the leading global cause of mortality, and recent evidence suggests a bidirectional relationship between systemic inflammation and periodontal disease (PD). **Specific Background:** Oral microbiota dysbiosis, particularly involving pathogens such as *P. gingivalis*, *A. actinomycetemcomitans*, and *T. forsythia*, has been implicated in CVD progression through inflammatory and metabolic pathways. **Knowledge Gap:** While previous studies have highlighted possible associations, limited data exist regarding the prevalence of these pathogens and their correlation with systemic inflammatory markers and cardiovascular risk factors in Middle Eastern populations. **Aim:** This study investigated the prevalence of key periodontal pathogens in patients with CVD and their relationship with systemic biomarkers and cardiovascular risk indicators. **Results:** A total of 150 CVD patients and 50 healthy controls were analyzed. Patients exhibited significantly higher prevalence of periodontal pathogens (74% *P. gingivalis*, 56% *A. actinomycetemcomitans*, 62% *T. forsythia*), elevated inflammatory markers (CRP, IL-6, TNF-α), dyslipidemia, and increased BMI compared with controls ($p < 0.001$). Pathogen prevalence correlated positively with CVD severity. **Novelty:** This study provides region-specific evidence linking periodontal pathogens to systemic inflammation and cardiovascular risk. **Implications:** The findings underscore the importance of integrating oral health care into cardiovascular disease prevention and management strategies.
Highlight :

- Periodontal pathogens are found more frequently in patients with CVD.
- Increased inflammatory markers are associated with disease severity.
- Risk factors such as high cholesterol increase the likelihood of CVD.

Keywords : Cardiovascular Disease, Periodontal Pathogens, P. Gingivalis, CVD Risk Factors, Inflammatory Markers

Introduction

Heart and blood vessel diseases (CVDs) kill and hurt more people than any other noncommunicable disease, making them a big global health issue [1]. Over the past few decades, the number of people under 55 who have CVDs has gone up greatly, especially those who have had a myocardial attack or a stroke [2]. A lot of data supports this trend, showing that being exposed to

cardiovascular risk factors early in life is a key part of getting the disease [3].

Being overweight or obese can make a lot of health problems worse, like heart disease, diabetes, some cancers, non-alcoholic fatty liver disease, and non-alcoholic steatohepatitis [4,5]. You can connect adipose tissue and CVDs in two ways: directly, and tangentially, through other health issues that are linked to fat. Because of this, being overweight or fat can make you more likely to get diabetes, bad cholesterol, and high blood pressure [6]. Obstructive sleep apnea caused by obesity can also raise the chance of CVD through low oxygen levels, irregular heartbeats, insulin resistance, and high blood pressure [7].

New data points to a connection between the microbiota in the mouth, obesity, and metabolic disorders, both in terms of the types of microbes involved and how the diseases start [8,9]. Oral microbiome dysbiosis—a change from harmless to possibly harmful species—is caused by a lot of different things working together [10,11]. Periodontal diseases (PDs), caused by opportunistic anaerobic bacteria, are chronic inflammatory and immune-mediated conditions that damage the gingiva, periodontal ligaments, and alveolar bone [12]. Numerous periodontopathogenic species have been identified, and research continues to explore their characteristics and pathogenic potential [13,14].

One idea is that CVDs and PDs are linked in more than one way. Some of these are systemic inflammation, the harmful effects of bacteria and their products in the bloodstream, and changes in the gut microbiome caused by germs from the mouth going there [15]. A lot of people believe that systemic inflammation is a main reason why gum disease and heart disease are connected [16,17]. Having high amounts of inflammation markers like erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and interleukin-6 (IL-6) has been linked to more heart disease and death [18]. There is some evidence that inflammation caused by gingivitis may play a role in arterial failure [19].

The hematogenous route makes it easier for mouth bacteria to spread to faraway places through bacteremia. These bacteria come from sore epithelium in periodontal pockets [20]. Bacteria like P. gingivalis, P. intermedia, A. actinomycetemcomitans, T. forsythensis, and T. denticola have been found in 20–70% of artery atheromas, according to new study [21]. Cross-sectional studies have shown over and over that people with gum disease are more likely to have atherosclerotic problems. For instance, the NHANES III group showed that people with serious periodontal disease were almost four times more likely to have a myocardial attack than people who did not have periodontitis [22]. Similarly, a study of 52,677 people with high blood pressure found a link between bad mouth health and a higher chance of CVD [23].

The oral cavity is now recognized as the second-largest microbial ecosystem in the human body, hosting over 500 identified bacterial species. These microbes play essential roles in maintaining systemic health and preventing disease onset [24]. Oral dysbiosis is linked to gum disease and is also becoming more and more linked to metabolic diseases like CVDs [25]. Deaths and illnesses caused by CVD are still major public health problems around the world [26]. Ischemic heart disease, stroke, and heart failure caused by high blood pressure are the main reasons people die from CVD [27].

Oral microbiota may serve as emerging indicators for both halitosis and systemic metabolic diseases. Working together with people from different fields could help find and treat mouth and systemic diseases, like CVDs, earlier. The study's goal is to find out how common it is for people of different ages and weights to have certain gum bacteria. These pathogens are P. gingivalis, A. actinomycetemcomitans, and T. forsythia. The study also wants to find out how periodontal disease and cardiovascular disease are related. It will do this by looking at risk factors like high blood pressure, lipid profiles, cholesterol levels, IL-6, TNF-α, and CRP, as well as cardiovascular risk assessments such as the Finnish Diabetes Risk Index (FINDRISC), Systematic Coronary Risk Evaluation (SCORE), and relative risk (RR).

Methodology

The cross-sectional observational study took place from January 1, 2024, to June 30, 2024. Its goal was to find out how common Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Tannerella forsythia were in people of different ages and body masses, as well as how they might be linked to cardiovascular disease (CVD) risk factors. Subgingival samples and gingival crevicular fluid were collected from patients diagnosed with periodontitis using sterile swabs, and preserved in appropriate transport media such as VMGA III or PBS to ensure the viability of the microorganisms. For microbial identification, samples were cultured on selective media: P. gingivalis was grown on blood agar or Brucella blood agar enriched with vitamin K and hemin, and incubated anaerobically at 37°C for 7–10 days; A. actinomycetemcomitans was cultured on tryptic soy agar (TSA) with blood under 5–10% CO_2 at 37°C for 48–72 hours; T. forsythia was isolated using fastidious anaerobe agar (FAA) with blood and N-acetyl muramic acid (NAM), incubated anaerobically at 37°C for 5–7 days. Gram staining was used for microscopic examination, revealing Gram-negative rods for P. gingivalis and T. forsythia, and Gram-negative coccobacilli for A. actinomycetemcomitans. Further identification was performed using biochemical assays: P. gingivalis was tested for protease activity via collagenase and BAPNA tests; A. actinomycetemcomitans was examined for leukotoxin (ltxA) production; and T. forsythia was evaluated using the gelatin hydrolysis and N-acetyl-β-glucosaminidase tests. In addition, systemic biomarkers were assessed to explore cardiovascular risk. Blood samples were collected to measure inflammatory markers CRP, IL-6, and TNF-α—using the sandwich ELISA technique. Lipid profile parameters, including total cholesterol, HDL, LDL, and triglycerides (mg/dL), were analyzed using a spectrophotometer. Cardiovascular risk was also assessed using standardized tools such as the Finnish Diabetes Risk Score (FINDRISC), Systematic Coronary Risk Evaluation (SCORE), and Relative Risk (RR).

Statistical Analysis

SPSS version 26 was used to look at the quantitative data. Rates and frequencies are used to show the outcomes. For factors that were spread out normally, two-tailed independent and dependent t-tests were used. It was possible to use the Mann-Whitney U test, the Wilcoxon test, and the Chi-square test on factors that were not spread out regularly. People used to think that a p-value less than 0.05 was statistically important.

Ethical Approval

It was okay with the human ethics committee at Al-Habbobi Teaching Hospital to do the study. People who took part in the study were told about it and asked to sign a form saying they agreed to take part. Also, the person was told that no one else would see his information.

Results

Comparison of Sociodemographic Characteristics of Study Participants (Age, Gender, BMI, Hypertension, and Diabetes) Between Patients and Healthy Controls with Statistical Significance.

In Table 1, you can see how the 150 cases and 50 healthy controls are different. Their BMI was higher (29.4 vs. 24.1, P<0.001), their blood pressure was higher (55% vs. 10%, P<0.001), and their diabetes was higher (45% vs. 7%, P<0.001). But neither the age nor the gender changed in a big way. That means there is a link between the illness and having diabetes, a higher BMI, or high blood pressure.

Variable	Patients Group (n=150)	Control Group (n=50)	p-value
Age (years)	58.7 ± 12.5	56.2 ± 11.3	0.321

Gender (M/F)	85 / 65	26 / 24	0.722
BMI (kg/m²)	29.4 ± 5.1	24.1 ± 3.7	< 0.001
Hypertension (%)	55%	10%	< 0.001
Diabetes (%)	45%	7%	< 0.001

Table 1. *Sociodemographic Characteristics (Age, Gender, BMI, Hypertension, and Diabetes) of the Study Participants.*

Prevalence of Periodontal Pathogens (P. gingivalis, A. actinomycetemcomitans, T. forsythia). Between Patients and Healthy Controls with Statistical Significance.

In Table 2, patients had much higher rates of P. gingivalis (74% vs. 28%, P<0.001), A. actinomycetemcomitans (56% vs. 20%, P<0.001), and T. forsythia (62% vs. 22%, P<0.001) than healthy controls. This shows that there is a strong link between these pathogens and the disease.

Pathogen	Patients (n = 150)	Healthy Controls (n = 50)	P-value
P. gingivalis (%)	74%	28%	< 0.001
A. actinomycetemcomitans (%)	56%	20%	< 0.001
T. forsythia (%)	62%	22%	< 0.001

Table 2. *Prevalence of Periodontal Pathogens (P. gingivalis, A. actinomycetemcomitans, T. forsythia).*

Inflammatory Markers (CRP, IL-6, TNF-α) CRP IL-6 TNF-α). Between Patients and Healthy Controls with Statistical Significance.

There was a strong link between the disease and high levels of these inflammatory markers, as shown in Table 3. Patients had much higher levels of CRP (14.5±6.2 mg/L vs. 3.2±1.1 mg/L, P<0.001), IL-6 (88.7±17.4 pg/mL vs. 26.4±6.5 pg/mL, P<0.001), and TNF-α (85.4±18.3 vs. 31.5±9.2 pg/mL, P<0.001).

Biomarker	Patients (n = 150)	Healthy Controls (n = 50)	P-value
CRP (mg/L)	14.5 ± 6.2	3.2 ± 1.1	< 0.001
IL-6 (pg/mL)	88.7 ± 17.4	26.4 ± 6.5	< 0.001
TNF-α (pg/mL)	85.4 ± 18.3	31.5 ± 9.2	< 0.001

Table 3. *Inflammatory Markers (CRP, IL-6, TNF-α) CRP IL-6 TNF-α).*

Cardiovascular Risk Factors (Cholesterol, HDL, LDL, Triglycerides) Between Patients and Healthy Controls with Statistical Significance.

Total Cholesterol, HDL, LDL, and Triglycerides are cardiovascular risk factors that are compared between patients and healthy groups in the table. Total Cholesterol, LDL, and Triglyceride levels are much higher in patients than in controls (P-value < 0.001). HDL values are lower in patients. These results show that patients have a higher chance of heart disease as shown in table 4.

Risk Factor	Patients (n = 150)	Healthy Controls (n = 50)	P-value
Total Cholesterol (mg/dL)	210.6 ± 43.5	180.2 ± 29.3	< 0.001
HDL (mg/dL)	42.5 ± 9.2	54.8 ± 11.3	< 0.001
LDL (mg/dL)	133.4 ± 35.7	103.2 ± 24.1	< 0.001
Triglycerides (mg/dL)	174.2 ± 56.1	120.8 ± 40.2	< 0.001

Table 4. *Cardiovascular Risk Factors (Cholesterol, HDL, LDL, Triglycerides).*

Association of Periodontal Pathogens with Cardiovascular Disease Between Severity, (Mild CVD,

Moderate CVD, Severe CVD),with Statistical Significance.

The table 5, shows a significant association between oral microorganisms and cardiovascular disease severity. P. gingivalis increases from 52% in mild to 84% in severe CVD ($P < 0.001$). A. actinomycetemcomitans and T. forsythia also show increased percentages with disease severity, with T. forsythia reaching 78% in severe CVD ($P < 0.001$). These results highlight the strong correlation between oral bacteria and CVD severity.

Periodontal Pathogen	Mild CVD (n = 50)	Moderate CVD (n = 50)	Severe CVD (n = 50)	P-value
P. gingivalis (%)	52%	71%	84%	< 0.001
A. actinomycetemcomitans (%)	45%	55%	63%	0.038
T. forsythia (%)	49%	66%	78%	< 0.001

Table 5. *Association of Periodontal Pathogens with Cardiovascular Disease Severity.*

Discussion

Heart disease and stroke have been the world's top causes of death for decades, affecting people of all races and cultures [28]. If you have the right tools, the World Health Organization (WHO) says that you can avoid or treat more than 75% of cardiovascular illnesses (CVDs) [29]. There wasn't a big difference in age between the groups in this study (58.7 ± 12.5 vs. 56.2 ± 11.3 years, $P = 0.321$). Gender distribution was similar ($P = 0.722$). However, patients had a significantly higher BMI (29.4 ± 5.1 vs. 24.1 ± 3.7 kg/m², $P < 0.001$) and a greater prevalence of hypertension (55% vs. 10%, $P < 0.001$) and diabetes (45% vs. 7%, $P < 0.001$) compared to healthy controls. The amount of T. denticola found depended on the person's body mass index (BMI). People of all ages did this. The only thing that was different between men and women was that men had more T. denticola than women did. The study found that P. gingivalis and P. intermedia was found about as often as each other. People who don't have type 2 diabetes are much less likely to have A. actinomycetemcomitans, F. nucleatum, and T. forsythia. According to another study [30], P. gingivalis was found more often in overweight people with type 2 diabetes? The study looks at how many types of germs are in the mouths of healthy people and people who have periodontal illnesses. It was found that only 28% of healthy controls have P. gingivalis, while 74% of cases do ($P > 0.001$). Only 20% of healthy people and 56% of people with the disease have A. actinomycetemcomitans ($P < 0.001$). This is because only 22% of healthy controls have T. forsythia, while 62% of cases do ($P < 0.001$). It is clear from this that there is a strong and statistically significant link between the disease and having germs in your mouth. Another study found that T. forsythia was more common in adults younger than 35 and A. actinomycetemcomitans was more common in adults older than 35. Males were more likely than females to have T. denticola, which was one of the different types of bacteria [31]. A study in people in the Middle East and North Africa who did not have advanced periodontitis found that P. gingivalis and P. intermedia were more common than A. actinomycetemcomitans. Statistics showed that there was a strong link between P. gingivalis and A. actinomycetemcomitans. There wasn't a strong link between A. actinomycetemcomitans and P. intermedia [32]. People with the disease had much higher amounts of CRP (14.5±6.2 mg/L vs. 3.2±1.1 mg/L, $P<0.001$), IL-6 (88.7±17.4 pg/mL vs. 26.4±6.5 pg/mL, $P<0.001$), and TNF-α (85.4±18.3 pg/mL vs. 31.5±9.2 pg/mL, $P<0.001$) compared to healthy controls. Lots of these inflammation factors in the blood are linked to the disease in a strong way. In a different study, people who took atorvastatin or simvastatin had lower amounts of periodontal indices and inflammation markers (IL-6, CRP, and TNF-α) in their blood [33,34]. IL-6, IL-8, MMPs, and prostaglandin E2 (PGE2) are some other chemicals that make the inflammation response stronger at the cellular level. Two important cytokines that do this are IL-1 and TNF-α. Chemokines in Parkinson's disease hurt cells and make them swell up. Experiments on animals have shown that cytokines like IL-1 and TNF-α are bad for you. They make the damage to periodontal tissues worse and are a main reason why the disease gets worse [34]. The pathogen causes oxidative stress and

then an inflammatory reaction in the blood vessels. Interferon-γ (IFN-γ), IL-1β, IL-6, and TNFα all grow in the EC. These are all pro-inflammatory factors. The monocytes can move and stick together better because of this, which helps AS form [35]. The study looked at blood pressure, cholesterol, HDL, LDL, and triglycerides levels in both sick and healthy people to see how they compared. These three types of cholesterol are much higher in patients than in controls (P-value < 0.001). HDL values are lower in patients. These results show that patients have a higher chance of heart disease. A review of 29 studies showed that there is a link between gingivitis and dyslipidaemia. Specifically, people with periodontitis had much higher amounts of TC, LDL, and TG, while their HDL values were lower[36]. Several pieces of data showed that people with dyslipidaemia had higher levels of TNF-α in their blood. This level was significantly linked to VLDL, triglycerides, and cholesterol, and it was negatively related to HDL cholesterol [37,38]. This study showed a significant association between oral microorganisms and cardiovascular disease severity. P. gingivalis increases from 52% in mild to 84% in severe CVD (P < 0.001). A. actinomycetemcomitans and T. forsythia also show increased percentages with disease severity, with T. forsythia reaching 78% in severe CVD (P < 0.001). These results highlight the strong correlation between oral bacteria and CVD severity. Also, T. forsythia and BspA raise blood levels of CRP and LDL while lowering HDL, which helps atherosclerosis grow even more [39]. This is becoming more and more clear that T. forsythia, the third and most well-known important part of the red complex bacteria that is linked to gum disease, is also linked to heart disease. A strong link has been found between T. forsythia and atherosclerosis in more than one study. At the time of the study, T. forsythia was found in 43.7% of arterial plaques in coronary vessels [40].

Conclusion

The findings show a strong link between gum infections and cardiovascular diseases (CVD). It was much more common for patients to have P. gingivalis, A. actinomycetemcomitans, and T. forsythia than for healthy controls, and it got worse as the CVD got worse. Periodontal infections were also linked to elevated systemic inflammatory markers (CRP, IL-6, TNF-α) and higher cardiovascular risk factors, including increased cholesterol and triglyceride levels. These findings support the hypothesis that periodontal infections contribute to the progression of CVD, highlighting the importance of oral health care as part of preventive and therapeutic strategies for cardiovascular diseases.

Med., vol. 2022, p. 8678967, 2022.

References

1. [1] P. N. Varelas, "Must Hypothalamic Neurosecretory Function Cease for Brain Death Determination? No: The UDDA Revision Series," Neurology, vol. 101, no. 3, pp. 137-139, 2023.
2. [2] J. A. Leopold and E. M. Antman, "Ideal Cardiovascular Health in Young Adults With Established Cardiovascular Diseases," Front. Cardiovasc. Med., vol. 9, p. 814610, 2022.
3. [3] A. M. Navar et al., "Earlier Treatment in Adults With High Lifetime Risk of Cardiovascular Diseases: What Prevention Trials Are Feasible and Could Change Clinical Practice? Report of a National Heart, Lung, and Blood Institute (NHLBI) Workshop," Am. J. Prev. Cardiol., vol. 12, p. 100430, 2022.
4. [4] X. Jin et al., "Pathophysiology of Obesity and Its Associated Diseases," Acta Pharm. Sin. B, vol. 13, no. 6, pp. 2403-2424, 2023.
5. [5] G. Leonov et al., "Oral Microbiome Dysbiosis as a Risk Factor for Stroke: A Comprehensive Review," Microorganisms, vol. 12, no. 8, p. 1732, 2024.
6. [6] A. Chait and L. J. Den Hartigh, "Adipose Tissue Distribution, Inflammation and Its Metabolic Consequences, Including Diabetes and Cardiovascular Disease," Front. Cardiovasc. Med., vol. 7, p. 522637, 2020.
7. [7] P. Poirier et al., "Obesity and Cardiovascular Disease: Pathophysiology, Evaluation, and

Effect of Weight Loss: An Update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease From the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism," Circulation, vol. 113, no. 6, pp. 898-918, 2006.
8. [8] Y. Wu et al., "Characterization of the Salivary Microbiome in People With Obesity," PeerJ, vol. 6, p. e4458, 2018.
9. [9] I. Schamarek et al., "The Role of the Oral Microbiome in Obesity and Metabolic Disease: Potential Systemic Implications and Effects on Taste Perception," Nutr. J., vol. 22, no. 1, p. 28, 2023.
10. [10] Z. Min et al., "Oral Microbiota Dysbiosis Accelerates the Development and Onset of Mucositis and Oral Ulcers," Front. Microbiol., vol. 14, p. 1061032, 2023.
11. [11] D. Ma et al., "Au\@Ag Nanorods-PDMS Wearable Mouthguard as a Visualized Detection Platform for Screening Dental Caries and Periodontal Diseases," Adv. Healthcare Mater., vol. 11, no. 10, p. 2102682, 2022.
12. [12] D. Bourgeois et al., "Periodontal Pathogens as Risk Factors of Cardiovascular Diseases, Diabetes, Rheumatoid Arthritis, Cancer, and Chronic Obstructive Pulmonary Disease—Is There Cause for Consideration?," Microorganisms, vol. 7, no. 10, p. 424, 2019.
13. [13] N. A. Abdulmuttaleb, A. A. Oliwi Nasir, and O. A. Mohsein, "Investigation of Genetic Variations in APLN and APLNR Genes and Their Potential Role in Cardiovascular Diseases," Reports Biochem. Mol. Biol., pp. 525-539, 2024.
14. [14] E. L. Veras et al., "Newly Identified Pathogens in Periodontitis: Evidence From an Association and an Elimination Study," J. Oral Microbiol., vol. 15, no. 1, p. 2213111, 2023.
15. [15] X. Peng et al., "Oral Microbiota in Human Systematic Diseases," Int. J. Oral Sci., vol. 14, no. 1, p. 14, 2022.
16. [16] D. Celik and A. Kantarci, "Vascular Changes and Hypoxia in Periodontal Disease as a Link to Systemic Complications," Pathogens, vol. 10, no. 10, p. 1280, 2021.
17. [17] Y. Leng et al., "Periodontal Disease Is Associated With the Risk of Cardiovascular Disease Independent of Sex: A Meta-Analysis," Front. Cardiovasc. Med., vol. 10, p. 1114927, 2023.
18. [18] I. Mozos et al., "Inflammatory Markers for Arterial Stiffness in Cardiovascular Diseases," Front. Immunol., vol. 8, p. 1058, 2017.
19. [19] A. Rahimi and Z. Afshari, "Periodontitis and Cardiovascular Disease: A Literature Review," ARYA Atherosclerosis, vol. 17, no. 5, p. 1, 2021.
20. [20] S. Kitamoto and N. Kamada, "Periodontal Connection With Intestinal Inflammation: Microbiological and Immunological Mechanisms," Periodontol. 2000, vol. 89, no. 1, pp. 142-153, 2022.
21. [21] I. Kannosh et al., "The Presence of Periopathogenic Bacteria in Subgingival and Atherosclerotic Plaques—An Age Related Comparative Analysis," J. Infect. Dev. Ctries, vol. 12, no. 12, pp. 1088-1095, 2018.
22. [22] W. G. Haynes and C. Stanford, "Periodontal Disease and Atherosclerosis: From Dental to Arterial Plaque," Arterioscler. Thromb. Vasc. Biol., vol. 23, no. 8, pp. 1309-1311, 2003.
23. [23] J. Kim et al., "Association Between Oral Health and Cardiovascular Outcomes in Patients With Hypertension: A Nationwide Cohort Study," J. Hypertens., vol. 40, no. 2, pp. 374-381, 2022.
24. [24] A. M. Abbas, I. H. Shewael, and O. A. Mohsein, "Lipoprotein Ratios as Biomarkers for Assessing Chronic Atherosclerosis Progression," Academia Open, vol. 10, no. 1, pp. 10-21070, 2025.
25. [25] M. Minty et al., "Oral Microbiota-Induced Periodontitis: A New Risk Factor of Metabolic Diseases," Rev. Endocr. Metab. Disord., vol. 20, pp. 449-459, 2019.
26. [26] D. Prasher, S. C. Greenway, and R. B. Singh, "The Impact of Epigenetics on Cardiovascular Disease," Biochem. Cell Biol., vol. 98, no. 1, pp. 12-22, 2020.
27. [27] N. A. Abdulmuttaleb, M. Q. Mohammed, and O. A. Mohsein, "Exploring the Connection Between Inflammatory Cytokines, Hypertension, and Diabetes in Angina Patients," Cytokines, vol. 14, no. 15, p. 16, 2024.
28. [28] H. Labibidi et al., "Cardiovascular Disease in Arab Americans: A Literature Review of

Prevalence, Risk Factors, and Directions for Future Research," Am. J. Prev. Cardiol., p. 100665, 2024.
29. [29] J. Stewart, G. Manmathan, and P. Wilkinson, "Primary Prevention of Cardiovascular Disease: A Review of Contemporary Guidance and Literature," JRSM Cardiovasc. Dis., vol. 6, p. 2048004016687211, 2017.
30. [30] M. Akherati et al., "Comparison of the Frequency of Periodontal Pathogenic Species of Diabetics and Non-Diabetics and Its Relation to Periodontitis Severity, Glycemic Control and Body Mass Index," Clin. Exp. Dent. Res., vol. 7, no. 6, pp. 1080-1088, 2021.
31. [31] D. Lateef, N. Nasser, and O. Mohsein, "The Relationships Between Aplein, Vaspin and Thyroid Hormone Levels in Obese Diabetic and Non-Diabetic Women," J. Exp. Clin. Med., vol. 41, no. 2, pp. 239-245, 2024.
32. [32] Z. Al Yahfoufi and W. Hadchiti, "Prevalence of Periodontal Pathogens in a Group of Participants From the Middle East and North Africa Geographic Region With Minimal Periodontal Disease," J. Int. Soc. Prev. Commun. Dent., vol. 7, no. Suppl 1, pp. S30-S35, 2017.
33. [33] S. S. Kadhim et al., "Statins Improve Periodontal Disease–Induced Inflammatory Changes and Associated Lipid Peroxidation in Patients With Dyslipidemia: Two Birds by One Stone," J. Int. Oral Health, vol. 12, no. 1, pp. 66-73, 2020.
34. [34] J. L. Ebersole et al., "Ageing Effects on Humoral Immune Responses in Chronic Periodontitis," J. Clin. Periodontol., vol. 45, no. 6, pp. 680-692, 2018.
35. [35] C. Sampath et al., "Porphyromonas Gingivalis Infection Alters Nrf2-Phase II Enzymes and Nitric Oxide in Primary Human Aortic Endothelial Cells," J. Periodontol., vol. 92, no. 7, pp. e54-e65, 2021.
36. [36] J. Xu and X. Duan, "Association Between Periodontitis and Hyperlipidaemia: A Systematic Review and Meta-Analysis," Clin. Exp. Pharmacol. Physiol., vol. 47, no. 11, pp. 1861-1873, 2020.
37. [37] I. Luchian et al., "The Role of Matrix Metalloproteinases (MMP-8, MMP-9, MMP-13) in Periodontal and Peri-Implant Pathological Processes," Int. J. Mol. Sci., vol. 23, no. 3, p. 1806, 2022.
38. [38] S. Jovinge et al., "Evidence for a Role of Tumor Necrosis Factor α in Disturbances of Triglyceride and Glucose Metabolism Predisposing to Coronary Heart Disease," Metabolism, vol. 47, no. 1, pp. 113-118, 1998.
39. [39] S. S. Chukkapalli et al., "Chronic Oral Infection With Major Periodontal Bacteria Tannerella Forsythia Modulates Systemic Atherosclerosis Risk Factors and Inflammatory Markers," Pathogens Dis., vol. 73, no. 3, p. ftv009, 2015.
40. [40] I. Razeghian-Jahromi et al., "Prevalence of Microorganisms in Atherosclerotic Plaques of Coronary Arteries: A Systematic Review and Meta-Analysis," Evid.-Based Complement. Altern. Med., vol. 2022, p. 8678967, 2022.