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A possible correlation between periodontal disease and systemic diseases: a clinical study

Saverio Ceraulo[1,2], Antonio Barbarisi[1*], Gianluigi Caccianiga[3], Manuela Lodico[4], Francesca Cremonini[3,5], Dorina Lauritano[3] and Francesco Carinci[3]

Abstract

Background Periodontal disease (PD) is a widespread inflammatory condition with potential systemic implications. Its association with diseases such as diabetes, cardiovascular conditions, and hypovitaminosis D suggests a complex interplay involving immune-inflammatory mechanisms. To evaluate the correlation between PD and systemic biomarkers—blood glucose, glycated hemoglobin, cholesterol, vitamin D, and TSH, promoting awareness of the importance of regular health checkups.

Methods Eighty patients underwent periodontal evaluation and blood testing. Statistical analysis was used to explore associations between PD and systemic alterations.

Results PD was significantly associated with higher glycemia ($p < 0.05$), and linked to altered cholesterol and vitamin D levels, and increasing age. TSH levels showed a trend toward lower levels in PD patients, warranting further investigation.

Conclusions This study supports a possible bidirectional relationship between PD and systemic health. Findings suggest PD may contribute to increased risk of conditions like diabetes and atherosclerosis. The observed link with systemic biomarkers highlights the need for integrated diagnostic and preventive strategies. Future research with larger, more diverse populations is essential to validate these associations and to explore the impact of treating systemic conditions on periodontal outcomes.

Keywords Periodontal disease, Glycated hemoglobin, Vitamin d, Thyrotropin, Cardiovascular disease, Diabetes mellitus, Thyroxine, Triiodothyronine, High-density lipoprotein cholesterol

Introduction

Periodontal disease (PD) is a chronic inflammatory condition of the tooth-supporting tissues, mainly caused by Gram-negative anaerobic bacteria [1, 2], which form a biofilm and initially induce reversible gingivitis [3] that, if untreated, progresses to periodontitis with irreversible tissue damage, leading to the destruction of the periodontium [4, 5]. Dental plaque accumulation, linked to gingivitis development [6], and the PD classification by the European Federation of Periodontology (EFP, 2017) are based on the disease's severity, complexity, tissue destruction, and rate of progression.

*Correspondence:
Antonio Barbarisi
a.barbarisi@campus.unimib.it
[1]Department of Medicine and Surgery, University of Milano-Bicocca, Monza 20100, Italy
[2]Fondazione IRCCS San Gerardo dei Tintori, Monza 20900, Italy
[3]Department of Translational Medicine, University of Ferrara, Ferrara 44121, Italy
[4]Department Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, University of Palermo, Palermo, Italy
[5]Postgraduate School of Orthodontics, University of Ferrara, Ferrara 44121, Italy

Several studies have shown a strong association between periodontal diseases and systemic conditions such as cardiovascular diseases, diabetes, obesity, pregnancy complications, and Alzheimer's disease [7–11]. This link may involve direct effects via bacterial dissemination or indirect effects via systemic inflammation [12], with modifiable risk factors including diabetes mellitus, smoking, alcohol, sedentary lifestyle, stress, osteoporosis/osteopenia, and viral infections, and potential mechanisms being shared risk factors, subgingival biofilm as a Gram-negative bacteria reservoir, and elevated inflammatory mediators [4].

Poor oral health, including dental caries, periodontal disease, or complete tooth loss, affects 3.5 billion people worldwide [13], with PD considered an age-related disease affecting about 5% of individuals at 35 years, 50% at 45 years, and 60% over 45 years [14–18], and in Italy affecting roughly 60% of the population (10–14% with severe PD) which, if undiagnosed or inadequately treated, can lead to progressive destruction of the tooth-supporting apparatus, impaired masticatory and phonatory function, tooth loss, and consequent esthetic and psychological impacts [19, 20].

One of the major diseases associated with the oral cavity and periodontal disease is cardiovascular disease, particularly atherosclerosis, which results from the accumulation of high levels of cholesterol on arterial walls. Cholesterol circulates in the blood within particles called lipoproteins. The absorption, synthesis, and metabolism of lipoprotein cholesterol vary with age. Periodontal disease and the ratio of triglycerides to high-density lipoprotein cholesterol high density (TG/HDL-C) are associated with cardiovascular disease, obesity, and metabolic syndrome [2]. In particular, 84% of the population with PD had a TG/HDL ratio > 2.3, which is 1.47 times higher than those without PD [21]. The association between periodontal disease and cardiovascular disease is supported by epidemiological and scientific evidence at present [22–25]. Scaling and root planing, performed during nonsurgical periodontal therapy, may induce bacteremia with subsequent activation of the humoral immune response: in patients with endocarditis, antibiotic prophylaxis is performed [2–26].

Diabetes mellitus (DM) is defined as a condition of chronic hyperglycemia due to a defect in insulin secretion by pancreatic β-cells, a decrease in insulin sensitivity, or a combination of both [27]. It is a rapidly increasing disease. Individuals with diabetes tend to develop a more severe form of periodontitis compared to non-diabetic individuals, with their risk of developing periodontitis being 2–3 times higher than that of healthy subjects [28]. Diabetes causes changes in immune cells such as neutrophils, monocytes and macrophages [26]. The impairment of phagocytosis and chemotaxis allows the bacteria to enter the periodontal pocket and destroy the periodontium. In addition, as the macrophage is susceptible to bacteria, it fails in its task of apoptosis, resulting in increased production of cytokines and proinflammatory mediators. Periodontal disease also leads to diabetic complications [29].

Caries and periodontal disease (PD) are linked to vitamin D deficiency (VDD), as low plasma $25(OH)D_3$ levels indicate immune imbalance and promote PD progression [30, 31]; VDD is associated with greater periodontal destruction, severe periodontitis, tooth loss, and elevated inflammatory biomarkers (IL-35, IL-17 A, TGF) [32], while adequate vitamin D supports oral health and treatment success [33].

The thyroid gland is a typical organ in which organ-specific autoimmune diseases frequently occur and chronic inflammation. Thyroid hormones (thyroxine T4, triiodothyronine T3 and calcitonin) regulate the oxidative system by increasing reactive species and decreasing the availability of antioxidants. These mechanisms share epidemiological associations with periodontitis and explain the impact of Thyroid-stimulating hormone (TSH) levels on periodontal disease [34]. Thyroid hormones play an important role in oxidative stress and inflammation in humans, because lower serum levels of TSH are associated with a higher prevalence of PD, while high TSH levels inhibit osteogenic differentiation of the periodontal ligament stem cells (PDLSCs) [35].

Unlike most studies that explore correlations between periodontal disease and systemic conditions such as cardiovascular disease, diabetes, pregnancy complications, and neurological, renal, hepatic, gastrointestinal, and respiratory disorders [6–10], this research distinguishes itself by using blood test parameters as the basis for evaluation. While previous works [36–39] emphasize the need for greater attention and preventive measures in dental procedures for patients with systemic pathologies, the objective of this study was to assess the prevalence of periodontal disease in a group of patients with altered values in specific blood tests—namely blood count, glucose, glycated hemoglobin, TSH, and vitamin D.

Materials and methods

Ethical approval

The study was conducted according to the guidelines of the Ethics Committee of the School of Medicine and Surgery at the Milano Bicocca University (protocol n. 11/17) and executed in conformity with the Declaration of Helsinki.

Study population and recruitment

80 patients (48 females, 32 males; mean age 59.6 years) attending the periodontology department of the dental clinic between January 2018 and June 2023 were

recruited through random sampling. A personal interview was carried out with all patients selected to explain the objectives of the study and make them aware of the method used and each patient was given a questionnaire with the explanation of this study. In the questionnaire it was written: the purpose of the research, risks, insurance coverage, the last of the study and the treatment of personal data. Data collection was carried out from February 2023 to June 2024.

Inclusion and exclusion criteria

Inclusion criteria were:

- male and female over 18 years.
- non-smokers patients.

Exclusion criteria were:

- patients with a previous diagnosis of diabetes or assuming drugs for diabetes' regulation.
- patients assuming Vitamin D or with a previous diagnosis of hypovitaminosis.
- patients with thyroid diseases and/or assuming drugs for these pathologies.

Data collection

Each patients was asked to present the results of the latest blood tests to assess the following levels: CBC, fasting blood glucose, glycated hemoglobin, total cholesterol, vitamin D (25 OH) and Thyrotropin (TSH) and a orthopantomography (OPT). Although an orthopantomography does not give all the details of bone loss, it is the most readily available radiographic investigation for the patient that provides a comprehensive overview of the bone situation. During the session, the following was performed:

a) Personal data collection;
b) The collection of clinical data relating to the state of the oral cavity;
c) Education and motivation for proper oral hygiene at home.
d) Motivation to keep blood test parameters within certain levels.

The chart is not only considered an information document important from a professional point of view, it is also a legal document, protection of both the patient who is required to sign each document, but also the operators and consequently of the dental clinic.

To collect data, we proceed by compiling and analyzing:

1) General anamnesis: it is an important document that allows us to collect all the information related to the general health status of the patients who can be useful to the dentist, to be able to reconstruct the patient's previous state of health and/or illness. It can be divided into personal and medical.
2) Orthopantomography(OPT): it is a panoramic scan that allows us to have a complete view of the patient's oral cavity and offer information such as, for example, missing teeth, the presence of fillings, prostheses or implants, presence of bone resorption, devitalized, malpositions, crowding, agenesis, presence of cysts.
3) Blood tests: it is essential to carefully analyze the values above Mentioned. In particular, the optimal values are:
   - Blood count: 13.5–18 g/dl (men), 12–16 g/dl (women).
   - Glycated haemoglobin (HbA1): 3.5–6.0.5.0% or 20–42 mmol/mol.
   - Blood glucose: 70–100 (m/dl).
   - Total cholesterol: < 190 mg/dl.
   - TSH: 0.350–5.500 μU/ml.
   - Vitamin D: 30–100 ng/ml.

Clinical examination

The diagnosis of periodontal disease was established according to the 2017 World Workshop classification, based on: clinical attachment loss (CAL) ≥ 1 mm in two or more non-adjacent teeth; probing pocket depth (PPD) ≥ 4 mm in at least two sites on different teeth; bleeding on probing (BoP) at ≥ 10% of sites; and radiographic evidence of alveolar bone loss ≥ 15% of root length or ≥ 2 mm from the CEJ to the alveolar crest on periapical or panoramic radiographs.

To assess the presence of plaque deposits on the surfaces of each tooth, and therefore vestibular, lingual, mesial and distal, the Plaque Index of Loe and Silness (1964) was adopted. The procedure involves dissolving erythrosine (in tablet form), rinsing it with water, and detecting surfaces with plaque. The four measurements taken are summed and divided by 4.

The plaque index per subject is calculated as the average of the indices of the individual dental elements. Specifically, the sum of the indices of the individual teeth is divided by the number of teeth considered. This method provides the clinical periodontist with an accurate assessment of the amount of bacterial plaque not removed. The health status of periodontal tissues was evaluated using the Periodontal Screening and Recording (PSR) system, developed by the American Academy of Periodontology and the American Dental Association. This rapid and effective procedure offers a time-efficient alternative to traditional periodontal examinations, making it practical for daily clinical use and enabling comprehensive periodontal assessments at acceptable costs. During the PSR,

all sites of all dental elements are probed using a periodontal probe after completing anamnestic surveys. The mouth is divided into sextants, and for each sextant, only one value (code) is recorded. This value represents the most severe condition observed in that sextant. Probing is performed using a simplified periodontal probe (Perioprobe) with a rounded tip of 0.5 mm in diameter and a colored band extending from 3.5 mm to 5.5 mm. The probe is gently inserted into the gum line, held parallel to the tooth's long axis, and slid along the tooth surface until resistance is encountered. The probing depth is read by observing the position of the colored band relative to the gum line. Each side of each tooth (buccal, mesial, lingual, and distal) is probed to assess furcation involvement.

Additionally, the "Bleeding on Probing" (BOP) index, which evaluates gingival bleeding during probing, was calculated. This index is considered an essential tool for accurate diagnosis and monitoring of periodontal health. All clinical measurements were performed by a single calibrated periodontist (intra-examiner kappa > 0.85), who underwent calibration sessions prior to the study to ensure methodological reliability.

Treatment protocol

Patients underwent treatment following the operative Protocol for Dye-Free Photodynamic Therapy:

- T1 (Baseline): Patients received nonsurgical periodontal therapy on the first and second quadrants (upper arch) following the Guided Biofilm Therapy (GBT) protocol, which includes plaque detection, air polishing with glycine and erythritol powders, and ultrasonic instrumentation. This approach enhances patient compliance and allows more effective removal of visible calculus by targeting disclosed plaque. Dye-free photodynamic therapy was then applied to the treated areas (hydrogen peroxide in periodontal pockets and irradiation with diode laser: 980 nM, peak power of 3 W, ton of 20 μs (microseconds), toff of 80 μs (microseconds), and average power of 0.6 W).
- T2 (1 week after T1): Nonsurgical periodontal therapy was performed on the third and fourth quadrants (lower arch), again using the GBT protocol, followed by dye-free photodynamic therapy.
- T3 (3 weeks after T2): Dye-free photodynamic therapy was applied to both the upper and lower arches.
- T4 (3 weeks after T3): A second session of dye-free photodynamic therapy was administered to the entire mouth (upper and lower arches).
- T5 (3 weeks after T4): A third full-mouth session of dye-free photodynamic therapy was performed.
- T6 (4 weeks after T5): Patients underwent a final evaluation, which included a reassessment of bacterial flora through phase-contrast microscopy and an update of periodontal clinical indices: Plaque Index (PI), Probing Pocket Depth (PPD), gingival recessions, and Bleeding on Probing (BoP).

Statistical analysis

Subsequently, each patient completed a questionnaire on the frequency of dental checkups and their knowledge of periodontal disease. Categorical variables were expressed as counts and percentages, while quantitative variables were presented as means and standard deviations. The Chi-square test or Fisher's exact test was used to compare individuals with and without periodontal disease for categorical variables. For continuous variables, comparisons were made using Student's t-test or the Wilcoxon-Mann-Whitney test. Statistically significant differences were identified by two-sided P-values below 0.05. Variables included in the multivariable logistic regression model were age and glycemia, as these were the only parameters with $p < 0.05$ in univariate analysis.

For the multivariate analysis, logistic regression was applied to model the likelihood of periodontal disease (PD = yes vs. PD = no) based on the systemic and clinical covariates that showed significance in the univariate analysis. Statistical analysis was conducted using the R Statistical Software.

A priori power analysis was performed using G*Power 3.1 software [40] estimate the minimum required sample size for detecting a medium effect size (Cohen's d = 0.5) with 80% power and α = 0.05.

Results

80 patients were recruited of which 48 were female and 32 males. The average age of the sample was 59.6 years. All the blood results, staging and grading of periodontitis are reported in Table 1.

Each patient was asked how often they go to the dentist, and it emerged that:

- 23 patients said they had regular check-ups with the dentist every 3 months.
- 20 patients every 4 months.
- 15 patients every 6 months.
- 20 patients 1 time a year.
- 2 patients every 2 years or more.

27.5% of patients undergo dental check-ups only when needed. Each patient was asked if they knew what periodontal disease is, and it emerged that:

- 54 of them were unaware of the disease

Table 1 Patients' blood results and periodontal disease classification

Patient	Genre (M/F)	Age (y)	Blood count* (normal if 13.5–18 g/dl in men, 12–16 g/dl in women/abnormal)	Glycemia (mg/dl)	Glycated hemoglobin (mmol/mol)	Total cholesterol (mg/dl)	Vit D (ng/ml)	TSH (μU/m)	PD (Y/*N*)	Staging	Grading
1	F	67	normal	88	5.8	243	25.6	1.71	Y	I	A
2	M	49	normal	92	3.7	193	9.2	2.05	Y	I	A
3	F	76	normal	192	5.5	163	25.7	1.856	Y	II	C
4	M	69	normal	176	4.5	175	28	1.996	Y	I	A
5	F	56	normal	81	5.4	221	15.8	1.145	Y	III	C
6	F	67	abnormal	119	4.7	266	12.5	0.649	Y	II	A
7	F	65	normal	99	3.9	231	43.9	1.074	Y	II	B
8	F	66	abnormal	326	6.7	160	26.2	1.232	Y	III	C
9	F	74	abnormal	86	5.3	179	18.9	0.731	Y	I	B
10	F	68	normal	81	5.2	296	35.5	1.261	Y	III	A
11	F	67	normal	80	4.8	290	26.5	2.594	Y	IV	B
12	M	67	normal	77	4.2	170	25.4	1.69	N		
13	M	64	normal	194	7.5	170	23.7	1.98	Y	IV	C
14	M	68	abnormal	118	3.9	127	8.3	2.6	Y	I	B
15	F	75	normal	117	3.7	192	32	2.9	Y	II	B
16	F	59	normal	93	3.5	211	26	2.633	N		
17	F	53	normal	88	5.4	205	29	1.85	Y	IV	A
18	F	62	abnormal	85	5.1	232	15	1.169	N		
19	M	67	abnormal	135	6.1	267	30	0.909	Y	IV	B
20	M	68	normal	82	4.7	190	32	2.02	Y	I	A
21	M	49	normal	83	4.9	147	27	1.90	Y	I	A
22	M	67	abnormal	109	6.0	143	25	2.588	Y	III	B
23	F	53	normal	90	4.3	232	22	3.11	N		
24	F	74	normal	129	6.8	186	15	1.34	Y	IV	B
25	F	70	abnormal	101	5.7	213	35.2	2.088	Y	II	A
26	M	74	normal	83	5.7	160	8	1.09	Y	III	C
27	F	55	normal	86	4.5	181	31.2	2.4	N		
28	F	59	normal	116	5.9	149	35	0.95	N		
29	F	61	normal	99	3.9	233	29	2.00	Y	IV	C
30	M	60	normal	98	5.8	207	40	1.011	Y	I	A
31	F	39	normal	85	4.8	240	37	2.066	N		
32	M	38	normal	81	6.3	176	35	1.449	N		
33	F	84	normal	86	6.2	162	38.3	0.651	Y	II	B
34	M	64	normal	88	5.1	167	12	1.097	Y	IV	C
35	M	52	normal	95	6.1	177	20	2.288	N		
36	F	51	normal	78	5.2	213	30	1.345	N		
37	F	55	abnormal	78	5.3	199	40	3.162	Y	IV	C
38	F	44	normal	82	5.9	174	27.6	1.052	Y	II	B
39	F	58	normal	70	6.7	305	5.3	2.871	N		
40	F	49	normal	93	5.4	189	27.8	1.150	N		
41	M	47	abnormal	101	6.8	192	25	1.833	N		
42	M	50	normal	85	5.9	242	23.2	1.072	N		
43	M	61	normal	111	6.9	271	8	2.031	Y	IV	C
44	M	35	abnormal	87	4.2	141	18	1.539	N		
45	F	74	normal	89	4.9	158	29.8	1.245	Y	III	A
46	F	59	normal	94	5.8	195	18.4	1.499	Y	I	A
47	M	59	normal	105	5.6	210	37.3	1.388	Y	II	C
48	F	67	abnormal	100	4.9	181	19.2	3.001	Y	IV	C
49	F	71	normal	85	5.1	165	27.8	2.117	Y	I	A
50	M	61	normal	107	5.9	178	25.9	1.034	N		
51	F	69	normal	98	4.6	186	17.9	1.935	N		

Table 1 (continued)

Patient	Genre (M/F)	Age (y)	Blood count* (normal if 13.5–18 g/dl in men, 12–16 g/dl in women/abnormal)	Glycemia (mg/dl)	Glycated hemoglobin (mmol/mol)	Total cholesterol (mg/dl)	Vit D (ng/ml)	TSH (μU/m)	PD (Y/*N*)	Staging	Grading
52	F	55	normal	105	3.2	174	28.4	2.903	Y	II	B
53	M	71	abnormal	81	6.4	136	38.2	3.561	N		
54	F	62	normal	93	5.2	129	19.2	1.479	Y	I	A
55	M	68	normal	106	7.3	184	38	2.037	Y	III	C
56	F	47	normal	71	5.8	174	29.3	1.920	N		
57	M	39	abnormal	98	4.3	193	23	1.846	N		
58	F	48	normal	86	4.6	129	37.4	2.450	N		
59	M	83	normal	119	5.1	230	9.2	2.009	Y	II	B
60	F	70	normal	94	4.9	183	18.3	2.301	Y	IV	B
61	F	72	normal	80	6.3	201	33	1.987	N	II	A
62	F	63	normal	82	4.8	195	22.3	2.03	N		
63	F	58	normal	104	7.2	248	28.9	1.022	Y	III	C
64	F	49	normal	118	7.3	159	27.3	0.778	Y	I	C
65	M	41	normal	92	6.1	132	13.9	0.328	SI	I	B
66	F	78	abnormal	78	5.8	198	16.2	1.045	Y	IV	A
67	M	64	normal	86	6.3	160	38.2	1.901	N		
68	F	72	abnormal	136	7.26	193	32.1	1.681	Y	II	C
69	M	59	normal	116	6.9	209	27.8	0.318	Y	IV	B
70	F	49	normal	92	6.5	216	25.3	1.982	Y	I	A
71	M	57	normal	84	6.3	184	21.7	0.447	N		
72	F	63	normal	75	5.6	138	19	1.324	Y	III	A
73	F	68	normal	79	6.5	180	18.3	2.008	Y	III	A
74	F	59	normal	92	5.2	204	28.5	1.680	Y	II	B
75	F	49	abnormal	103	5.8	230	18.2	1.361	Y	II	B
76	F	51	normal	85	6.4	179	5.9	4.089	N		
77	M	73	normal	109	5.9	163	13.8	2.068	Y	I	A
78	M	62	normal	114	7.8	170	39.2	1.058	Y	III	C
79	M	68	normal	74	5.7	158	14.3	3.278	NO		
80	F	53	normal	90	6.5	207	10.2	0.876	SI	III	B

*The blood count values are indicated as 'normal' if they fall within the normal ranges of 13.5 to 18 g/dl for men and 12 to 16 g/dl for women. Any results outside these ranges are marked as 'abnormal'

– The remaining 26, on the other hand, said they knew what it was, but in broad strokes.

Patients who were aware of periodontal disease were asked if they knew about the correlation between periodontal disease and systemic diseases. It emerged that:

– 12 answered yes
– 14 said no.

The grade and stage, according to the new periodontal classification, of periodontitis patients are summarized:

- 27.78% of patients with periodontal disease were classified as stage I;
- 25.93% of patients with periodontal disease were classified as stage II;
- 22.22% of patients with periodontal disease were classified as stage III;
- 24.07% of patients with periodontal disease were classified as stage IV.

Among patients with hypovitaminosis D (< 30) and periodontal disease:

- 37.5% were classified as Grade A, in particular 60% of these with Stage I;
- 35.0% were classified as Grade B, in particular 35.71% of these with Stage II;
- 27.5% were classified as Grade C, with 45.45% of them having Stage IV.

Among patients with altered cholesterol levels and periodontal disease:

- 40.74% were classified as Grade A, in particular 45.45% of these had Stage I.
- 33.33% were classified as Grade B, in particular 55.56% of these had Stage II;
- 25.93% were classified as Grade C, with 42.86% of them having Stage IV.

Among patients with altered blood glucose levels in conjunction with periodontal disease, it is possible to highlight:

- 17.39% were classified in Grade A, in particular 50% of these have Stage I on a par with Stage II;
- 39.13% were classified as Grade B, in particular 44.44% of these have Stage II;
- 43.48% were classified as Grade C, in particular 40% of these have Stage III.

In particular:

- glucose average in men was 102.77 mg/dl
- glucose average in women was 99,12 mg/dl
- glucose average in men with periodontitis was 112,11 mg/dl
- glucose average in women with periodontitis was 104,06 mg/dl.

Biological mechanisms linking periodontal disease to systemic conditions have been investigated in the literature (Table 2).

This study contributes valuable data on the relationship between periodontal disease and systemic parameters, aligning with—but also differing from—existing literature. All findings are summarized in Tables 3 and 4.

Study's limitations

The study's limitations are summarized in the table below (Table 5).

Statistical analysis

This study included 80 patients, 49 (61.3%) females and 31 (38.8%) males. Among these patients, 53 (66,25%) reported PD. By performing univariable analysis (Table 6), there was a statistically significant difference between two groups based on age, with patients with PD (Mean = 3.8, SD = 9.6) older than patients without PD (Mean = 55.0, SD = 10.4). Furthermore, glycemia was found significantly higher in patients with PD (M = 107.3 mg/dl, SD = 40.0) compared to subjects without PD (M = 87.2 mg/dl, SD = 10.5). There was not any other variable with statistically significant difference between two groups (Table 2).

In the multivariable analysis (Table 7), age was confirmed associated with an increased risk of PD (AdjOR = 4.2; 95% CI =[1.51–12.82], $p = 0.007$) as well as glycaemia (AdjOR = 3.25; 95% CI =[1.18–9.68], $p = 0.026$).

Discussion

In the literature, numerous correlations have been established between periodontal disease and systemic conditions such as cardiovascular disease, diabetes, pregnancy complications, and neurological, renal, hepatic, gastrointestinal, and respiratory diseases [6–10]. Consequently, several studies [36–39] agree that the presence of certain systemic pathologies in patients requires increased attention during dental procedures, as well as preventive measures, to ensure optimal healing of mucosal tissues.

In this study, blood tests performed within six months prior to the visit were considered. After collecting all data, the study objectives were achieved. The first key finding is that, out of 80 patients, 54 suffered from periodontal disease, including 35 women and 19 men.

Statistical analysis revealed a significant difference in age between the two groups, with patients affected by periodontal disease being older than those without. Additionally, glycemia levels were significantly higher in patients with periodontal disease compared to those without. No other variables showed statistically significant differences between the two groups.

Furthermore, it was found that patients with altered levels of vitamin D, cholesterol, and blood sugar were the most affected by periodontal disease. Patients with hypovitaminosis were more susceptible to developing periodontal disease; most studies show that periodontitis is associated with lower levels of vitamin D compared to individuals with a healthy oral cavity [31].

In our study, controlling periodontal disease was notably more difficult in patients with altered cholesterol levels. It is well established that individuals with periodontitis have a TG/HDL ratio approximately 1.47 times higher than those without periodontitis [2, 35]. Among patients with altered glycated hemoglobin levels, most were classified as having Stage III, Grade C periodontal disease. Blood test results showed the average values for each parameter examined. Patients with periodontal disease exhibited higher average glucose levels than healthy individuals, consistent with existing literature [27].

Among men, both healthy and those with periodontitis, average glucose levels were higher compared to women, supporting findings from previous studies. Indeed, numerous studies have reported that periodontal disease adversely affects glycemic control, contributing to complications such as cardiovascular disease and end-stage kidney disease.

The average total cholesterol was higher in women (199.73 mg/dl) than in men (181.35 mg/dl), exceeding the threshold limit. However, there was little difference between healthy women and those with periodontitis.

Table 2 Biological mechanisms linking periodontal disease to systemic conditions

Parameter	Biological Mechanism	Reference
Blood Glucose	- **Effects of hyperglycemia on periodontitis**: Chronic hyperglycemia in diabetic patients increases the production of advanced glycation end products (AGEs). These AGEs bind to their receptors (RAGEs), triggering an inflammatory cascade. This leads to increased secretion of pro-inflammatory cytokines (e.g., IL-1β, TNF-α) and matrix metalloproteinases (MMPs), which contribute to periodontal tissue destruction. - **Effects of periodontitis on blood glucose**: Pathogenic periodontal bacteria and their byproducts, such as lipopolysaccharides (LPS), induce systemic inflammation. This exacerbates insulin resistance, further impairing glycemic control.	[41, 42]
Cholesterol	- **Effects of dyslipidemia on periodontitis**: Oxidized LDL (oxLDL) enhances macrophage activation and promotes the release of inflammatory cytokines, worsening tissue destruction in periodontitis. - **Effects of periodontitis on lipid metabolism**: Chronic systemic inflammation caused by periodontitis disrupts lipid metabolism, leading to increased triglycerides and LDL levels while decreasing HDL levels.	[43, 44]
Cardiovascular Disease	- **Direct mechanisms**: Periodontal pathogens, such as *Porphyromonas gingivalis* and *Tannerella forsythia*, can enter the bloodstream through inflamed gums and contribute to the formation of atherosclerotic plaques. - **Indirect mechanisms**: Chronic systemic inflammation caused by periodontitis (elevated CRP, IL-6, and TNF-α) accelerates atherosclerosis and endothelial dysfunction.	[45, 46]
TSH (Thyroid-Stimulating Hormone)	- **Effects of hypothyroidism on periodontitis**: Hypothyroidism, characterized by elevated TSH levels, reduces osteoclastic activity and alters bone metabolism, increasing the risk of alveolar bone loss. - **Effects of periodontitis on thyroid function**: Chronic periodontal inflammation may contribute to thyroid dysfunction through immune dysregulation and the activation of systemic inflammatory cytokines.	[47, 48]
Vitamin D	- **Effects of Vitamin D deficiency on periodontitis**: Vitamin D stimulates the production of antimicrobial peptides, such as cathelicidins and defensins, which protect against periodontal pathogens. A deficiency impairs this immune defense, promoting bone destruction. - **Effects of periodontitis on Vitamin D**: Chronic inflammation may alter Vitamin D metabolism, reducing its bioavailability and amplifying periodontal disease progression.	[49, 50]

Table 3 Systemic conditions and PD in literature findings and in this study findings

Systemic Condition	Literature Findings (from Systematic Reviews/Meta-analyses)	Study Findings
Diabetes (Glycemia and HbA1c)	- PD increases HbA1c by ~0.29% [51] - OR for diabetes in PD patients: 1.86 [52]	- Glycemia significantly higher in PD patients: 107.3 mg/dl vs. 87.2 mg/dl ($p < 0.001$) - HbA1c not significantly different (5.6 vs. 5.4 mmol/mol; $p = 0.406$)
Cardiovascular Disease (Cholesterol)	- PD associated with higher total cholesterol: MD ~ 7.79 mg/dl [53] - Elevated TG/HDL ratio in PD [54]	- Slightly higher cholesterol in PD group: 194.1 mg/dl vs. 189.7 mg/dl ($p = 0.636$), not significant
Vitamin D Deficiency	- PD associated with lower vitamin D: MD − 7.66 ng/ml [55] - OR for PD in hypovitaminosis D: ~1.33 [56]	- Vitamin D slightly lower in PD group: 24.4 ng/ml vs. 25.3 ng/ml ($p = 0.676$), not significant
Thyroid Dysfunction (TSH)	- Lower TSH linked to increased PD risk [57]: OR ~ 1.72 - Thyroid dysfunction affects periodontal inflammation and bone loss [58]	- Lower TSH in PD group: 1.6 µU/ml vs. 2.0 µU/ml ($p = 0.053$), trend approaching significance

Conversely, in men, cholesterol levels were higher in patients with periodontal disease compared to healthy individuals.

Analysis of average vitamin D levels revealed that both men and women had levels below the sufficiency threshold. Women with periodontal disease had higher average vitamin D levels (25.57 ng/ml) than men with periodontitis (22.65 ng/ml), suggesting that low vitamin D levels are more strongly associated with periodontal disease.

Average TSH levels fell within the normal range for both healthy individuals and those with periodontitis. However, patients with periodontal disease had lower average TSH levels (1.604 µU/mL in men and 1.703 µU/mL in women). Consistent with the literature [34], lower TSH levels were associated with significantly higher probabilities of developing periodontitis. Therefore, maintaining TSH levels within the normal range is crucial, especially in patients with hypothyroidism, as it improves outcomes in implantology, orthodontics, and periodontics.

Table 4 Summary of systemic parameters in relation to periodontal Disease – Comparison between literature and study findings

Parameter	Literature Review Summary	This Study (PD vs. No PD)	Statistical Significance
Age	Older age is a well-established risk factor for PD [59]	63.8 vs. 55.0 years	$p < 0.001$
Glycemia	↑ Glycemia in PD; bidirectional link with diabetes (OR: 1.86) [60, 61]	107.3 vs. 87.2 mg/dl	$p < 0.001$
HbA1c	↑ HbA1c in PD by ~ 0.24–0.29% [62, 63]	5.6 vs. 5.4 mmol/mol	NS ($p = 0.406$)
Cholesterol	↑ Total cholesterol in PD by ~ 7.8 mg/dl [64]	194.1 vs. 189.7 mg/dl	NS ($p = 0.636$)
Vitamin D	↓ Vitamin D in PD by ~ 7.6 ng/ml [65, 66]	24.4 vs. 25.3 ng/ml	NS ($p = 0.676$)
TSH	↓ TSH associated with higher PD risk (OR ~ 1.7); impact on bone metabolism and inflammation [67, 68]	1.6 vs. 2.0 µU/ml	~$p = 0.053$ (borderline)

Table 5 Limitations of the study

Limitation Category	Specific Limitation
Sample size	The work has a small sample size, which can limit the generalizability of the results.
Demographic restrictions	The study focuses exclusively on Italian patients, reducing the diversity of the sample.
Confounding factors	The low socioeconomic status and educational level of patients from a public hospital may influence the findings.
Lack of a control group	The study does not include a control group of smokers, diabetic patients, or individuals with other conditions related to periodontal disease.

Table 7 Multivariable analysis

Variables	Adjusted OR	95%CI	*p*-value
Age			0.007**
> 62 years vs. <=62 years	4.2	[1.51–12.82]	
Glycaemia			0.026*
> 92(mg/dl) vs. <=92(mg/dl)	3.25	[1.18–9.68]	

The analysis also revealed that most patients had not undergone blood tests for a significant period—up to three years in some cases. This investigation proved especially beneficial for patients with altered levels in one or more of the six parameters examined. A notable number of patients with altered parameters also suffered from periodontal disease. These patients were informed of the potential relationship between periodontal and systemic diseases and were advised to consult their physician for further evaluation.

Table 6 Univariable analysis

Variables/ Disease	Categories/ M(SD)	Periodontal Disease			
		NO ($n = 27$)	YES ($n = 53$)	Total ($n = 80$)	*p*-value
Gender	F	15 (55.6%)	34 (64.2%)	49 (61.3%)	0.615
	M	12 (44.4%)	19 (35.8%)	31 (38.8%)	
Age (years)	Mean (SD)	55.0 (10.4)	63.8 (9.6)	60.8 (10.7)	< 0.001***
Blood count (g/dl)	normal	22 (81.5%)	41 (77.4%)	63 (78.8%)	0.891
	abnormal	5 (18.5%)	12 (22.6%)	17 (21.2%)	
Glycaemia (mg/dl)	Mean (SD)	87.2 (10.5)	107.3 (40.0)	100.5 (34.4)	< 0.001***
Glycated hemoglobin (mmol/mol)	Mean (SD)	5.4 (0.9)	5.6 (1.1)	5.5 (1.0)	0.406
Total cholesterol (mg/dl)	Mean (SD)	189.7 (37.8)	194.1 (39.9)	192.6 (39.0)	0.636
Vitamin D (ng/ml)	Mean (SD)	25.3 (9.0)	24.4 (9.6)	24.7 (9.3)	0.676
TSH (µU/ml)	Mean (SD)	2.0 (0.9)	1.6 (0.7)	1.8 (0.8)	0.053
Staging	I	0 (0%)	15 (28.3%)	15 (18.8%)	0.722
	II	1 (3.7%)	13 (24.5%)	14 (17.5%)	
	III	0 (0%)	12 (22.6%)	12 (15%)	
	IV	0 (0%)	13 (24.5%)	13 (16.2%)	
Grading	A	1 (3.7%)	19 (35.8%)	20 (25%)	1.000
	B	0 (0%)	18 (34%)	18 (22.5%)	
	C	0 (0%)	16 (30.2%)	16 (20%)	

The findings of this study reveal both convergences and divergences with the existing literature on the relationship between periodontal disease and systemic health parameters. Consistent with previous studies, glycemia was significantly elevated in patients with periodontal disease, reinforcing the well-documented bidirectional relationship between periodontal disease and diabetes. The highly significant p-value (< 0.001) further supports this association. Although not statistically significant, the observed trend toward lower TSH levels in patients with periodontal disease ($p = 0.053$) aligns with recent findings, suggesting that subclinical hyperthyroidism may contribute to periodontal inflammation.

In contrast, this study did not identify significant differences in cholesterol and vitamin D levels between patients with and without periodontal disease, diverging from much of the existing literature. Several possible explanations may account for this discrepancy, including

the limited sample size ($n = 80$), which may not have been sufficient to detect subtle metabolic variations, and variability in patient lifestyle or medication use, which could obscure underlying associations. Furthermore, vitamin D levels were generally low across both groups, suggesting a widespread insufficiency that may have diluted any intergroup differences. These divergent findings may also reflect specific characteristics of the study population—Italian adults—who may share dietary habits or healthcare access that influence systemic markers. The significant age difference between groups is another important factor to consider, as age itself may confound associations with systemic biomarkers.

Despite these limitations, the clinical relevance of the study is clear: the findings underscore the importance of screening for systemic risk factors in patients with periodontitis, particularly regarding hyperglycemia and thyroid function. While cholesterol and vitamin D levels did not show significant differences, they remain biologically plausible factors and warrant further investigation. Overall, this study highlights the necessity of integrating systemic health assessments into periodontal evaluation and management. The strong association with glycemic control and emerging evidence linking thyroid function to periodontal disease emphasize the potential for more integrated medical-dental care. The discrepancies with previous literature, especially regarding lipid and vitamin D profiles, underscore the need for larger, multicenter studies with detailed stratification for confounding variables such as age, medication use, and socioeconomic status.

Emphasis was placed on motivation: maintaining oral health is essential to prevent the formation of infectious foci in various parts of the body. To achieve this, patients were educated on proper home oral hygiene practices, including the use of chemical agents to reduce plaque levels. As part of primary prevention, patients were asked about the frequency of their dental check-ups and their knowledge of periodontal disease. The results highlighted that periodontal disease is still an underestimated condition, with significant misinformation regarding its implications. Patients were instructed and motivated to consistently use home oral hygiene devices, such as electric toothbrushes, dental floss, interdental brushes, tongue cleaners, and water flossers, to prevent or, for those with periodontitis, manage the disease.

Primary prevention is particularly important for fragile and/or hospitalized patients. The challenges faced by frail, non-self-sufficient, or non-ambulatory elderly patients often exacerbate systemic pathological conditions. Prosthetic rehabilitation plays a critical role in improving their quality of life and social activity [69].

Patients aware of periodontal disease were asked if they knew about its correlation with systemic diseases: 12 answered yes, while 14 said no. This highlights the importance of educating patients about the risks associated with periodontitis and the effects of poor oral hygiene on their overall health. Dental professionals must emphasize the importance of a healthy diet, avoiding harmful habits such as smoking and excessive alcohol consumption, and engaging in moderate, consistent physical activity. Furthermore, patients should be motivated and instructed to control and remove bacterial plaque through proper home hygiene practices to prevent and manage periodontal pathologies that may worsen their condition.

Clinical implications

The findings suggest that periodontal assessments may serve not only in maintaining oral and dental health but also as an important screening tool for the early detection of systemic disease risks. Therefore, integrating periodontal examinations into routine health check-ups for individuals at systemic risk may improve clinical outcomes."

Conclusions

Within the limitations of this study, the findings indicate significant associations between periodontal disease (PD) and elevated glycemia, altered cholesterol and vitamin D levels, and older age. Additionally, a trend toward lower TSH levels was observed in PD patients, suggesting that potential thyroid–periodontal interactions warrant further investigation. These results highlight the importance of an interdisciplinary approach to PD prevention and management, integrating oral health assessments with systemic health evaluations. Dental professionals play a key role in this process through patient education, personalized oral hygiene strategies, and appropriate medical referrals.

Abbreviations

PD	Periodontal disease
TG	Triglycerides
HDL-C	High-density lipoprotein cholesterol high density
DM	Diabetes mellitus
VDD	Vitamin D deficiency
TSH	Thyroid-stimulating hormone
PDLSCs	Periodontal ligament stem cells
OPT	Orthopantomography
HbA1	Glycated haemoglobin
CAL	Clinical attachment loss
PPD	Probing pocket depth
BoP	Bleeding on probing
PSR	Periodontal Screening and Recording
GBT	Guided Biofilm Therapy
Microseconds	µs
PI	Plaque Index
PPD	Probing Pocket Depth
AGEs	Advanced glycation end products
LPS	Lipopolysaccharides
oxLDL	Oxidized LDL

Supplementary Information

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Supplementary Material 1.

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Declarations

Ethics approval and consent to participate
The study was conducted according to the guidelines of the Ethics Committee of the School of Medicine and Surgery at the Milano Bicocca University, (protocol n. 11/17) and it was executed in conformity with the Declaration of Helsinki. A consent to participate was given to each patient. Informed consent was obtained from all subjects involved in the study.

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