

Original Article

Heart rate variability as a predictor of autonomic dysfunction and cardiovascular risk in periodontitis

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Abstract

Periodontitis is a chronic inflammatory disease damaging the supportive structure of teeth. It has many systemic impacts including cardiac autonomic dysfunction. Heart Rate Variability (HRV) measures an objective analysis of the extent of autonomic regulation and where decreased parasympathetic activity coupled with increased sympathetic predominance was determined to correlate well with risk in cardiovascular function. This research ascertains periodontitis and its correlation to autonomic dysfunction by HRV analysis. In total, 54 periodontitis patients were involved in the study, categorized under four groups, namely Gingivitis (n=14), Mild Periodontitis (n=13), Moderate Periodontitis (n=13), and Severe Periodontitis (n=14). Kubios HRV software version 3.5 was used for the analysis of time-domain and frequency-domain parameters of lead II ECG for HRV analysis. The indices of SNS and PNS were calculated for the assessment of autonomic balance. The correlation between the HRV parameters with the severity of periodontal disease was performed statistically. The SNS index was increased with periodontitis severity (Gingivitis: 1.09 ± 0.60 , Mild Periodontitis: 4.25 ± 2.4 , Moderate Periodontitis: 3.82 ± 2.2 , Severe Periodontitis: 4.45 ± 1.5 ; $p < 0.001$), which reflected enhanced sympathetic activation. On the other hand, the PNS index was significantly reduced (0.55 ± 0.91 in Gingivitis to -0.98 ± 0.59 in Severe Periodontitis; $p < 0.001$), indicating parasympathetic withdrawal. SDNN, a marker of overall autonomic tone, decreased significantly ($p = 0.025$), while high-frequency (HF) power, indicative of vagal activity, showed a strong negative correlation with periodontitis severity ($Rho = -0.58$, $p < 0.001$). These findings suggest progressive autonomic dysfunction with increasing periodontal inflammation. Significant autonomic dysfunction, including elevated sympathetic hyperactivity and diminished parasympathetic regulation, is associated with periodontitis and lowers heart rate variability. Higher cardiovascular risk is correlated with the advancement of periodontal disease, underscoring the necessity of HRV evaluation as a possible biomarker. Future studies should examine if treating periodontal disease can enhance systemic health and restore autonomic balance.

Keywords: periodontitis, heart rate variability, autonomic dysfunction, sympathetic dominance, parasympathetic activity, cardiovascular risk

Introduction

Periodontal disease is a very common chronic inflammatory condition that causes progressive tissue destruction and eventual loss of the teeth-supporting structures [1]. It is mainly caused by a dysbiotic oral microbiome, wherein pathogenic bacteria such

as *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Aggregatibacter actinomycetemcomitans* trigger an exaggerated immune response [2]. This leads to the production of inflammatory cytokines, matrix metalloproteinases (MMPs), and reactive oxygen species (ROS), which contribute to periodontal ligament degradation, alveolar bone resorption, and clinical attachment



loss (CAL) [1, 2]. Periodontitis has been traditionally considered a localized oral disease; however, more recent studies have increasingly pointed to its systemic significance. In the United States, approximately 42% of adults aged 30 years and older have some form of periodontal disease, with 7.8% experiencing severe periodontitis [3]. Globally, the prevalence of periodontal disease ranges from 20% to 50%, making it a significant public health concern [4]. Due to the chronic inflammatory nature of periodontitis and its ability to modulate immune responses beyond the oral cavity, its potential role in influencing systemic pathophysiology, particularly CVD, has gained considerable attention in recent decades [5].

The relationship of periodontitis with CVD is complex, multifactorial, and involving both direct dissemination of microbes via the bloodstream and systemic inflammatory pathways [6]. Periodontal pathogens gain entry into the bloodstream through bacteraemia, contributing to endothelial dysfunction, plaque formation in the arteries, and upregulation of inflammatory mediators such as CRP, IL-6, and TNF- α [7]. These inflammatory cascades speed up the course of atherosclerosis and enhance the risk of myocardial infarction, stroke, and other cardiovascular events. In addition to systemic inflammation, it has been recently found that the dysfunctional state of the autonomic nervous system can play a very important role in mediating the association of periodontitis with cardiovascular health [8]. The ANS controls vital physiological functions, such as heart rate, vascular tone, and blood pressure, through its sympathetic and parasympathetic branches. Studies have shown that periodontitis patients have an imbalance in autonomic function, which is characterized by decreased parasympathetic activity (vagal tone) and increased sympathetic dominance, being strong predictors of cardiovascular morbidity and mortality [9]. HRV is a well-established marker of autonomic function that has been applied to assess cardiac autonomic regulation in systemic diseases, yet its potential utility in periodontitis remains largely unexplored.

Although there is growing awareness of the oral-systemic connection, a significant research gap persists in understanding the exact mechanistic link between periodontitis and cardiac autonomic dysfunction. Most of the investigations focused more on inflammation and metabolic disturbances rather than on the effect of periodontitis upon autonomic regulation. Additionally, despite its widespread application in cardiology to detect autonomic balance and assess cardiovascular risk, HRV analysis has not gained a prominent

position within periodontal diseases [10]. This study intends to help bridge that gap by more fully conducting HRV analysis in patients with varying degrees of periodontitis and evaluating its potential as an early indicator of autonomic dysfunction and cardiovascular risk.

By incorporating periodontal assessments with advanced autonomic function testing, the research will provide novel insights into bidirectional interactions between oral health and cardiovascular physiology. The findings may have important clinical implications, promoting a paradigm shift toward interdisciplinary healthcare in which dental practitioners and medical professionals collaborate to identify and manage systemic health risks associated with periodontitis.

Material and methods

Study design and setting

The present study was a cross-sectional investigation to assess cardiac autonomic dysfunction in periodontitis patients. The research was conducted at Nandha Medical College and Hospital, Erode, India. It was conducted after recruiting participants on the basis of specific eligibility criteria. This site provided access to a diverse population of patients and the diagnostic and analytical tools required for comprehensive assessments of periodontal and autonomic function.

Participants and eligibility criteria

A total of 54 patients were recruited in the study, all of whom had a confirmed diagnosis of periodontitis. The inclusion criteria were that the patients must be within the age group of 30 to 65 years to ensure that the most susceptible population for systemic complications caused by periodontitis was recruited. Both male and female subjects who fulfilled these age and diagnostic criteria were eligible for inclusion.

Participants who have had neurological disorders, pre-existing autonomic dysfunction, or diabetes-related neuropathy were excluded as these conditions would interfere with the outcome of HRV. Individuals with acute dental conditions, such as toothache, swelling, or periodontal abscesses, were also excluded, as these conditions could affect autonomic responses independently. Further, no individual was taken in whose general medical conditions were systemic like bleeding disorders, jaundice, hepatitis, drug allergies, autoimmune disorders, cancer, or symptomatic cardiovascular and

respiratory diseases. Women in the stage of pregnancy and handicapped people with bodily defects not permitting them to abide by study protocol were not enrolled.

Data collection and clinical examination

Demographic, medical, and periodontal assessments were done for all participants. Then a test of HRV was conducted to assess cardiac autonomic dysfunction. A structured questionnaire was used in recording demographic data of each participant, such as age, gender, and medical history. Parameters of the general health of the participants will be considered as a confounder, such as blood pressure, heart rate, and BMI.

The severity of periodontal disease was calculated using the score of Community Periodontal Index (CPI) [11]. Moreover, the extent of gingival recession and mobility was checked using periodontal probe and rear surface mouth mirror. The loss in clinical attachment with periodontal pocket depth, if any was measured with greater care for a proper categorization of the patient's level of periodontitis.

Heart rate variability analysis

HRV analysis was performed to assess cardiac autonomic function, which is influenced by the sympathetic and parasympathetic nervous systems. For this, a lead II electrocardiogram (ECG) recording was obtained using a Multichannel Physiopac – PP 8 machine. Participants were asked to rest for 15 minutes before the recording to ensure physiological stabilization. The ECG was recorded for five minutes, following the Task Force Guidelines on HRV measurement.

Once the ECG signals were captured, the R-R interval (time between two successive heartbeats) was extracted and any artifacts or ectopic beats were filtered to ensure data accuracy. The ECG signals were analysed using Kubios HRV software version 3.5 that enabled a comprehensive analysis of time-domain and frequency-domain parameters. Standard analysis in the time domain includes three important HRV variables: Standard Deviation of NN intervals, Root Mean Square of Successive Differences, and pNN50, which measures the percentage of adjacent NN intervals differing by more than 50 milliseconds. This provides an indication of overall autonomic tone as well as parasympathetic activity.

Frequency-domain analysis was carried out by decomposing the HRV signals into the low-frequency

range (LF, 0.04–0.15 Hz) and the high-frequency range (HF, 0.15–0.4 Hz), reflecting the contributions of sympathetic and parasympathetic activity, respectively. The ratio LF/HF was also computed as an index of autonomic balance. To further differentiate autonomic responses, Parasympathetic Nervous System (PNS) and Sympathetic Nervous System (SNS) indices were calculated.

Statistical analysis

All the data that were collected and entered in Microsoft Excel. All data were analyzed by SPSS software version 22.0. Descriptive statistics for relevant variables were performed, including calculating mean, standard deviation (SD), and standard error of the mean (SEM). Pearson's correlation test as well as Spearman's Rho correlation test was applied to assess the relationship between periodontitis severity and HRV parameters.

Results

This study evaluated the impact of periodontitis on cardiac autonomic dysfunction through Heart Rate Variability (HRV) analysis, highlighting significant alterations in autonomic regulation among patients with periodontal disease.

The findings indicate that patients with periodontitis exhibit notable autonomic dysfunction, primarily characterized by reduced parasympathetic activity, increased sympathetic dominance, and impaired overall HRV. These autonomic changes show progressively increased association with the severity of periodontal disease, which suggests that chronic periodontitis contributes to systemic dysregulation of autonomic function and predisposes individuals to cardiovascular complications.

In this section, the demographic and clinical characteristics of study participants are provided, followed by an elaboration of patterns of HRV-based autonomic dysfunction, mainly focusing on time-domain and frequency-domain HRV parameters, as well as their relationship to the severity of periodontitis and stress index.

Demographic and clinical characteristics of the study population

A demographic profile regarding age, gender, and body mass index of the study population was also

Table 1: Baseline characteristics of the study population.

Parameter	Gingivitis (n=14)	Mild periodontitis (n=13)	Moderate periodontitis (n=13)	Severe periodontitis (n=14)
Mean Age (years)	39.5±5.2	42.3±4.8	46.7±5.6	51.2±4.9
BMI (kg/m ²)	24.8±3.1	25.6±3.7	26.2±3.9	27.5±4.1
CPI Score	2.1±0.5	3.4±0.7	4.1±0.8	4.9±0.6
CAL (mm)	1.5±0.3	2.8±0.4	4.2±0.5	5.6±0.5

collected to exclude potential confounding variables that might have an impact on HRV parameters. This baseline characteristic analysis of the study population indicated that patients with severe periodontitis were significantly older and also had higher BMI values than those with mild or moderate periodontitis. Age-related autonomic decline and obesity-related metabolic stress may be some of the causes of progression of periodontitis and its associated autonomic dysfunction (Table 1).

The steady rise in CPI and CAL scores with the progression of periodontitis. Since both obesity and ageing are established risk factors for autonomic dysregulation and cardiovascular disease, their interplay with periodontal disease severity does warrant integration of periodontal care into more generalized systemic health monitoring frameworks.

Periodontitis and autonomic dysfunction: evaluation by HRV

Parasympathetic activity (PNS index) with periodontitis progression

This index provides a measure of direct vagal tone and parasympathetic modulation of heart rate, which was significantly reduced in periodontitis patients, especially in the moderate to severe group. The reduction in PNS index indicates a progressive impairment in parasympathetic control over cardiac function, meaning less capacity to counterbalance sympathetic overactivation (Table 2).

The statistically significant correlation between severity of periodontitis and the PNS index suggests that increased parasympathetic function. Therefore, the patients with a smaller PNS index have signs of autonomic impairment, enhanced cardio stress, and increased sensitivity to arrhythmias and cardiovascular diseases.

Sympathetic activity (SNS index) with periodontitis progression

While the parasympathetic function decreased with worsening periodontal disease, the SNS index showed progressive increased value. Such sympathetic overactivation is an established indicator of cardiovascular risk because sympathetic overactivity leads to increased heart rate, vasoconstriction, and release of pro-inflammatory cytokines (Table 3).

The increase in SNS index with periodontitis severity suggests autonomic dysregulation, which is the loss of parasympathetic influence met with an exaggerated sympathetic response.

Such autonomic imbalances have been strongly implicated in hypertension, endothelial dysfunction, and atherogenesis, further supporting the potential role of periodontitis as a risk factor for cardiovascular disease (Figure 1).

HRV frequency-domain parameters and periodontitis severity

Frequency-domain HRV analysis gives a quantitative estimation of sympathetic and parasympathetic

Table 2: Association between periodontitis and PNS index.

Study groups	Mean PNS index±SD	p-value
Gingivitis	0.55±0.91	<0.001 ***
Mild periodontitis	-0.47±0.46	
Moderate periodontitis	-0.90±0.85	
Severe periodontitis	-0.98±0.59	

Note: *** – denotes very highly significant p-value.

Table 3: Association between periodontitis and SNS index.

Study groups	Mean SNS index $\pm$ SD	p-value
Gingivitis	1.09 $\pm$ 0.60	<0.001 ***
Mild periodontitis	4.25 $\pm$ 2.4	
Moderate periodontitis	3.82 $\pm$ 2.2	
Severe periodontitis	4.45 $\pm$ 1.5	

Note: *** – denotes very highly significant p-value.

contributions to heart rate regulation. The findings showed that the high-frequency power was significantly reduced, thereby supporting parasympathetic dysfunction in periodontitis patients (Table 4).

These findings confirm that periodontitis patients exhibit substantial impairment in both short-term and long-term autonomic function, predisposing them to cardiovascular risks.

Time-domain HRV analysis and its association with periodontitis

Time-domain HRV parameters are well established markers of the autonomic nervous system function. They provide the crucial information of heart rate fluctuation over time, which is directly influenced by the balance between parasympathetic and sympathetic nervous activity. In the present study, time-domain

HRV parameters were used to estimate the degree of autonomic dysfunction in periodontitis patients.

Findings indicate that the SDNN value was statistically significant at $p=0.025$, signifying a drop in the periodontitis patient group as their periodontal condition worsened, which reflected a decrease in overall heart rate variability. Impaired cardiac autonomic responsiveness with increased sympathetic predominance and a loss of autonomic flexibility can be seen to be related to an increased risk of CVD.

In contrast, Mean RR intervals and RMSSD did not present with statistically significant correlations with periodontitis severity. However, values do follow a pattern of declining, and therefore, increasing periodontal disease severity is associated with poor short-term parasympathetic modulation of heart rate. Reduction in vagal tone raises the susceptibility to arrhythmias,

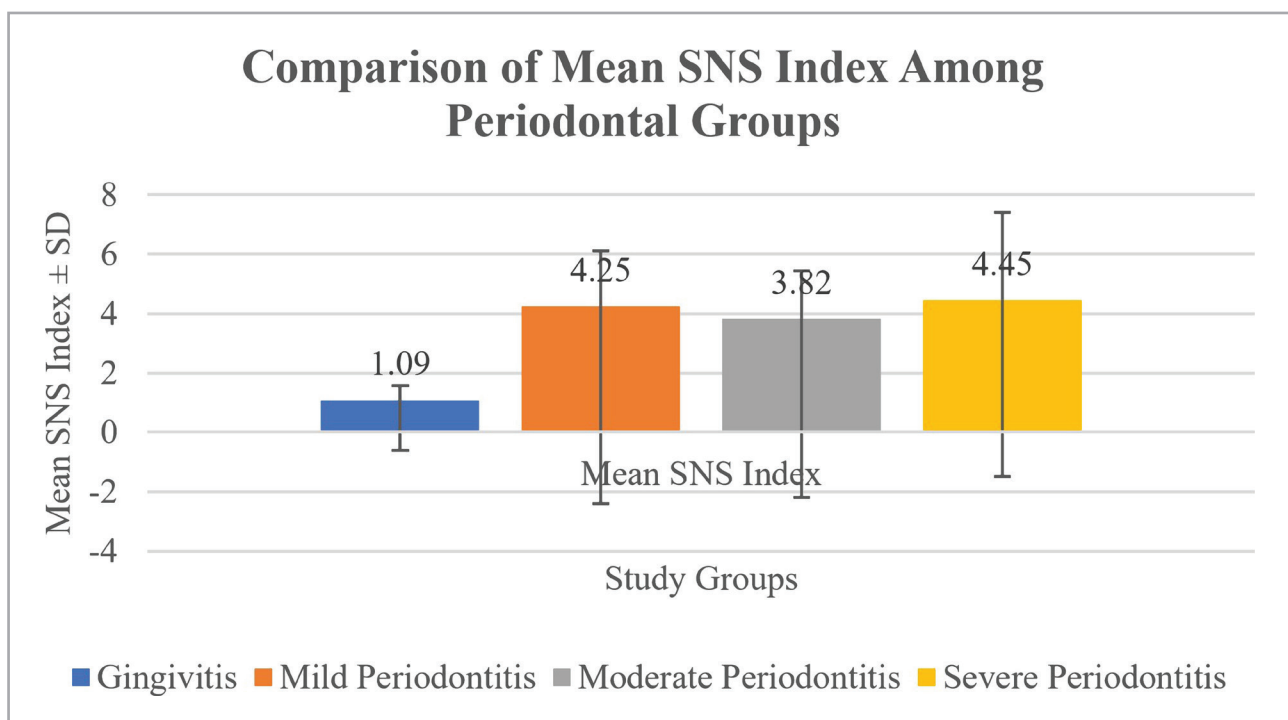


Figure 1: Comparison of mean SNS index among periodontal groups.

Table 4: Correlation between periodontitis and Frequency-Domain HRV parameters.

HRV parameter	Correlation (Rho)	p-value
LF/HF ratio	0.06	0.54
Power LF	-0.19	0.05 *
Power HF	-0.58	<0.001 ***
Power VLF	-0.24	0.02

Note: Power VLF reduction (p=0.02) confirms that periodontitis influences long-term autonomic modulation; * – Power LF reduction (p=0.05) suggests a loss of short-term autonomic regulation; *** – Power HF values (p<0.001) indicate a strong reduction in vagal control, correlating with parasympathetic suppression.

disturbances in blood pressure, and other cardiovascular complications (Table 5).

- *SDNN reduction and its implications:*

SDNN is the gold-standard marker of autonomic control. A reduction in periodontitis patients indicates that the cardiovascular system is less adaptable to physiological stressors. Low SDNN values are associated with higher cardiovascular morbidity and mortality, especially in the presence of inflammatory conditions like periodontitis.

- *Declining RMSSD and its association with vagal tone:*

RMSSD is an indicator of parasympathetic activity and short-term HRV changes. Although it was not statistically significant in this study, a negative correlation suggests that periodontitis patients experience reduced vagal activity, further supporting the hypothesis of autonomic imbalance and increased cardiovascular risk.

Taken together, these findings underscore the systemic impact of periodontitis, linking it to altered autonomic regulation and potential cardiovascular dysfunction

Correlation between periodontitis and stress index

In addition to time-domain and frequency-domain HRV parameters, this study also explored the relationship between periodontitis severity and autonomic stress index. The stress index is an HRV-derived

parameter that quantifies sympathetic overactivity, particularly in response to chronic inflammation and systemic stress.

The correlation between periodontitis and stress index was not statistically significant, at p=0.11, but showed a positive trend; therefore, patients with severe periodontitis may be at increased sympathetic dominance, which is probably caused by systemic inflammation, increased oxidative stress, and cytokine-mediated autonomic dysfunction. This trend fits with previous studies indicating that chronic inflammatory diseases lead to autonomic imbalance, thereby causing cardiovascular complications (Table 6).

Chronic inflammation as a driver of autonomic stress:

The positive correlation between CPI score, an index for periodontitis severity, and stress index was consistent with the hypothesis that chronic inflammatory diseases, like periodontitis, enhance autonomic stress. Although this association was not statistically significant, the trend indicates that periodontitis could induce minor but detectable alterations in autonomic control.

Mechanisms linking periodontitis to autonomic stress:

- Inflammatory cytokines (e.g., TNF- α , IL-6) activate the hypothalamic-pituitary-adrenal (HPA) axis leading to increased sympathetic activation and lower HRV;

Table 5: Correlation between HRV time-domain parameters and periodontitis.

HRV parameter	Correlation (Rho)	p-value
Mean RR (ms)	-0.06	0.57
Mean HR (bpm)	0.05	0.63
SDNN (ms)	-0.012	0.025 *
RMSSD (ms)	-0.11	0.28

Note: * – denotes significant p-value.

Table 6: Correlation between HRV stress index and CPI score.

Dependent variable	Stress index correlation (Rho)	p-value
CPI score	0.16	0.11

- Periodontal pathogens activate systemic endotoxemia initiating the autonomic stress response with disruption of cardiovascular homeostasis;
- The chronic pain and psychological distress which are a natural consequence of periodontitis, may also act to enhance sympathetic activity further driving the pathophysiological relationship of periodontitis with autonomic dysfunction.

Discussion

This study established a very significant relationship between periodontitis and cardiac autonomic dysfunction as suggested by the alterations in HRV. There was a progressive increase in the SNS index with a decrease in the PNS index, leading to a decrease in HRV and increasing the risk for cardiovascular disease with an increase in the severity of periodontitis. This is in agreement with the study by Fang SC et al. (2019), which indicated that low HRV is a strong predictor of cardiovascular mortality, underlining the role of autonomic imbalance in systemic disease [12].

Similarly, Amato M et al. (2025) found that chronic inflammation in periodontal disease exacerbates metabolic and cardiovascular dysfunction, reinforcing the hypothesis that periodontitis contributes to systemic health deterioration beyond the oral cavity [13]. Inflammation caused by periodontal pathogens, especially *Porphyromonas gingivalis*, has been associated with endothelial dysfunction, atherosclerosis, and cardiac autonomic dysregulation (Bhuyan R et al., 2022; Martínez-García M et al., 2021) [14, 15].

The present study further strengthens the evidence about the imbalance of autonomic activity in periodontitis patients with time and frequency HRV analysis. Reduced HF power or decreased parasympathetic activity and increased LF power or increased sympathetic activity are consistent with Segovia M et al. (2011), who found that periodontal disease-related autoantibodies change the β 1-adrenergic receptor function and lead to reductions in HRV and enhanced cardiovascular vulnerability [16]. Additionally, Pietropaoli D et al. (2023) demonstrated that HRV alterations in periodontitis pa-

tients mirror those found in hypertensive and diabetic individuals, suggesting a shared pathway of autonomic dysfunction [17]. Conversely, Irigoyen MC et al. (2012) noted that while autonomic impairment is common in type 2 diabetes and hypertension, its association with periodontitis remains underexplored, underscoring the need for more interdisciplinary research on oral-systemic connections [18].

This study further supports the correlation between periodontitis, stress, and HRV impairment by Gupta K et al. (2022), who demonstrated that dental procedures induce significant sympathetic activation, leading to transient cardiovascular risk [19]. Jamilian A et al. (2016) also reported that malocclusion treatment improved HRV and stress response, indicating that oral interventions can modulate autonomic function [20]. The findings of this study also resonate with those of Haque MM et al. (2022), who suggested that targeted periodontal therapy, combined with interventions to enhance parasympathetic tone, may restore autonomic balance and reduce cardiovascular burden [21]. However, Gheorghe DN et al. (2022) previously hypothesized that autonomic dysfunction in periodontitis patients might be secondary to metabolic disturbances rather than a direct effect of oral inflammation, a theory that requires further longitudinal validation [22].

The graded autonomic pattern was most evident in the composite indices. The mean PNS index fell from 0.55 ± 0.91 in participants with gingivitis to -0.98 ± 0.59 in those with severe periodontitis ($p < 0.001$), whereas the mean SNS index increased from 1.09 ± 0.60 to 4.45 ± 1.50 ($p < 0.001$). This reciprocal change is consistent with progressive vagal withdrawal and sympathetic predominance. The accompanying reduction in SDNN ($p = 0.025$) and the inverse correlation between HF power and periodontal severity (Spearman's $\rho = -0.58$, $p < 0.001$) further support an association between greater periodontal burden and diminished autonomic flexibility. These findings are clinically relevant because reduced HRV has been linked to adverse cardiovascular outcomes; nevertheless, the cross-sectional design does not establish causality or show that periodontal treatment will restore autonomic function.

Although the study is certainly in line with most available literature on oral-systemic health interactions, large-scale long-term studies are needed to really

help determine if periodontal treatment can restore some kind of balance in autonomic functions. Research for the future should focus on molecular markers of inflammation, neural modulation, and the effect of periodontal therapy on cardiovascular results. Vianello E *et al.* (2024) thus were able to suggest [23]. Considering the burden of global periodontitis and its systemic implications, incorporating HRV assessment in periodontal evaluations might increase the chances of early diagnosis and prevention strategies, thus improving patient care.

Conclusion

This study shows that periodontitis is associated with impaired cardiac autonomic regulation, with more pronounced dysfunction as periodontal disease becomes more severe. The findings indicate a shift toward sympathetic predominance, reduced parasympathetic influence, and loss of overall autonomic flexibility. The pattern observed across the heart rate variability measures supports a relationship between periodontal inflammation and an unfavorable cardiovascular autonomic profile, although not every measure changed consistently. These findings suggest that periodontal disease may have systemic consequences beyond the oral cavity and underline the importance of early periodontal assessment and management within cardiovascular risk prevention. As the cross-sectional design permits only an association to be identified, further longitudinal and interventional studies are needed to determine whether periodontal treatment can improve autonomic regulation and reduce cardiovascular risk.

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Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The study protocol was reviewed and approved by the Institutional Ethics Committee of SRM Medical College Hospital and Research Centre, SRM Institute of Science and Technology (SRMIST), Kattankulathur, Chengalpattu District, Tamil Nadu, India, on 23 October 2024 (Ethics Committee registration no. ECR/8934/INST/TN/2013/RR-19). The approval was granted for a period of three years. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Consent to participate

Written informed consent was obtained from all the participants.

References

1. Martínez-García M, Hernández-Lemus E. Periodontal Inflammation and Systemic Diseases: An Overview. *Front Physiol.* 2021;12:709438. Published 2021 Oct 27. doi:10.3389/fphys.2021.709438
2. Abdulkareem AA, Al-Taweel FB, Al-Sharqi AJB, Gul SS, Sha A, Chapple ILC. Current concepts in the pathogenesis of periodontitis: from symbiosis to dysbiosis. *J Oral Microbiol.* 2023;15(1):2197779. Published 2023 Apr 2. doi:10.1080/20002297.2023.2197779
3. Periodontal Disease in Adults (Age 30 or Older). *Nih.gov.* Published 2018. <https://www.nidcr.nih.gov/research/data-statistics/periodontal-disease/adults>
4. Nazir M, Al-Ansari A, Al-Khalifa K, Alhareky M, Gaffar B, Almas K. Global Prevalence of Periodontal Disease and Lack of Its Surveillance. *ScientificWorldJournal.* 2020;2020:2146160. Published 2020 May 28. doi:10.1155/2020/2146160
5. Wu Q, Zhang W, Lu Y, *et al.* Association between periodontitis and inflammatory comorbidities: The common role of innate immune cells, underlying mechanisms and therapeutic targets. *International Immunopharmacology.* 2024;128:111558. doi:<https://doi.org/10.1016/j.intimp.2024.111558>
6. Nguyen CM, Kim JW, Quan VH, Nguyen BH, Tran SD. Periodontal associations in cardiovascular diseases: The latest evidence and understanding. *J Oral BiolCraniofac Res.* 2015;5(3):203-206. doi:10.1016/j.jobcr.2015.06.008
7. Saliem SS, Bede SY, Cooper PR, Abdulkareem AA, Milward M, Abdullah BH. Pathogenesis of periodontitis – A potential role for epithelial-mesenchymal transition. *Japanese Dental Science Review.* 2022;58:268-278. doi:<https://doi.org/10.1016/j.jdsr.2022.09.001>
8. Bellocchi C, Carandina A, Montinaro B, *et al.* The Interplay between Autonomic Nervous System and Inflammation across Systemic Autoimmune Diseases. *Int J Mol Sci.* 2022;23(5):2449. Published 2022 Feb 23. doi:10.3390/ijms23052449

9. Ribeiro AB, Santos-Junior NN, Luiz JPM, et al. Cardiovascular and Autonomic Dysfunction in Murine Ligature-Induced Periodontitis. *Sci Rep*. 2020;10(1):6891. Published 2020 Apr 23. doi:10.1038/s41598-020-63953-1
10. Drury RL, Simonetti SA. Heart Rate Variability in Dental Science. *Front Med (Lausanne)*. 2019;6:13. Published 2019 Feb 6. doi:10.3389/fmed.2019.00013
11. Cutress TW, Ainamo J, Sardo-Infirri J. The community periodontal index of treatment needs (CPITN) procedure for population groups and individuals. *Int Dent J*. 1987;37(4):222-233.
12. Fang SC, Wu YL, Tsai PS. Heart Rate Variability and Risk of All-Cause Death and Cardiovascular Events in Patients With Cardiovascular Disease: A Meta-Analysis of Cohort Studies. *Biological Research For Nursing*. 2019;22(1):109980041987744. doi:https://doi.org/10.1177/1099800419877442
13. Amato M, Polizzi A, Viglianisi G, Leonforte F, Mascitti M, Isola G. Impact of Periodontitis and Oral Dysbiosis Metabolites in the Modulation of Accelerating Ageing and Human Senescence. *Metabolites*. 2025;15(1):35. Published 2025 Jan 9. doi:10.3390/metabol15010035
14. Bhuyan R, Bhuyan SK, Mohanty JN, Das S, Juliana N, Juliana IF. Periodontitis and Its Inflammatory Changes Linked to Various Systemic Diseases: A Review of Its Underlying Mechanisms. *Biomedicines*. 2022;10(10):2659. Published 2022 Oct 21. doi:10.3390/biomedicines10102659
15. Martínez-García M, Hernández-Lemus E. Periodontal Inflammation and Systemic Diseases: An Overview. *Front Physiol*. 2021;12:709438. Published 2021 Oct 27. doi:10.3389/fphys.2021.709438
16. Segovia M, Ganzinelli S, Reina S, Borda E, Sterin-Borda L. Role of anti- β 1 adrenergic antibodies from patients with periodontitis in cardiac dysfunction. *Journal of Oral Pathology & Medicine*. 2011;41(3):242-248. doi:https://doi.org/10.1111/j.1600-0714.2011.01090.x
17. Pietropaoli D, Cairo F, Citterio F, et al. Practical Guidelines for Patients with Hypertension and Periodontitis. *High Blood Press Cardiovasc Prev*. 2023;30(1):7-16. doi:10.1007/s40292-022-00553-2
18. Irigoyen MC, Casarini DE, Morris M, Montano N. Autonomic nervous system, inflammation, and diabetes: mechanisms and possible interventions. *Exp Diabetes Res*. 2012;2012:894157. doi:10.1155/2012/894157
19. Gupta K, Kumar S, AnandKukkamalla M, et al. Dental Management Considerations for Patients with Cardiovascular Disease-A Narrative Review. *Rev Cardiovasc Med*. 2022;23(8):261. Published 2022 Jul 20. doi:10.31083/j.rcm2308261
20. Jamilian A, Kiaee B, Sanayei S, Khosravi S, Perillo L. Orthodontic Treatment of Malocclusion and its Impact on Oral Health-Related Quality of Life. *The Open Dentistry Journal*. 2016;10(1):236-241. doi:https://doi.org/10.2174/1874210601610010236
21. Haque MM, Yerex K, Kelekis-Cholakis A, Duan K. Advances in novel therapeutic approaches for periodontal diseases. *BMC Oral Health*. 2022;22(1). doi:https://doi.org/10.1186/s12903-022-02530-6
22. Gheorghe DN, Camen A, Popescu DM, et al. Periodontitis, Metabolic and Gastrointestinal Tract Diseases: Current Perspectives on Possible Pathogenic Connections. *J Pers Med*. 2022;12(3):341. Published 2022 Feb 24. doi:10.3390/jpm12030341
23. Vianello E, Emanuela Galliera. New Molecular Mechanisms and Markers in Inflammatory Disorders. *International Journal of Molecular Sciences*. 2024;25(12):6506-6506. doi:https://doi.org/10.3390/ijms25126506