Received: 2 January 2021 | Revised: 3 March 2021 | Accepted: 4 March 2021

DOI: 10.1002/JPER.21-0004

JOURNAL OF Periodontology

ORIGINAL ARTICLE

Periodontitis and its higher levels of severity are associated with the triglyceride/high density lipoprotein cholesterol (TG/HDL-C) ratio

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Abstract

Background: Periodontitis and the Triglyceride/High Density Lipoprotein Cholesterol (TG/HDL-C) ratio have both been associated with cardiovascular disease, metabolic syndrome, and obesity. Additionally, the ratio is a possible substitute for predicting insulin resistance. This study investigated the association between periodontitis, its severity levels (exposures), and the TG/HDL-C ratio (outcome).

Methods: A cross-sectional study of public health service users in Brazil considered socioeconomic-demographic characteristics, lifestyle behavior, and general and oral health conditions. Anthropometric measurements and blood pressure were also measured. Systemic biomarker data were obtained, as well as assessment of periodontal diagnosis and its severity. The TG/HDL-C ratio was calculated using the serum triglyceride level over HDL cholesterol and the cut-off point, TG/HDL-C ≥2.3 serving as the cutoff indicting dyslipidemia. Logistic and linear regressions were used to statistically analyze the data.

Results: A total of 1011 participants were included, with 84.17% having periodontitis and 49.85% having a TG/HDL-C ratio ≥2.3. For individuals with periodontitis, the odds of TG/HDL-C ratio ≥2.3 were 1.47 times greater than in those without periodontitis ($OR_{Adjusted} = 1.47$, 95% CI: 1.02–2.14). Similar results were found for those with moderate and severe periodontitis, with a slight increase in the measurement magnitude with disease severity.

Conclusion: A positive relationship between periodontitis and the TG/HDL-C ratio ≥2.3 was found, suggesting a possible association with periodontal disease severity.

KEYWORDS
epidemiology, periodontal medicine, periodontitis, public health

1 | INTRODUCTION

Periodontitis is defined as a chronic, multifactorial, inflammatory disease driven by tooth-borne bacterial biofilms, resulting in a chronic, destructive and at times non-self-limiting inflammatory responses.[1] Periodontitis is influenced and modulated by numerous risk factors, and if not controlled results in periodontal attachment loss and alveolar bone resorption.[1,2]

Periodontitis, in its mild form, affects about 45% to 50% of adults, with 60% of adults over 65 years affected.[3] The most severe forms of periodontitis affects 11.2% of the global adult population and is considered the sixth most common disease worldwide, representing a significant economic, social and health care burden.[3] Periodontitis is a health outcome that is an example of worldwide social inequality.[3,4]

Over the last 5 decades, numerous epidemiological studies have shown that periodontitis is associated with many common chronic diseases related to aging and premature mortality,[5] such as cardiovascular diseases, cancer, respiratory diseases, cerebrovascular diseases/stroke, Alzheimer's disease and diabetes[5–9]

There is also evidence that periodontitis alters the profile of serum lipoproteins.[10,11] Periodontal inflammation results in release of inflammatory mediators into the bloodstream, which contributes to chronic, low-level systemic inflammation that can influence systemic health. Low density lipoprotein cholesterol and triglyceride levels are known to increase in response to inflammation, in contrast to HDL-C levels.[11,12] Previous studies suggest that the triglyceride/high density lipoprotein cholesterol ratio (TG/HDL-C) is strongly associated with cardiovascular disease, metabolic syndrome, obesity and is a simpler substitute marker for predicting insulin resistance[13–15]

Insulin resistance, characterized by reduced sensitivity of the body's cells to the actions of insulin, results in chronic complications of diabetes.[16–19] In addition, insulin resistance, which is closely related to obesity, is more common in individuals with type 2 diabetes mellitus, and an important cause of hyperglycemia.[19] It also causes an excessive flow of free fatty acids from adipose tissue into the bloodstream to directly impact the development of macrovascular complications such as cardiovascular diseases (CVD), in addition to increasing the production and release of very low density lipoprotein cholesterol in the liver, resulting in dyslipidemia.[16,18,20] Thus, the goal of this study was to investigate associations between periodontitis, its severity levels, and the TG/HDL-C ratio.

2 | MATERIALS AND METHODS

Individuals for this cross-sectional study were recruited from basic health units in the city of Feira de Santana, Bahia, Brazil, from 2017 to 2019. The research protocol was approved by the Ethics Committee of the State University of Feira de Santana and the study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2013.

All participants who met the eligibility criteria signed an Informed Consent Form. The inclusion criteria included individuals of both genders, over 18 years old and registered in basic health units. Individuals were excluded if:they were diagnosed with neoplasia, HIV, pregnancy, required antibiotic prophylaxis prior to periodontal examination, used anti-inflammatories in the previous 6 months before the examination, received prior periodontal treatment or used antibiotics 6 months before the examination.

2.1 | Calculation of the sample size

To calculate the minimum sample size, the following parameters were considered: confidence level of 95%, study power of 80%, 1:1 ratio between exposure and non-exposure to periodontitis. Thus, assuming a frequency of the worst condition of the TG/HDL-C ratio of 25.5% for the group not exposed to periodontitis and a frequency of 38.4% for the group exposed to periodontitis (with findings from a pilot study on the topic, not published), the minimum group size was determined to be 221, with an additional 20% added for possible loss of information. Thus, the total sample size was determined to be 508 individuals.

2.2 | Data collection procedures

Information on socioeconomic-demographic characteristics, lifestyle behavior and general and oral health conditions were obtained through interviews.

Serum biomarkers were obtained from medical records. Biomarkers included complete blood count, total cholesterol, low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), very low density lipoprotein cholesterol (VLDL-C), triglycerides, and fasting blood glucose. Individuals who had biomarkers collected more than three months after collection of clinical data were referred to the laboratory for retesting.

Body weight was obtained using an anthropometric digital scale*. The height was recorded directly using a wall-mounted stadiometer. The Body Mass Index (BMI) was calculated from the individuals' height and weight.[21] The waist circumference, midpoint between the iliac crest and the lower costal ridge, were measured with a measuring tape when the individual was erect, with a relaxed abdomen, with the arms at the sides and the feet together.[22]

Blood pressure (BP) was measured with a calibrated sphygmomanometer and stethoscope†. BP was measured three times, with a 1-minute pause between measurements, in a calm environment and with the participants correctly positioned. BP was calculated as the arithmetic mean of the last two measurements.[23]

The oral evaluation, performed by a calibrated dentist (I.S.G.F.), included periodontal clinical parameters from all teeth, with six sites per tooth: mesio-vestibular, mid-vestibular, disto-vestibular, mesio-lingual, medium-lingual, disto-lingual, except for the third molars. The following parameters, were obtained: the probing depth,[24] gingival recession,[25] clinical attachment level[25] and bleeding on probing.[26] Visible plaque was recorded at four sites (mesial, distal, buccal, palatal/lingual) per tooth.[26]

2.3 | Periodontitis and its severity levels

Using the periodontitis diagnostic criteria from the US Center for Disease Control and the American Academy of Periodontics (CDC/AAP) in the United States of America,[27,28] the participants were classified according to periodontitis severity (mild, moderate, severe periodontitis and without periodontitis). Individuals were also dichotomized as having no periodontitis or any periodontitis (mild, moderate, and severe).

2.4 | Dependent variable – triglyceride/high density lipoprotein cholesterol (TG/HDL-C) ratio

The TG/HDL-C ratio was obtained by determining the ratio of serum triglyceride and cholesterol-HDL values for each individual.[29] To obtain cut-off values, participants with metabolic syndrome were compared to the group without the syndrome. Receiver-operating characteristic (ROC) analysis was used to establish optimal cut-off values and according to the distribution of this continuous variable in the sample, the median TG/HDL-C ratio was selected as the cutoff point for classifying participants into group with TG/HDL-C ratio < 2.3 and group TG/HDL ratio-C ≥ 2.3, the latter category considered dyslipidemic.

2.5 | Independent covariables

The covariables were distributed according to a hierarchical level based on the theoretical model of social determination of health.[30] At the distal level, the socioeconomic characteristics were education level (in years of study), occupation (having a job or not/retired), family income (in minimum wages), household density (number of people in the household) and marital status (having a partner or not). At the intermediate level, the covariables were related to general and oral health conditions, and lifestyle behaviors. Covariables included the following diseases (yes or no—self-reported): arterial hypertension, diabetes mellitus, cardiovascular disease, liver disease, history of stroke, lung disease, kidney disease, systemic infection and metabolic syndrome.[31] BMI (< 25 kg/m^š or ≥ 25 kg/m^š and < 30 kg/m^š or ≥ 30 kg/m^š), waist circumference (< 102 or < 88 cm, or ≥ 102 or ≥ 88 cm, men and women, respectively)[31] and blood pressure (< 85 or < 130 mmHg, or ≥ 85 or ≥ 130 mmHg),[31] consultation with the dentist in the last year (yes or no), physical activity (yes or no), smoking habit (yes, smoker/ex-smoker, or not), and alcoholic beverage consumption (yes, drink/have drank or not). At the proximal level, demographic and health care information considered included: age (in years), race/skin color (white and non-white), sex (male and female), use of medication for cholesterol and triglyceride (yes or no), and flossing $\geq$ one time per day (yes or no).

2.6 | Statistical analysis

Descriptive analysis of periodontitis, its severity levels, and the TG/HDL-C ratio ≥ 2.3 was performed with simple and relative frequencies for categorical covariables and measurements of central tendency and dispersion for continuous ones, based on the normality distribution of covariables using Kolmogorov-Smirnov test. The degree of comparability between the groups, exposed and unexposed/outcome and non-outcome, was performed through bivariate analysis using Pearson's chi-square test, based on the normality distribution of covariables using Kolmogorov-Smirnov test, with a significance level of 5%.

The hierarchical analysis was performed after selecting the covariables with a significance level $\leq 20\%$ through bivariate analysis. The collinearity between the covariables was assessed using the variance matrix, using Pearson's correlation coefficient.

Initially, in block I – distal hierarchical level, the socioeconomic covariables were evaluated in the model, with those selected that had a $P \leq 0.20$. Then, in block II – intermediate hierarchical level, the covariables related to

lifestyle behavior and health condition were tested, and those covariables that had a $P \leq 0.20$ were also selected. Finally, for block III – proximal hierarchical level, the demographic covariables and those related health care information were tested, and those with a $P \leq 0.05$ value were selected for the final model. In all these stages, the epidemiological importance of the covariable in the association under study was also a criterion of choice.

Additionally, the association between periodontitis, its severity levels, and the TG/HDL-C ratio ≥ 2.3 was assessed by means of stratified analysis and logistic regression modeling, obtaining the crude and adjusted Odds Ratio (OR), their respective 95% confidence intervals (95% CI), with a 5% significance level. For this purpose, the following statistical models between oral disease and TG/HDL-C ratio ≥ 2.3 were used: without periodontitis versus periodontitis, without periodontitis versus mild periodontitis, without periodontitis versus moderate periodontitis, and without periodontitis versus severe periodontitis. Subsequently, multiple and simple linear regression was used with the calculation of the beta coefficient and its respective 95% CI.

The initial selection of confounding and modifying covariables was made based on a theoretical model of causality between the exposures and the outcome, also from the hierarchical level analysis. Thus, the following covariables were selected as confounding: educational level, smoking habit, consultation with the dentist in the last year, liver disease, fasting blood glucose, blood pressure, use of medication for cholesterol and triglyceride, age and sex. In addition, the maximum likelihood ratio test ($P < 0.05$) was used to analyze the effect-modifying covariables and the presence of confounding covariables was verified with the use of the backward strategy, the one that produced a change in the association measurement of at least 10%. In all stages, the Hosmer-Lemeshow test was used to assess the quality of the fit of the analysis model. The data analysis used version 15 of the statistical program STATA[‡].

3 | RESULTS

The final sample included 1011 participants, 332 men and 679 women, aged 18-89 years, (median age of 54 years – interquartile ranges of 43 and 65 years), mean ± standard deviation (SD) of 53.15 ± 14.63 years and with an occurrence of periodontitis of 84.17% (851). The TG/HDL-C ratio ranged from 0.11 to 15.23, median of 2.33, interquartile intervals of 1.52 and 3.54, and mean 2.79 ± 1.86. ROC analysis established optimal cut-off value of 2.38 (Supplementary file – Figure 1). The frequency of the TG/HDL-C ratio ≥ 2.3 was 49.85% (504).

Statistically significant differences ($P \leq 0.05$) were noted between the presence of periodontitis and the TG/HDL-C ratio ≥ 2.3 depending on age, education level, smoking habit, diabetes mellitus, hypertension, fasting blood glucose, diagnosis of metabolic syndrome, waist circumference and blood pressure (Tables 1 and 2). Covariables that differed ($P \leq 0.05$) only according to the exposure were current occupation, lung disease and systemic infection. Covariables that showed a difference only for the outcome were sex, skin color race, consultation with the dentist in the last year, liver disease and cardiovascular disease.

Total cholesterol and LDL-C showed a statistically significant difference ($P \leq 0.05$) when both the exposure groups and the outcome groups were compared (Tables 1 and 2). The TG/HDL-C ratio ≥ 2.3 was higher in participants with periodontitis ($P < 0.01$) compared to those without the disease. Likewise, the TG/HDL-C ratio ≥ 2.3 was significantly higher in individuals with moderate and severe periodontitis ($P \leq 0.05$) when compared to those without periodontitis (Table 2).

The association between periodontitis and the TG/HDL-C ratio ≥ 2.3, assessed through hierarchical analysis, remained positive and statistically significant at all levels assessed (Table 3). In block I, distal hierarchical level, the covariables education level, current occupation and household density were selected as confounders. The association measurement estimated that the odds that participants with periodontitis had a TG/HDL-C ratio ≥ 2.3 was 1.75 times greater than those without periodontitis: $OR_{adjusted} = 1.75$, 95% CI; 1.23-2.49. In block II, the covariable education level was incorporated with those of the intermediate hierarchical level such as smoking habit, alcoholic beverage consumption, consultation with the dentist in the last year, liver disease, cardiovascular disease, lung disease, systemic infection, waist circumference, history of stroke and fasting blood glucose. In this adjusted model, the odds of the TG/HDL-C ratio ≥ 2.3 in the group with periodontitis was 1.57 times higher compared to those without periodontitis: $OR_{adjusted} = 1.57$, 95% CI: 1.08-2.27. In block III, the final model, the covariables age, gender, race/skin color, flossing at least once a day and use of medication to control cholesterol and triglycerides were selected for the proximal hierarchical level and were incorporated into the previous model. In this case, the odds of the TG/HDL-C ratio ≥ 2.3 in those with periodontitis was 1.47 times higher than in those without periodontitis: $OR_{adjusted} = 1.47$, 95% CI: 1.02-2.14.

The covariable cardiovascular disease was also included in the final model, due to the epidemiological importance in the main association. The Hosmer-Lemeshow statistical test indicated good quality of the regression models.

The associations between the levels of moderate and severe severity of periodontitis and the TG/HDL-C ratio

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TABLE 1 Number (*n*) and percentage (%) of the main characteristics of the participants according to the presence of periodontitis

Characteristics	Periodontitis		
	No 160 (100%)	Yes 851 (100%)	*P**
Age			
≥54 years	48 (30.00)	465 (54.64)	<0.01
Sex			
Male	47 (29.38)	285 (33.49)	0.31
Race/Skin Color			
Black	138 (86.25)	718 (84.37)	0.54
Education level			
Up to 4 years of study	37 (23.13)	311 (36.55)	<0.01
Family income[a]			
<1 minimum wage	39 (24.38)	178 (20.92)	0.33
Household density			
More than three people per household	69 (43.13)	342 (40.19)	0.49
Current occupation			
Unemployed or Retired	79 (49.38)	283 (33.25)	<0.01
Marital status			
Without companion	76 (47.50)	399 (46.89)	0.89
Smoking habit (in the last 6 months)			
Yes	35 (21.88)	302 (35.49)	<0.01
Alcoholic beverage consumption (at least 3 times a week in the last 6 months)			
Yes	77 (48.13)	361 (42.42)	0.18
Physical activity (at least 3 times a week)			
No	100 (62.50)	565 (66.39)	0.34
Consultation with the dentist in the last year (at least one)			
No	70 (43.75)	393 (46.18)	0.57
Flossing at least once a day			
No	82 (51.25)	486 (57.46)	0.15
Diabetes Mellitus			
Yes	67 (41.88)	486 (57.11)	<0.01
Hypertension			
Yes	57 (35.63)	463 (54.41)	<0.01
Liver disease			
Yes	10 (6.25)	43 (5.05)	0.53
Lung Disease			
Yes	8 (5.00)	12 (1.41)	<0.01
Cardiovascular disease			
Yes	16 (10.00)	108 (12.69)	0.34
Kidney disease			
Yes	9 (5.63)	62 (7.29)	0.45
Systemic Infection			
Yes	14 (8.75)	27 (3.17)	<0.01
History of Stroke			

(Continues)

TABLE 1 (Continued)

Characteristics	Periodontitis		
	No 160 (100%)	Yes 851 (100%)	*P**
Yes	11 (6.88)	34 (4.00)	0.10
Body mass index			
≥ 30 kg/mš	36 (22.50)	209 (24.56)	0.23
≥ 25 and < 30 kg/mš	48 (30.00)	304 (35.72)	0.08
LDL cholesterol			
> 130 mg/dL	41 (25.62)	262 (30.79)	0.19
Total cholesterol			
> 190 mg/dL	60 (37.50)	399 (46.89)	0.03
Cholesterol and triglyceride medication			
Yes	11 (6.88)	68 (7.99)	0.63
Fasting blood glucose			
> 99 mg/dL	63 (39.38)	460 (54.05)	<0.01
Metabolic syndrome			
Yes	45 (28.13)	411 (48.30)	<0.01
Waist circumference			
≥ 102 or ≥ 88 cm	65 (40.63)	427 (50.18)	0.03
Blood pressure			
≥ 85 or ≥ 130 mmHg	77 (48.13)	537 (63.10)	<0.01

*P value = Statistical significance level: $P \leq 0.05$.

[a]Average value of the minimum wage at the time of data collection: R $ 963.00 (equivalent to US $ 274.36 in the period).

≥ 2.3 were then tested (Table 4). Crude and adjusted association measurements, both through logistic and linear regression, showed positive associations. The adjusted logistic regression models demonstrated that the odds of individuals with moderate periodontitis having a TG/HDL-C ratio ≥ 2.3 was 1.52 times higher than among those without periodontitis: $OR_{adjusted} = 1.52$, 95% CI; 1.03-2.25, and for participants with severe periodontitis of 1.57 times greater: $OR_{adjusted} = 1.57$, 95% CI; 1.03-2.37.

Multiple linear regression showed that both with the presence of periodontitis and with the increase in the level of severity of periodontitis, it was observed that there was an increase in the TG/HDL-C ratio ≥ 2.3. The individual having only the diagnosis of periodontitis showed an increase of 0.32 in the TG/HDL-C ratio ≥ 2.3 ($P = 0.04$). For the association between moderate periodontitis and TG/HDL-C ratio ≥ 2.3, an increase of 0.31 in the ratio value ($P = 0.05$) was noted. For participants diagnosed with severe periodontitis, the increase in the value of this ratio was 0.34 ($P = 0.05$). This analysis suggests a possible association between periodontitis severity and the TG/HDL-C ratio ≥ 2.3.

The Hosmer-Lemeshow statistical test was used to verify the goodness of fit for each model. The P value ranged from 0.37 to 0.57, revealing that the null hypothesis was rejected and indicating the good quality of the regression models employed.

4 | DISCUSSION

This study showed that periodontitis is positively associated with a TG/HDL-C ratio ≥ 2.3, corroborating the previous study of Kwon et al.,[32] conducted in Korea, using population data from the 2012-2014 Korean National Health and Nutrition Examination Survey – KNHANES. The present study also showed a positive association between periodontitis severity and the TG/HDL-C ratio ≥ 2.3.

The association of periodontitis with the TG/HDL-C ratio ≥ 2.3 may be relevant to the pathogenesis of cardiovascular diseases, metabolic syndrome, obesity and insulin resistance.[13–15] The TG/HDL-C ratio has been correlated with small, dense LDL-C, an atherogenic lipoprotein with high capacity to promote oxidative modifications.[33,34] Individuals having both periodontitis and TG/HDL-C ratio ≥ 2.3 may have an even greater risk for several important chronic diseases. When the levels of periodontitis are considered, the presence of moderate periodontitis added to this ratio a lower value (0.31) than that when the diagnosis of the periodontal condition was severe periodontitis

TABLE 2 Number (*n*) and percentage (%) of the main characteristics of the participants according to the presence of the triglyceride/high density lipoprotein cholesterol (TG/HDL-C) ratio

Characteristics	TG/HDL-C Ratio		
	<2.3507 (%)	≥ 2.3504 (%)	*P**
Age			
≥54 years	222 (43.79)	291 (57.74)	<0.01
Sex			
Male	147 (28.99)	185 (36.71)	0.01
Race/Skin Color			
Black	439 (89.59)	417 (82.74)	0.01
Education level			
Up to 4 years of study	156 (30.77)	192 (38.10)	0.01
Family income[a]			
<1 minimum wage	109 (21.50)	108 (21.43)	0.98
Household density			
More than three people per household	205 (40.43)	206 (40.87)	0.89
Current occupation			
Unemployed or Retired	187 (36.88)	175 (34.72)	0.47
Marital status			
Without companion	236 (46.55)	239 (47.42)	0.78
Smoking habit (in the last 6 months)			
Yes	150 (29.59)	187 (37.10)	0.01
Alcoholic beverage consumption (at least 3 times a week in the last 6 months)			
Yes	216 (42.60)	222 (44.05)	0.64
Physical activity (at least 3 times a week)			
No	338 (66.67)	327 (64.88)	0.55
Consultation with the dentist in the last year (at least one)			
No	208 (41.03)	255 (50.60)	<0.01
Flossing at least once a day			
No	274 (54.04)	297 (58.93)	0.12
Diabetes Mellitus			
Yes	239 (47.14)	314 (62.30)	<0.01
Hypertension			
Yes	218 (43.00)	302 (59.92)	<0.01
Liver disease			
Yes	18 (3.55)	35 (6.94)	0.01
Lung Disease			
Yes	9 (1.78)	11 (2.18)	0.64
Cardiovascular disease			
Yes	51 (10.06)	73 (14.48)	0.03
Kidney disease			
Yes	32 (6.31)	39 (7.74)	0.37
Systemic Infection			
Yes	17 (3.35)	24 (4.76)	0.26
History of Stroke			

(Continues)

TABLE 2 (Continued)

Characteristics	TG/HDL-C Ratio		
	<2.3507 (%)	≥ 2.3504 (%)	*P**
Yes	17 (3.35)	28 (5.56)	0.09
Body mass index			
≥ 30 kg/mš	114 (22.49)	131 (25.99)	0.18
≥ 25 and < 30 kg/mš	178 (35.11)	174 (34.52)	0.71
LDL cholesterol			
> 130 mg/dL	99 (19.53)	204 (30.48)	<0.01
Total cholesterol			
> 190 mg/dL	188 (37.08)	271 (53.77)	<0.01
Cholesterol and triglyceride medication			
Yes	21 (4.14)	58 (11.51)	<0.01
Fasting blood glucose			
> 99 mg/dL	211 (41.62)	312 (61.90)	<0.01
Metabolic syndrome			
Yes	129 (25.44)	327 (64.88)	<0.01
Waist circumference			
≥ 102 or ≥ 88 cm	229 (45.17)	263 (52.18)	0.03
Blood pressure			
≥ 85 or ≥ 130 mmHg	278 (54.83)	340 (67.46)	<0.01
Periodontitis			
Yes	407 (80.28)	444 (88.10)	<0.01
Mild Periodontitis			
Yes	2 (0.39)	–	–
Moderate Periodontitis			
Yes	238 (46.94)	253 (50.20)	<0.01
Severe Periodontitis			
Yes	167 (32.94)	191 (37.90)	<0.01

*P value = Statistical significance level: $P \leq 0.05$.

[a]Average value of the minimum wage at the time of data collection: R $ 963.00 (equivalent to US $ 274.36 in the period).

(0.34), further a possible association with disease severity, to be investigated in future.

There is evidence that individuals with periodontitis release inflammatory mediators from periodontal tissues into the bloodstream, capable of generating low-intensity systemic inflammation, influencing systemic health.[7] This systemic inflammation interferes with the increase in LDL-C and triglyceride levels, in contrast to the decrease in HDL-C levels.[12] These lipoprotein and lipid changes affect numerous processes that promote lipolysis and positive regulation of circulating triglycerides that contribute to a severe pro-inflammatory state, changes in inflammatory responses to the challenge of the periodontal pathogen and affect immune functions at different stages by various mechanisms.[35,36]

The relationship of TG/HDL-C ratio and periodontitis to insulin resistance may contribute to systemic outcomes, since it is common in individuals diagnosed with diabetes mellitus, metabolic disorders, obesity, and is an important causal factor of hyperglycemia.[16] In this condition, host cells have reduced sensitivity to the actions of insulin. Insulin resistance is also a causal factor in the excessive flow of free fatty acids from adipose tissue into the bloodstream, resulting in dyslipidemia and the development of cardiovascular disease.[16] In addition, insulin resistance reduces the production of some protective enzymes, favoring increased leukocyte adhesion to endothelial cells and resulting in increased vasoconstriction, inflammation and procoagulant changes, which in turn favors the development of atherosclerotic lesions, the main cause of cardiovascular diseases.[17,18,20,37] The actions of insulin resistance also cause damage to microvascular endothelial cells with impairments in angiogenesis and vasoreactivity.[19]

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TABLE 3 Hierarchical analysis of the association between periodontitis and triglyceride/high density lipoprotein cholesterol (TG/HDL-C) ≥ 2.3 ratio

Covariables according to the hierarchical level	Periodontitis x TG/HDL-C ≥ 2.3 ratio		
	Odds ratio (95% confidence interval)	*P**	Model quality[a]
Block I - DISTAL LEVEL	1.75 (1.23-2.49)[b]	<0.01	0.51
Education level: up to 4 years of study	1.32 (1.02-1.73)	0.04	
Current occupation: unemployed or retired	0.97 (0.75-1.27)	0.84	
Household density: > 3 people per household	1.03 (0.80-1.33)	0.81	
Block II - INTERMEDIATE LEVEL	1.57 (1.08-2.27)[c]	0.02	0.40
Education level: up to 4 years of study	1.16 (0.88-1.52)	0.31	
Smoking habit: yes	1.28 (0.96-1.70)	0.09	
Alcoholic beverage consumption: yes	0.97 (0.74-1.28)	0.84	
Consultation with the dentist in the last year: yes	0.68 (0.53-0.88)	<0.01	
Liver disease: yes	1.84 (0.99-3.40)	0.06	
Cardiovascular disease: yes	1.30 (0.86-1.97)	0.21	
Lung disease: yes	0.92 (0.35-2.41)	0.86	
Systemic infection: yes	1.13 (0.56-2.25)	0.73	
Waist circumference: ≥ 102 or ≥ 88 cm	1.30 (1.01-1.68)	0.05	
Stroke history: yes	1.35 (0.70-2.62)	0.37	
Fasting blood glucose : > 99 mg/dL	2.11 (1.63-2.74)	<0.01	
Block III - PROXIMAL LEVEL	1.47 (1.02-2.14)[d]	0.04	0.62
Education level: up to 4 years of study	1.09 (0.82-1.46)	0.55	
Smoking habit: yes	1.14 (0.86-1.51)	0.37	
Consultation with the dentist in the last year: yes	0.68 (0.52-0.88)	<0.01	
Liver disease: yes	1.82 (1.01-3.32)	0.05	
Cardiovascular disease: yes	1.22 (0.82-1.83)	0.33	
Waist circumference: ≥ 102 or ≥ 88 cm	1.50 (1.12-2.00)	0.01	
Fasting blood glucose : > 99 mg/dL	1.88 (1.43-2.46)	<0.01	
Age: ≥ 54 years	1.27 (0.96-1.67)	0.10	
Male	1.57 (1.15- 2.13)	<0.01	
Race/skin color: black	0.86 (0.60-1.24)	0.43	
Flossing at least once a day: no	1.11 (0.85-1.45)	0.44	
Use cholesterol and triglyceride medication: yes	2.29 (1.34-3.92)	<0.01	

**P* value: significance level ≤ 0.05.

[a]Hosmer-Lemeshow to assess the goodness of fit for the final model; .

[b]Adjusted model for the covariables in the same block plus covariables belonging to the previous levels.

[c]Adjusted model for the covariables in the same block plus covariables belonging to the previous levels.

[d]Adjusted model for the covariables in the same block plus covariables belonging to the previous levels.

TABLE 4 Logistic regression analysis, with crude and adjusted association measurement, 95% confidence interval (95% CI), and simple and multiple linear regression analysis, with the beta coefficient, 95% CI, of the association between periodontitis, moderate periodontitis, severe periodontitis and triglyceride/high density lipoprotein cholesterol (TG/HDL-C) ≥ 2.3 ratio

ANALYSIS MODEL	Crude odds ratio (95% CI)	*P**	Adjusted odds ratio (95% CI)	*P**	Beta coefficient (95% CI)	*P**	Adjusted beta coefficient (95% CI)	*P**
Periodontitis and TG/HDL-C ≥ 2.3	1.81 (1.28-2.57)	<0.01	1.50 (1.03-2.17)[a]	0.03	0.51 (0.20-0.83)	<0.01	0.32 (0.01-0.63)[b]	0.04
Moderate periodontitis and TG/HDL-C ≥ 2.3	1.77 (1.23-2.55)	<0.01	1.52 (1.03-2.25)[b]	0.03	0.47 (0.15-0.80)	<0.01	0.31 (0.01-0.63)[b]	0.05
Severe periodontitis and TG/HDL-C ≥ 2.3	1.91 (1.30-2.80)	<0.01	1.57 (1.03-2.37)[b]	0.04	0.58 (0.24-0.93)	<0.01	0.34 (0.01-0.69)[b]	0.05

**P* value: significance level ≤ 0.05.

[a]Adjusted by education level, smoking habit, consultation with the dentist in the last year, liver disease, fasting blood glucose, blood pressure, use of cholesterol and triglyceride medication, age and sex.

[b]Adjusted by education level, smoking habit, consultation with the dentist in the last year, liver disease, fasting blood glucose, use of cholesterol and triglyceride medication, age and sex; *P* value for the model fit test: Periodontitis and TG/HDL-C ($P = 0.57$); Moderate periodontitis and TG/HDL-C ($P = 0.51$); Severe periodontitis and TG/HDL-C ($P = 0.37$).

Association investigations using TG/HDL-C ratio has been addressed in several previous studies in adults, young people and children.[13,14,38–42] In these investigations, this ratio was associated with an increased risk of cardiovascular disease, extension of coronary heart disease, insulinemia, insulin resistance, cardiometabolic risk, obesity, and severity of sickle cell anemia.

Thus, the results of the present study represent important findings for health, and they have good internal validity. The study's strengths include the examination of the periodontal condition, which was performed by assessing all the teeth present, avoiding classification errors such as underestimation of periodontitis.[28] In addition, the criteria used to define periodontitis and its severity levels is recognized worldwide, which allows for comparisons between studies.[27,28] Another strength of the present study is the hierarchical analysis for the evaluation of the main association, as careful selection of confounding covariables, both based on statistical tests and through the construction of a theoretical-conceptual model improves measurement accuracy.[43,44]

It is known that age, sex, smoking habit, glycemic level, arterial hypertension and use of medication for dyslipidemia are factors that interfere when associating periodontitis with outcomes such as the TG/HDL-C ratio.[32] In addition, the number of visits to the dentist for treatment and prevention of oral disease,[45] as well as liver disease[46] has an influence on studied conditions. Finally, the confounding level of education, since the lower the number of years of study, the occurrence of both the exposure and the outcome is greater.[47,48]

The cross-sectional study design is a limitation of this investigation, since it does not allow the evaluation of the temporal connection between periodontitis exposure and the outcome, the TG/HDL-C ratio ≥ 2.3. Cross-sectional study design does not permit inferences to be made of causality and directionality between exposure and outcome; however, it is a relevant hypothesis generator for future investigations. Another limitation of the study is the number of participants that made it mandatory to reduce the number of confounders selected for the multiple analysis, avoiding over-adjustment, in the associations between the severity levels of periodontitis, moderate and severe, and the TG/HDL-C ratio ≥ 2.3, as well as preventing the estimate of the association measurement for the group with mild periodontitis. Likewise, subgroup analysis by gender could not be performed, as the power of the study would be compromised. Finally, other factors not considered, such as genetics, may have introduced residual confounding.[49] Nevertheless, the results are applicable to individuals having general conditions similar to the population that the sample of the present study represents.

5 | CONCLUSION

The findings of this study showed a positive association between both moderate and severe periodontitis and a TG/HDL-C ratio ≥ 2.3. These results reinforce an association of periodontitis with the TG/HDL-C ratio. Since the TG/HDL-C ratio can be easily determined from conventional blood analyses, additional longitudinal studies can assess the effect of periodontal therapy on this outcome. Such studies will determine if periodontal therapy would assist in the control, prevention and early treatment of atherogenic and metabolic diseases.

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Notes

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ACKNOWLEDGMENTS

Thanks to the undergraduate and graduate students who assisted the data collection, especially. Our special thanks to Samilly Miranda, Josicélia Batista, Sarah Conceição, Marcela Moreira and Michelle Oliveira.

CONFLICT OF INTEREST AND FINANCIAL DISCLOSURE

The authors also declare no conflicts of interest related to the study.

Financial support for this research was provided by the Research Support Foundation of the State of Bahia (FAPESB), Salvador, Bahia, Brazil; The National Council for Scientific and Technological Development (CNPq), Brasilia, Brazil, and Feira de Santana State University, Bahia, Brazil.

AUTHOR CONTRIBUTIONS

All authors contributed equally to this manuscript.

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Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Gomes-Filho IS, Santos PNP, Cruz SS, et al. Periodontitis and its higher levels of severity are associated with the triglyceride/high density lipoprotein cholesterol (TG/HDL-C) ratio. *J Periodontol*. 2021;1-13.