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Measurement of atherosclerosis markers in individuals with periodontitis

Angar Soronzonbold [1,*,†], **Erkhbilguun Munkhkherlen** [1,*,†], **Khongorzul Batchuluun** [2,3], **Oyun-Enkh Puntsag** [4], **Uurtuya Shuumarjav** [3,5], **Bayarchimeg Batbayar** [4]

[1]School of Dentistry, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia
[2]Department of Histology, School of Biomedicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia
[3]Institute of Biomedical Sciences, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia
[4]Department of Periodontics and Endodontics, School of Dentistry, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia
[5]Department for Graduate Education Policy and Management, Graduate School, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia

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***Correspondence:**
Angar Soronzonbold
School of Dentistry, Mongolian National University of Medical Sciences, Zorig Street, Ulaanbaatar 14210, Mongolia.
Email: pmm17d011@st.mnums.edu.mn
Tel: +976-86061676
Fax: +976-(11)321249

Erkhbilguun Munkhkherlen
School of Dentistry, Mongolian National University of Medical Sciences, Zorig Street, Ulaanbaatar 14210, Mongolia.
Email: pmm17d052@st.mnums.edu.mn
Tel: +976-88750217
Fax: +976-(11)321249

[†]These authors contributed equally to this work as first authors.

ABSTRACT

Purpose: The inflammatory response due to inflammatory cytokines, bacterial pathogens, and the altered lipoprotein metabolism in patients with periodontitis indicates that infection with periodontal anaerobic bacteria may influence atherogenesis *in vitro* and *in vivo*. We aimed to explore the effect of periodontitis concerning clinical and ultrasound markers of early atherosclerosis.
Methods: In this case-control study, a total of 30 systemically healthy adults (15 with periodontitis and 15 without periodontitis) over 40 years of age were studied. Periodontitis was determined by measuring the clinical attachment level (CAL) and radiographic bone loss (RBL). Conventional cardiovascular risk factors, including body mass index, serum levels of total cholesterol (TCH), triglycerides (TG), and high-density and low-density lipoprotein (HDL and LDL, respectively) cholesterol were evaluated. Carotid artery intima-media thickness (IMT) was measured using ultrasonography.
Results: The mean values of the CAL and carotid IMT were 5.02±0.9 mm and 0.084±0.01 cm vs. 1.6±0.61 mm and 0.072±0.02 cm in the periodontitis and healthy groups, respectively, reflecting statistically significant differences (P=0.001 and P=0.037, respectively). There were statistically significant differences in the serum levels of TCH, TG, and LDL between the 2 groups (P=0.017). The CAL and RBL were positively associated with carotid IMT and serum cholesterol levels, except for HDL, whereas tooth loss was not associated with any markers (P<0.05). Compared to the healthy group, participants with periodontitis exhibited 2.09 times higher odds (95% confidence interval, 1.22–3.59) of having subclinical atherosclerosis.
Conclusions: The presence of periodontitis increased the risk of atherosclerosis.

Keywords: Alveolar bone loss; Atherosclerosis; Carotid intima-media thickness; Chronic periodontitis; Periodontal attachment loss

ORCID iDs
Angar Soronzonbold
https://orcid.org/0000-0002-8195-0248
Erkhbilguun Munkhkherlen
https://orcid.org/0000-0002-6733-0456
Khongorzul Batchuluun
https://orcid.org/0000-0001-6176-9313
Oyun-Enkh Puntsag
https://orcid.org/0000-0002-8216-3289
Uurtuya Shuumarjav
https://orcid.org/0000-0002-9951-2457
Bayarchimeg Batbayar
https://orcid.org/0000-0001-8826-7989

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

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INTRODUCTION

Periodontitis is an inflammatory condition that negatively affects the tooth-supporting tissues, including gingiva, periodontal ligaments, and alveolar bone. It is one of the main causes of tooth loss [1]. The etiology and pathophysiology of periodontitis are complex. At the microbial level, a dramatic shift from a symbiotic microenvironment to a dysbiotic microbial community leads to a dysregulated host immune response or local inflammation. In parallel, genetic and environmental factors, as well as systemic health status, also play roles in the pathogenesis of periodontitis through an altered immune response [2]. The prevalence of periodontitis was reported to be 71.1% in the Mongolian population, according to the National Oral Health Survey in 2013 [3].

Atherosclerosis, the central pathology of cardiovascular diseases, is a chronic inflammatory disease that is mainly characterized by fibrotic plaques in arterial blood vessels [4]. The traditional risk factors of atherosclerosis include age, family history, gender, smoking, hypercholesterolemia, elevated low-density lipoprotein (LDL) cholesterol, diabetes mellitus, and hypertension [5]. Numerous case-control, cross-sectional, and cohort studies have suggested that periodontal disease is related to cardiovascular disease, including atherosclerosis [6-9]. One recent study revealed an increased stroke risk in people with severe periodontitis [8]. The inflammatory response due to inflammatory cytokines and bacterial pathogens, as well as altered lipoprotein metabolism in periodontitis patients, suggests that infection with periodontal Gram-negative, anaerobic bacteria may influence atherogenesis *in vitro* and *in vivo* [10]. Furthermore, clinical studies have suggested that periodontal treatment has positive effects on atherosclerosis markers and attenuates systemic inflammation [11]. In addition, a recent study suggested that improvements in the periodontal condition were associated with reduced progression of carotid atherosclerosis [12].

The carotid intima-media thickness (IMT) is a widely used and clinically validated marker of atherosclerosis [13]. A study reported that the adjusted mean carotid IMT increased with the severity of periodontitis among Korean adults [14]. Although several studies have reported an association between increased IMT and periodontal disease, there is limited evidence in people with normal body mass index (BMI) or Mongolians.

Therefore, the objectives of the present study were to evaluate the clinical markers of atherosclerosis, including carotid IMT, and to determine the relationship between periodontal status and atherosclerosis markers.

MATERIALS AND METHODS

Study population and selection criteria

The study population consisted of patients from the Central Dental Hospital of the Mongolian National University of Medical Sciences. Participants provided written informed consent according to the Declaration of Helsinki, 2013. Over 3 months (from December 2021 to February 2022), 15 systemically healthy patients with periodontitis and 15 systemically healthy adults without periodontitis were included in the study.

The inclusion criteria for healthy people included: 1) >40 years of age, 2) >16 teeth present in the mouth, and 3) no history of tooth extraction due to periodontitis. The inclusion criteria

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for periodontitis patients included: 1) >40 years of age, 2) >16 teeth present in the mouth, and 3) a clinical attachment level (CAL) of >3 mm at more than 10 sites regardless of periodontal pocket depth. The exclusion criteria comprised: 1) the presence of known systemic disease, 2) regular medication use or pregnancy, and 3) systemic antibiotic treatment and a history of any type of periodontal treatment within the previous 3 months.

Questionnaire and anthropometric measurements

The participants answered a questionnaire concerning health issues, medication use, past dental history, smoking, and education. None of the participants reported any known diabetes or cardiovascular disease. BMI values were calculated by dividing weight (in kg) by height squared (m^2).

Assessment of periodontal status

A single trained dentist examined the number of teeth in each patient. Next, the dentist measured CAL with a manual probe (University of North Carolina 15) at 6 points in 6 index teeth (buccal-mesial, mid-buccal, buccal-distal, lingual-mesial, mid-lingual, and lingual-distal); these measurements were made on upper first molars (#16, 26) or second molars (#17, 27), a central or lateral incisor (#12, 11, 21, 22), the lower first molars (#36, 46) or second molars (#37, 47), and a central or lateral incisor (#32, 31, 41, 42) [15]. An adjacent tooth was selected if the index tooth was missing.

The radiographic bone loss (RBL) of alveolar bone was assessed by dentists using panoramic radiographs taken using a digital panoramic tomography machine (Pax-Primo, Vatech Global, Seoul, Korea). RBL, defined as a 2-mm distance from the most coronal portion of the alveolar bone crest to the cementoenamel junction, was measured on the mesial and distal sides of all present teeth [16].

Determination of atherosclerosis markers

Blood pressure was measured using a calibrated aneroid sphygmomanometer, and the average of 2 measurements was used for the analysis. Serum levels of triglycerides (TG), high-density lipoprotein (HDL) and LDL, and total cholesterol (TCH) were assessed using standardized biochemical tests. IMT measurements were obtained from the right common carotid artery (CCA). All ultrasound examinations were performed by a trained radiologist using an ultrasound system (PT5200 Portable Color Doppler Ultrasound Scanner, Perlong, Nanjing, China) with a 5- to 12-MHz linear transducer. The patient was examined in the supine position with the head slightly hyperextended and tilted 45° to the left. The IMT measurements were obtained on the posterior wall of the right and left CCA along a 1-cm section proximal to the bifurcation. The IMT was defined as the distance from the leading edge of the lumen-intima interface to the leading edge of the media-adventitia interface [17]. Two measurements were taken in the selected area, and the maximum IMT was recorded. The cut-off value for increased IMT was calculated as 0.754 mm [18].

Statistical analysis

A descriptive analysis was conducted for each variable. The Shapiro-Wilk test was used for assessing the distribution of continuous variables. The Student's *t*-test was used for 2 independent samples to analyze quantitative variables. Associations among the different quantitative variables were evaluated using Pearson correlation coefficients. Odds ratios (ORs) and confidence intervals (CIs) were calculated with exact conditional logistic regression. SPSS version 22.0 (IBM Corp., Armonk, NY, USA) was used to perform statistical analyses. A *P* value <0.05 was considered to indicate statistical significance.

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RESULTS

Subject characteristics

Fifteen patients aged 40 to 54 years (11 women and 4 men) with chronic periodontitis, and 15 systemically healthy controls aged 39 to 49 years (13 women and 3 men) were included in this study. No significant differences were observed among the groups regarding age, gender, smoking status, BMI, and systolic or diastolic blood pressure (P>0.05) (**Table 1**).

Evaluation of periodontal status and atherosclerosis markers

The periodontal parameters (including CAL, RBL, and the total number of missing teeth) and serum levels of TG, TCH, and LDL cholesterol were significantly higher in patients with periodontitis than in healthy individuals (P<0.05) (**Tables 2** and **3**). However, a statistically significant difference in the level of HDL was not found (P>0.05) (**Table 3**). The IMT of the carotid artery was approximately 0.1 mm greater in the periodontitis group than in the healthy group (P<0.05) (**Figure 1**).

Correlation between periodontal status and atherosclerosis markers

Serum levels of TG, TCH, LDL cholesterol, and IMT were positively associated with CAL and RBL (P<0.05). While the number of missing teeth was not significantly correlated with cholesterol levels and IMT (P>0.05) (**Tables 4** and **5**), the CAL and RBL were found to have ORs of 2.09 (P=0.007; 95% CI, 1.22–3.59) and 1.19 (P=0.008; 95% CI, 1.05–1.35) for increased IMT (**Table 6**).

Table 1. Characteristics of chronic periodontitis and healthy individuals

Parameter	Periodontitis patients (n=15)	Healthy individuals (n=15)	*P* value
Age (yr)	47.67±6.25	44±5.27	0.093
Gender (men/women)	4/11	2/13	0.55
Smoker	5	2	0.36
BMI (kg/m^2)	26.52±1.92	25.34±1.63	0.084
SBP (mmHg)	121.07±5.16	116.08±9.36	0.29
DBP (mmHg)	77.67±10.51	80.02±10.66	0.54

Values are presented as mean ± standard deviation.
BMI: body mass index, DBP: diastolic blood pressure, SBP: systolic blood pressure.

Table 2. Periodontal parameters in the study groups

Parameter	Periodontitis patients (n=15)	Healthy individuals (n=15)	*P* value
CAL (mm)	5.03±0.92	1.60±0.61	0.001[a]
RBL (%)	38.97±8.91	23.50±6.12	0.001[a]
No. of missing teeth	5.67±4.27	1.40±0.08	0.007[a]

Values are presented as mean ± standard deviation.
CAL: clinical attachment level, RBL: radiographic bone loss.
[a]Statistically significant difference between the study groups.

Table 3. Serum cholesterol levels

Parameter	Periodontitis patients (n=15)	Healthy individuals (n=15)	*P* value
Triglycerides (mmol/L)	1.38±0.87	0.74±0.35	0.013[a]
Total cholesterol (mmol/L)	5.5±1.02	4.68±0.96	0.031[a]
LDL (mmol/L)	3.14±0.76	2.28±0.66	0.003[a]
HDL (mmol/L)	1.54±0.41	1.67±0.28	0.313

Values are presented as mean ± standard deviation.
LDL: low-density lipoprotein, HDL: high-density lipoprotein.
[a]Statistically significant difference between the study groups.

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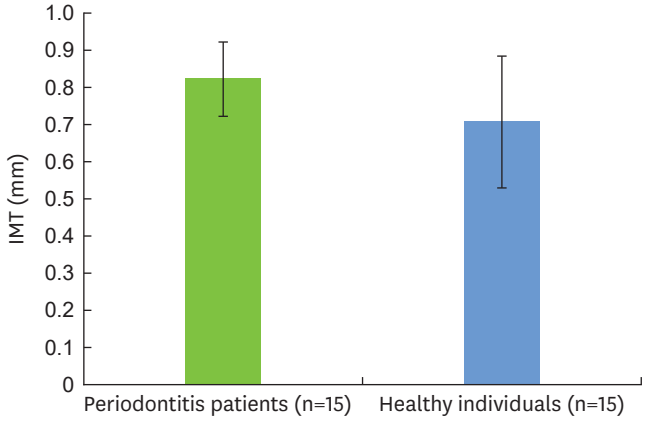

Figure 1. Carotid IMT in the study groups.
IMT: intima-media thickness.

Table 4. Correlation between periodontal parameters and serum cholesterol levels

Parameter	Triglycerides (mmol/L)	Total cholesterols (mmol/L)	LDL (mmol/L)	HDL (mmol/L)
CAL (mm)	0.42[a)]	0.51[a)]	0.61[a)]	−0.08
RBL (%)	0.36[a)]	0.46[a)]	0.51[a)]	−0.12
No. of missing teeth	0.09	0.35	0.21	0.28

CAL: clinical attachment level, HDL: high-density lipoprotein, RBL: radiographic bone loss, LDL: low-density lipoprotein.
[a)]Statistically significant correlation.

Table 5. Correlation between periodontal parameters and serum cholesterol levels

Parameter	IMT (mm)	*P* value
CAL (mm)	0.39[a)]	0.03
RBL (%)	0.42[a)]	0.02
No. of missing teeth	0.12	0.53

CAL: clinical attachment level, IMT: intima-media thickness, RBL: radiographic bone loss.
[a)]Statistically significant correlation.

Table 6. ORs for the relationships of demographic characteristics, cholesterol levels, and periodontal parameters with increased intima-media thickness

Parameter	OR (95% CI)	*P* value
Age (yr)	1.15 (0.96–1.38)	0.13
BMI (kg/m^2)	1.41 (0.90–2.18)	0.129
Triglycerides (mmol/L)	4.19 (0.84–20.79)	0.079
Total cholesterol (mmol/L)	1.49 (0.71–3.15)	0.3
LDL (mmol/L)	2.82 (0.94–8.47)	0.065
HDL (mmol/L)	0.20 (0.02–2.19)	0.19
CAL (mm)	2.09 (1.22–3.59)	0.007[a)]
RBL (%)	1.19 (1.05–1.35)	0.008[a)]
No. of missing teeth	1.41 (0.90–2.22)	0.14

BMI: body mass index, CAL: clinical attachment level, CI: confidence interval, HDL: high-density lipoprotein, LDL: low-density lipoprotein, OR: odds ratio, RBL: radiographic bone loss.
[a)]Statistically significant.

DISCUSSION

In this study, we evaluated clinical markers of atherosclerosis, including the serum levels of TG, TCH, LDL cholesterol, HDL cholesterol, and carotid IMT in patients with and without periodontitis. During periodontitis, local pro-inflammatory cytokines, produced by neutrophils and macrophages, including tumor necrosis factor, interleukin-1, and interleukin-6, can induce an acute-phase response in the liver by entering the systemic

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circulation, resulting in altered lipid metabolism [19]. This provides a scientific basis for the increased risk of atherosclerosis in patients with periodontitis.

Recent studies have shown that periodontitis and atherosclerosis have common pathogenic risk factors, including age, smoking, and diabetes mellitus. It has been suggested that avoiding smoking and reducing insulin resistance could benefit both conditions [20]. In a study conducted by Zeng et al. [21], patients with both type 2 diabetes and periodontitis were shown to have a higher incidence of carotid atherosclerosis.

The present study showed that the serum levels of TG, TCH, and LDL were elevated in subjects with chronic periodontitis, indicating that hyperlipidemia was significant in conditions of periodontitis. Previous studies have also reported that TG and LDL cholesterol levels were higher in periodontitis subjects [10, 12, 13]. Similarly, a study by Griffiths and Barbour [22] found that subjects with periodontitis had changes in their lipoprotein profiles. These results support the proposal that patients with chronic periodontitis are more susceptible to hyperlipidemia.

This study revealed that the adjusted mean IMT of the carotid artery was higher in chronic periodontitis patients. An abnormally increased IMT may represent a state of subclinical atherosclerosis and peripheral arterial disease [14]. According to the American Heart Association, an IMT value of more than 1.0 mm is regarded as abnormal. Previous studies have found that individuals with severe periodontitis are more likely to have subclinical atherosclerosis, due to elevated cholesterol levels and increased IMT.

In conclusion, this study suggests that the presence of chronic periodontitis may increase the risk of atherosclerosis by elevating the cholesterol levels and the IMT, independent of age, gender, and BMI.

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