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"ASSESSMENT OF ATHEROSCLEROSIS INDICATORS IN INDIVIDUALS WITH PERIODONTITIS: A CASE-CONTROL INVESTIGATION"

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Background: It is suggested that periodontitis contributes to vascular inflammation, which accelerates the development of atherosclerosis. This study investigates the impact of periodontitis on clinical and ultrasound markers of carotid atherosclerosis.

Methods: The study involved 60 systemically healthy patients aged over 45 years (30 with chronic periodontitis and 30 without it) at a university dental school. Traditional cardiovascular risk factors for atherosclerosis were assessed, and carotid intima-media thickness (IMT) was measured via ultrasound.

Results: The internal carotid IMT was 0.77 mm in the periodontal disease group and 0.81 mm in the control group, with no statistically significant differences between them (P = 0.537). However, significant differences were found in the presence of carotid atheroma plaques, which correlated with the severity of periodontitis (P = 0.002). Logistic regression analysis revealed significant differences in age and periodontitis related to the presence of atheroma plaques in the carotid intima.

Conclusion: The severity of periodontitis appears to influence the presence of carotid atheroma plaques.

Gingival inflammation has become a growing focus in understanding the impact of oral health, particularly periodontitis, on cardiovascular diseases.[1-7]Periodontal disease is an infectious disorder characterized by the damage to the tissues supporting the teeth, caused by a long-term inflammatory reaction in a susceptible host.[8]Ridker and Silvertown have presented evidence that supports the involvement of inflammation in cardiovascular diseases.

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In this context, chronic inflammation, like that seen in periodontal disease, could contribute to atherosclerosis by influencing the risk, onset, and advancement of vascular events.[9-12]

The progression of atherosclerosis and the triggering of cardiovascular events involve a combination of risk factors, such as age, smoking, hypertension, hypercholesterolemia, elevated low-density lipoprotein (LDL) cholesterol, low high-density lipoprotein (HDL) cholesterol, diabetes, and elevated triglycerides, lipoproteins, homocysteine, and coagulation factors like fibrinogen and plasminogen activator inhibitors. Predisposing factors include obesity, a sedentary lifestyle, a family history of early coronary disease, male sex, mental disorders, and various socioeconomic and ethnic factors.[13-16]

Research has indicated that dental and periodontal diseases may be linked to atherosclerosis. Specifically, it has been suggested that the chronic inflammation associated with periodontitis could contribute to the development of atherosclerosis. [1,17]Periodontitis and overall poor oral health indeed play a role in the progression of cardiovascular disease. Additionally, meta-analyses have shown that the degree of systemic bacterial exposure from periodontitis correlates with an increased risk of atherosclerosis.[10]

The intima-media thickness (IMT) of the carotid artery, a histopathologically validated marker for atherosclerosis, has gained significant attention. This measurement is closely linked to diseases of the coronary and cerebral arteries, making it a strong predictor of both cardiovascular and cerebrovascular ischemic events.[18-26]

In 2001, Beck et al.[18] examined carotid IMT in relation to periodontitis as part of the Atherosclerosis Risk in Communities study, which included 6,017 individuals with an average age of 62. The study found that severe periodontitis, defined as more than 30% of sites with gingival attachment loss greater than 3 mm, was associated with a 1.31 times higher likelihood of having an IMT greater than 1 mm compared to those without periodontitis.

Currently, there are no established definitive diagnostic markers for cardiovascular disease risk in relation to periodontitis and carotid IMT in individuals without coronary heart disease.[18,26-28] This study investigates the link between periodontitis and carotid artery IMT, as well as the clinical, metabolic, and inflammatory markers related to atherosclerosis in individuals without cardiovascular disease.

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MATERIAL AND METHODS

Patients

The study involved patients from the Rama Dental College,Hospital and Research Centre, Kanpur. Each participant signed a written informed consent before participating in the study. Over 14 months (from January 2024 to June 2024), 30 systemically healthy individuals with chronic periodontitis (6 males and 24 females, ages 32 to 70 years; average age: 58.2 ± 9.8 years) and 30 systemically healthy individuals without periodontitis (9 males and 21 females, ages 30 to 69 years; average age: 57.2 ± 12.2 years) were enrolled in the study.

General inclusion criteria included individuals aged 45 years or older. The criteria for inclusion in the chronic periodontitis group were: 1) having at least 16 teeth and 2) having at least 10 sites with a probing depth (PD) greater than 5 mm. For the control group, inclusion criteria were: 1) no clinical signs of periodontal disease or history of periodontal disease and 2) having at least 16 teeth present.

Exclusion criteria were: 1) the presence of known systemic diseases (such as diabetes mellitus, cardiovascular, renal, liver, or lung disease, or hypertension), 2) a history of any acute or chronic infection, as determined by clinical examination and routine lab tests, or 3) having received systemic antibiotics within the previous 3 months, using regular medications, being pregnant, or engaging in intense physical activity.

An in-depth medical history was gathered for each participant through an interview. Participants completed a questionnaire regarding health issues, medication use, alcohol consumption, smoking habits, and education. Smoking status was categorized as: 1) current smoker, 2) former smoker, or 3) non-smoker. Educational level was used as a proxy for social status. None of the participants reported having known heart disease or diabetes. Body mass index (BMI) was calculated using the anthropometric data (weight in kilograms divided by height squared in meters), with individuals having a BMI over 29.9 kg/m^2 considered obese.

Research assistants measured blood pressure using a calibrated aneroid sphygmomanometer, and the average of two measurements was used in the analysis. Hypertension was defined as a self-reported history of diagnosed hypertension, the use of antihypertensive medications, or a mean systolic blood pressure of ≥140 mmHg or a mean diastolic blood pressure of ≥90 mmHg.

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Glucose, triglycerides, HDL cholesterol, LDL cholesterol, total serum cholesterol, C-reactive protein (CRP), and glycated hemoglobin (HbA1c) levels were measured in serum using commercial enzymatic kits and standardized biochemical testing methods.

Clinical Examination

A calibration exercise was conducted to guarantee satisfactory inter-examiner repeatability, and a single trained expert (SF-M) in periodontitis evaluated all clinical parameters. Bleeding on probing (BOP), a sign of active periodontal inflammation, was included of the assessment. With the exception of the third molars, this was accomplished by evaluating the gingival recession and PD at six different tooth sites: mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, and disto-lingual. Clinical periodontal disease was classified as either aggressive or chronic periodontitis, and PD was evaluated using a periodontal probe.

Healthy individuals with no history of periodontal disease (clinical attachment level [CAL] ≤ 3 mm at each site) were placed in the control group. Clinical data collected included probing depth (PD) and cemento-enamel junction (CEJ) measurements at six sites for all teeth, with CAL calculated as the sum of PD and gingival recession scores.

Bleeding on probing (BOP) was recorded as the full-mouth gingival BOP score (the number of sites with BOP divided by the total number of sites in the mouth, multiplied by 100).

Periodontitis was diagnosed based on the percentage of sites with CAL > 3 mm: 1% to 32% was classified as mild, 33% to 66% as moderate, and 67% to 100% as severe.

Ultrasound Exploration

IMT measurements were taken from the right common carotid artery (CCA). All ultrasound examinations were conducted by a trained radiologist (JDB-S) using an ultrasound system with a 5- to 12-MHz linear transducer. The radiologist was unaware of the patient's periodontal status. The following examination protocol, which is known to be accurate and reproducible, was used:

1. The patient was positioned in a supine posture with their head slightly hyperextended and tilted 45° to the left. To optimize image quality, several technical considerations were made to ensure clear visualization of the vessel wall: a) the ultrasound beam was perpendicular to the vessel, b) focus was adjusted in the region of interest (posterior

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vessel wall), c) the gain was set at the lowest possible level to prevent lumen artifacts, and d) the image was magnified (2x) for better discrimination of the vessel wall.

2. To measure IMT, an optimal longitudinal image of the right CCA was captured, and measurements were taken on the far (posterior) wall of the vessel, along a 1-cm section proximal to the bifurcation. IMT was defined as the distance from the leading edge of the lumen-intima interface to the leading edge of the media-adventitia interface. Only the intima (the echogenic layer) and the media (the hypoechoic layer) were included in the measurement.
3. Three measurements were taken from the selected carotid segment, with the measurement corresponding to the maximum IMT recorded.

Carotid plaque, defined by the appearance of the largest focal lesion, was classified based on: 1) surface characteristics, 2) echogenicity, and 3) texture. Surface characteristics were categorized as: 1) smooth, 2) mildly irregular (height variations ≤0.4 mm), 3) markedly irregular (height variations >0.4 mm), and 4) ulcerated (a discrete depression >2 mm in width extending into the media). Lesion echogenicity was categorized as hypoechoic, isoechoic, hyperechoic, or calcified.

Texture was categorized as either homogeneous or heterogeneous. In cases with multiple focal lesions, the largest lesion on each side was measured. Participants were then grouped into one of three categories: 1) no plaque, 2) intermediate-risk plaque, or 3) high-risk plaque. Those with no plaque were identified as having a smooth intimal surface and no focal thickening. High-risk plaque was defined by the presence of a markedly irregular or ulcerated surface, or hypodense or heterogeneous plaques covering more than 50% of the total plaque volume, as these features are linked to clinical symptoms. Other plaques, such as hyperdense, calcified, homogeneous plaques, or those with a mildly irregular surface, were classified as intermediate risk. If an individual had multiple types of plaques, the plaque risk was determined by the most severe type.

For some analyses, carotid findings were grouped into two categories: detectable or minimal atherosclerosis. Detectable atherosclerosis was defined as being present in participants with carotid wall thickness in the upper two tertiles or in the intermediate- or high-risk plaque groups.

Statistical Analyses

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The sample size for the study was calculated based on the assumption of a clinically significant difference in carotid IMT of 0.09 mm. Using this mean difference, with $\alpha = 0.05$, s = 0.14 mm, and a power of 80%, the required sample size was determined to be 39 individuals in each group.

Data were analyzed using statistical software. A descriptive analysis was performed for each variable. The associations between different qualitative variables were examined using the Pearson chi-square test. For quantitative variables, the Student t-test was applied to two independent samples, with variance homogeneity checked for each case. A bivariate analysis was conducted, with the binary outcome variable "presence of carotid plaques" being assessed. Odds ratios and confidence intervals were computed using exact conditional logistic regression. Statistical significance was considered when $P \leq 0.05$.

RESULTS

Table 1:HomogeneityofGroupsbyDemographicCharacteristics

Characteristics	**Periodontal Disease Group(n=30)**	**Control Group(n=30)**	**P-value**
Age,mean±SD	58.21±9.79	57.22±12.19	0.726
Sex, n(%) **Male** **Female**	6(20) 24(80)	9(30) 21(70)	0.372
Educationlevel,n(%) None **Primary** **Secondary** **University**	6(20) 18(60) 4(13.33) 2(6.67)	1(3.33) 20(66.67) 8(26.67) 1(3.33)	0.146
Smoking habit, n(%) Smoker **Former smoker** **Never-smoker**	7(23.33) 3(10) 20(66.67)	5(16.67) 4(13.33) 21(70)	0.777
Alcohol consumption, n(%) **Yes** **No**	9(30) 21(70)	9(30) 21(70)	1.000
BMI (kg/m^2),mean±SD	28.64±11.37	28.52±4.14	0.957
Systolic bloodpressure,mean±SD	118.0±24.2	122.0±30.0	0.910

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Diastolicbloodpressure,mean±SD	70.58±26.2	70.5±29.3	0.253
Regularphysical activity,n(%) **Yes** **No**	14(46.67) 16(53.33)	17(56.67) 13(43.33)	0.437
Family history of cardiovascular disease,n(%) **Yes** **No**	8(26.67) 22(73.33)	10(33.33) 20(66.67)	0.572

Student t testandPearsonx^2 test.

Table 1 displays the demographic characteristics, as well as data on patient education level, habits, BMI, systolic blood pressure, and family history. The group with periodontal disease showed significantly higher levels of total cholesterol and HbA1c compared to the control group (Table 2). No significant differences were found between the two groups in terms of the other hemostatic parameters (Table 2).

Table 2: Test Variables in the Study Groups

Laboratory variables	Periodontal Disease Group (n=30;mean ± SD)	Control Group (n=30;mean ± SD)	P Value
Glucose(mg/Dl)	106.41±23.18	109.59±37.80	0.742
Serum creatinine(mg/dL)	0.78±0.13	0.79±0.21	0.773
Triglycerides(mg/dL)	98.05±43.98	122.19±49.13	0.141
Total cholesterol (mg/dL)	244.70±39.55	209.12±26.98	0.003
LDL cholesterol (mg/dL)	153.91±34.99	136.91±16.41	0.142
HDL cholesterol (mg/dL)	70.77±27.33	61.18±9.91	0.278
hs-CRP(mg/L)	1.07±0.67	0.95±0.61	0.677
Leukocytes(n)	6.57±1.65	7.15±1.78	0.283

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HbA1c(%)	5.84±0.53	5.46±0.49	0.024
Platelets(n)	202.80±46.57	232.06±57.03	0.075

Carotid ultrasound measurements indicated an intima thickness of 0.76 ± 0.18 mm in individuals with periodontal disease, compared to 0.81 ± 0.26 mm in the control group. This difference was not statistically significant (P = 0.537) (Table 3). In terms of carotid atheromatous plaques, 17 individuals with periodontal disease (56.7%) had plaques, while only 6 individuals in the control group (20%) had plaques, with the difference between the two groups being statistically significant (P = 0.002).

Table 3: Comparison of IMT and Presence of Carotid Plaques in Study Groups

Characteristics	**PeriodontalDisease Group(n=30)**	**Control Group(n=30)**	**P Value**
IMT(mm),mean±SD	0.76±0.18	0.81±0.26	0.537
Carotidplaques,n(%) **Yes** **No**	17(56.67) 13(43.33)	6(20) 24(80)	0.002

Student t test and Pearson x^2 test.

The ultrasound findings for individuals with carotid atheromatous plaques in both the periodontal disease group and the control group revealed no statistically significant differences in terms of the number of plaques, their surface characteristics, or ultrasound features (Table 4).

Table 4: Carotid Ultrasound Variables(n=23 carotid plaques)in the Study Groups

Carotid Ultrasound Variables	**Periodontal disease group (n=17 carotid plaques)**	**Control Group (n=6 carotid plaques)**	**P value**
Single or multiple carotid plaques,n(%)	11(64.70) 6(35.30)	5(83.33) 1(16.67)	0.395
Plaque-media thickness(mm),mean±SD	2.06±0.98	1.57±0.33	0.247
Carotid plaque	11(64.70)	6(100)	0.412

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surface,n(%) **Smooth and well defined** **Slightly irregular** **Very irregular** **Ulcerated(>2mm)**	4(23.53) 1(5.88) 1(5.88)	0(0) 0(0) 0(0)	
Ultrasound characteristics ,n(%) **Hypoechoic** **Isoechoic** **Hyperechoic** **Calcified**	4(23.53) 0(0) 10(58.82) 3(17.64)	0(0) 0(0) 2(33.33) 4(66.67)	0.066
Echostructure,n(%) **Homogenous** **Heterogenous**	14(82.35) 3(17.64)	6(100) 0(0)	0.280
Risk of cerebrovascular event,n(%) **Moderate risk** **High risk**	13(76.47) 4(23.53)	6(100) 0(0)	0.192

Student t test and Pearson x^2 test.

Significant differences were found between periodontal condition and the presence of atheromatous plaques, specifically related to the severity of periodontal involvement (P = 0.038) (Table 5).

Table 5: Relationship Between Periodontal Characteristics and Presence of Carotid Plaques inthePeriodontalDiseaseGroup(n=30)

Periodontal Characteristics	Presence of Carotid Plaques (n=17)	Absence of Carotid Plaque(n=13)	P Value
Numberof teeth,mean ± SD	23.66±3.85	23.86±3.73	0.887
Bleeding index,mean ± SD	24.31±17.22	27.17±22.64	0.772
CAL(mm),mean ± SD	4.37±0.58	4.02±0.54	0.087
PD(mm),mean ± SD	5.03±0.92	4.47±0.56	0.068

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Numberofpockets≥4mm,mean± SD	4.74±4.92	10.37±11.56	0.082
Number of pockets≥6mm,mean± SD	1.17±2.11	1.32±3.41	0.899
Periodontal disease,n(%) **Mild** **Moderate** **Severe**	6(35.30) 6(35.30) 5(29.40)	10(76.92) 3(23.08) 0(0)	0.038

Student t test and Pearson x^2 test.

Table 6: Logistic Regression Model for Presence of Carotid Plaques

Variables	**Odds Ratio**	**95% Confidence Interval**	P Value
Age	7.02	1.77 to 27.80	0.005
Sex	0.48	0.14 to 1.81	0.287
Smoking	0.75	0.21 to 2.88	0.690
Periodontal disease	5.22	1.66 to 16.52	0.005
BMI	1.52	0.47 to 4.83	0.466
Systolic blood pressure	0.28	0.57 to 1.52	0.145
Diastolicbloodpressure	0.74	0.24 to 2.33	0.602
Regularphysical activity	1.02	0.36 to 2.93	0.952
Cardiovasculardisease	1.02	0.33 to 3.22	0.953
Glucose(mg/dL)	1.65	0.51 to 5.28	0.405
Triglycerides(mg/dL)	1.62	0.97 to 27.52	0.731

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Total cholesterol (mg/dL)	0.93	0.32 to 2.64	0.888
LDL cholesterol (mg/dL)	2.26	0.60 to 8.48	0.227
HDL cholesterol (mg/dL)	0.18	0.02 to 2.08	0.195
hs-CRP(mg/L)	0.38	0.023to 3.57	0.395
Leukocytes(n)	0.28	0.03 to 2.67	0.275
HbA1c(%)	3.43	0.29 to 40.12	0.325
Platelets(n)	0.77	0.13 to 4.66	0.790

Table 6 outlines the results of the logistic regression analysis, showing that both patient age and the presence of periodontitis were significantly associated with the presence of atheromatous plaques.

DISCUSSION

This study explored periodontal disease as a potential risk factor for atherosclerosis by examining the link between chronic periodontal disease and early changes in the carotid arteries. The findings revealed significant differences in the severity of periodontal disease based on the presence of atheromatous plaques in the carotid intima, as detected through ultrasound in systemically healthy individuals.

The relationship between periodontitis and atherosclerosis is of great interest, though the results remain debated, with some studies finding no causal connection and others suggesting a strong link. The discrepancies in findings could be attributed to differences in study populations (such as age, ethnicity, and location) and variations in how periodontitis is assessed, with some research focusing only on gingival inflammation.[3,12,31,32]

Ultrasound measurements have been shown to correlate with histologic findings, and an increased intima-media thickness (IMT) is associated with vascular risk factors and advanced atherosclerosis.[20,22] Consequently, IMT is becoming more commonly used for risk assessment. An increase in carotid IMT, as measured by ultrasound, is linked to a higher risk of acute myocardial infarction and cerebrovascular events like stroke in patients with no prior

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vascular disease, suggesting that subclinical atherosclerosis may be present in many individuals with periodontitis.[27]

The relationship between periodontitis and carotid IMT was investigated by Becketal.[18]. People with periodontitis had a greater chance of having an elevated IMT than people without the condition. However, there were no variations in media thickness between the two groups in our series. Therefore, more research in this area is required.

Age is a key factor linked to both periodontal disease and cardiovascular disease.[3] A study in Japan involving 1,763 individuals aged 38 to 88 years found that subclinical aortic atherosclerosis, as assessed by magnetic resonance imaging, was present in 50% of participants and increased with age.[4] Data from the population-based Health in Pomerania study showed that when comparing individuals with high versus low levels of periodontal disease, the prevalence of carotid artery plaques increased by 15% among males under 59 years old, while it increased only 5% in those aged 59 and older.[6]

Similarly, Cairo et al.[27] reported that the odds of higher carotid IMT were more than eight times greater in individuals under 40 with periodontitis compared to age-, sex-, obesity-, and smoking-matched controls who were periodontally healthy. While we assessed periodontal disease based on clinical measures, microbiological factors are also significant. In this regard, Desvarieux et al.[5], as part of the Oral Infections and Vascular Disease Epidemiology Study, found that colonization by *Actinomyces israelii*, *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola* was significantly linked to increased carotid IMT.

The data regarding periodontal intervention and the immediate rise in serum markers of inflammation may indicate that intensive periodontal treatment could lead to serious adverse effects.[34] A recent study examined the outcomes of periodontal interventions in individuals with heart disease, suggesting that these treatments do not result in more severe adverse events than would be expected in the general population over a 25-month period.[10] Moreover, this study showed that routine non-surgical periodontal therapy does not lower the risk of severe cardiovascular events.

Several recent studies[35,36] have suggested a link between periodontal disease and obesity. Increasingly, research is identifying newly recognized risk factors for systemic diseases that are also linked to periodontal disease, with obesity emerging as a risk factor for periodontal disease.[35,36] To further understand the relationship between obesity and periodontal disease, additional studies with larger sample sizes, using more comprehensive fat analysis measures

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beyond BMI, and adjusting for various confounding factors through multiple regression models, are necessary.

In our study, patient age and the presence of periodontitis showed statistically significant differences in relation to the presence of atheroma plaques, but other factors did not show significant differences. These results should be interpreted with caution due to the small sample size and the disproportionate number of females compared to males in the heterogeneous population. Therefore, further research is needed to validate these findings.

Conclusion

Ultrasound measurement of carotid artery IMT is a straightforward, non-invasive method that reveals significant differences in the presence of atheroma plaques based on the severity of periodontal disease.

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