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Is there an association between periodontal disease and acute myocardial infarction? A cross-sectional study

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Aim: The aim of the present study was to investigate the association between periodontal disease and acute myocardial infarction (AMI).

Study design: A total number of 120 patients were selected for the study. Sixty patients who were examined immediately following an episode of myocardial infarction were selected as the test group and 60 patients suffering from chronic coronary heart disease were selected as the control group for the study. The study was conducted with the help of a medical history, periodontal examination and analysis of enzyme profile of the patient.

Results: Results of multiple logistic regression analysis, without adjusting for confounding factors, showed that plaque index (PI) ≥ 2, periodontal disease index (PDI) ≥ 4 and low density lipoproteins were associated with AMI. Former smokers showed a significantly lower risk for AMI. After adjusting for age, current smoking, diabetes, hypertension, low density lipoproteins and high density lipoproteins, the results showed that PI ≥ 2 and PDI ≥ 4 were not significantly associated with AMI.

Conclusion: PI ≥ 2 and PDI ≥ 4 showed a significantly positive association with AMI, when the confounding factors were not adjusted. However, once the confounding factors were adjusted, PI ≥ 2 and PDI ≥ 4 showed no association. This shows that risk factors such as smoking and hyperlipidemia have a more profound association with AMI than periodontal disease.

■ Introduction

The effect of oral health on the rest of the body was proposed by Assyrians as early as the seventh century B.C. William Hunter's focal infection theory was widely accepted in the period from 1900 to 1950, which was known as the era of focal infection. In the 1940s and 1950s, this theory fell into disrepute because Hunter and other advocates were unable to explain how focal oral sepsis produced systemic maladies. The period from 1950 to 1989 was known as the era of retreat. After Mattila's report on the rela-

tionship of periodontal inflammation to systemic conditions in 1989[1], the focal infection theory was supported with evidence. This opened a new era of periodontal medicine.

Periodontal diseases are bacterial infections in which certain bacteria play an important role in the development of inflammatory processes. Periodontal infections may cause vascular events via lipopolysaccharides and inflammatory cytokines, contributing to the pathogenesis of cardiovascular disease[2]. Periodontal pathogens themselves have been shown to increase platelet aggregation and thromboembolic events.

The aim of the present study was to investigate the association between periodontal disease and acute myocardial infarction (AMI).

■ Study design

There were a total number of 120 patients. Sixty patients who were examined immediately following an episode of AMI were selected as a test group, and 60 patients suffering from chronic coronary heart disease (CHD) were selected as a control group for the study at the Vijaya Heart Foundation, Chennai-600026, India. All patient gave informed consent to their participation in the study, and the study design was approved by the ethical commitee of Meenakshi University.

■ Group I (Test group)

This group consisted of 60 individuals who were diagnosed as suffering from AMI.

■ Group II (Control group)

This group consisted of 60 patients who were diagnosed as suffering from chronic CHD.

■ Inclusion criteria for patient selection

1. Patients with AMI were verified by typical changes in their electrocardiogram (ECG) and an increase in serum enzymes aspartate transaminase (AST), creatine phosphokinase (CPK) and CPK isoenzyme (CPK-MB) together with or without chest discomfort consistent with AMI.
2. Patients suffering from chronic CHD should not have suffered from acute coronary events in the previous 6 months.

■ Exclusion critera

During dental examination, third molars were excluded from the study. Patients with respiratory disease were excluded from the study.

■ Study design

Medical history

A medical history was taken regarding medical status and smoking habits.

Periodontal examination

AMI patients were clinically examined 6–7 days after admission to the coronary care unit. Clinical examination of chronic CHD patients was carried out during their hospital visit.

The clinical parameters recorded were:

- Plaque index (PI, Silness and Loe[3])
- Periodontal disease index (PDI, Ramfjord[4]).

Lab analysis

Blood samples from all patients were collected and tested in the biochemical lab of the hospital using an autoanalyser (Roche No.917) and the values of the following variables were recorded:

- High density lipoprotein (HDL)
- Low density lipoprotein (LDL)
- Serum glutamate oxaloacetate transaminase (SGOT)
- Creatine phosphokinase (CPK)
- Creatine phosphokinase isoenzyme (CPK-MB).

Statistical analysis

Means and standard deviations were estimated for continuous variables in each study group. Mean values were compared by Student *t* test. Proportions were estimated for different characteristics in each study group. Proportions were compared by using chi-square test with Yates' correction:

$$\text{Formula } x^2 = \frac{\Sigma (O - E)^2}{E}$$

where O = observed frequency, and E = expected frequency.

Variable	Group I Mean ± SD	Group II Mean ± SD	*P* value *
Age (Range)	54.50 ± 7.30 (37–72)	57.70 ± 9.70 (35–81)	0.04 (Sig)
PI	2.13 ± 0.33	1.71 ± 0.49	< 0.0001 (Sig)
PDI	4.78 ± 0.83	3.34 ± 1.13	< 0.0001 (Sig)
HDL	40.70 ± 11.50	39.30 ± 8.50	0.43 (NS)
LDL	158.90 ± 27.70	78.50 ± 32.40	< 0.0001 (Sig)

Table 1 Mean, standard deviation and test of significance of mean values between group I and group II

PI: plaque index
PDI: periodontal disease index
HDL: high density lipoprotein
LDL: low density lipoprotein
** Student t test was used to compare the mean values between group I and group II.*
Sig: significant, P < *0.05*
NS: not significant, P > *0.05*

Variable		Group I No (%)	Group II No (%)	*P* value *
Smoking habit				
	Non-smoker	15 (25)	6 (10)	
	Current smoker	41 (68.3)	3 (5)	#
	Former smoker	4 (6.7)	51 (85)	< 0.0001 (Sig)
Diabetes				
	Yes	37 (61.7)	40 (66.7)	0.70 (NS)
	No	23 (38.3)	20 (33.3)	
Hypertension				
	Yes	31 (51.7)	34 (56.7)	0.71 (NS)
	No	29 (48.3)	26 (43.3)	

Table 2 Distribution of various parameters in group I and group II

** Chi-square test with Yates' continuity correction was used to calculate the* P *value*
 # Without continuity correction
Sig: significant, P < *0.05*
NS: not significant, P > *0.05*

Univariate and multiple logistic regression analysis were done to identify the risk factors for the development of MI. In the present study, $P < 0.05$ was considered as the level of significance.

■ Results

As shown in Table 1, the mean age in group I (54.5 ± 7.3) was significantly lower than the mean age in group II (57.7 ± 9.7) ($P = 0.04$). The age range for group I was 37–72 and that for group II was 35–81.

The mean PI score in group I (2.13 ± 0.33) was significantly higher than group II (1.71 ± 0.49) ($P < 0.0001$). The mean PDI score in group I (4.78 ± 0.83) was significantly higher than group II (3.34 ± 1.13) ($P < 0.0001$).

As shown in Table 2, the proportion of current smokers in group I (68.3%) was higher than in group II (5%). The proportion of former smokers was greater in group II (85%) than in group I (6.7%). There was a significant difference in the proportion of former smokers and current smokers between group I and group II ($P < 0.0001$).

The proportion of patients with diabetes in group II (66.7%) was higher than in group I (61.7%), but there was no significant difference between the two groups ($P = 0.70$). The proportion of patients with hypertension in group II (56.7%) was greater than in group I (51.7%), but the difference was not statistically significant ($P = 0.71$).

As depicted in Table 3, results of univariate logistic regression analysis (ULRA) showed that the factors such as age (OR = 0.96, $P = 0.045$), current smoking (OR = 5.47, P = 0.03), former smoking (OR = 0.03, $P < 0.0001$), PI ≥ 2 (OR = 4.50, $P = 0.0002$), PDI ≥ 4 (OR = 16.71, $P < 0.0001$) and LDL (OR = 1.06, $P < 0.0001$) were significantly associated with AMI.

Table 3 Results of univariate logistic regression analysis

Independent variable	Regression coefficient (± SE)	*P* value	Odds ratio
Age (years)	-0.04 (± 0.02)	0.045 (Sig)	0.96
Sex – Male	-1.01 (± 0.53)	0.06	0.37
Smoking Current Former	 1.70 (± 0.77) -3.46 (± 0.71)	 0.03 (Sig) < 0.0001 (Sig)	 5.47 0.03
Diabetes	-0.22 (± 0.38)	0.57	0.80
Hypertension	-0.20 (± 0.37)	0.58	0.82
PI (≥ 2)	1.50 (± 0.40)	0.0002 (Sig)	4.50
PDI (≥ 4)	2.82 (± 0.51)	< 0.0001 (Sig)	16.71
HDL	0.01 (± 0.02)	0.44	1.02
LDL	0.06 (± 0.01)	< 0.0001 (Sig)	1.06

Dependent variable: acute myocardial infarction vs chronic coronary heart disease
SE: standard error
PI: plaque index
PDI: periodontal disease index
HDL: high density lipoprotein
LDL: low density lipoprotein
Sig: significant, P < *0.05*

Table 4 Results of multiple logistic regression analysis

Independent variable	Regression coefficient (± SE)	*P* value	Odds ratio
PI (≥≥2)	3.80 (± 1.79)	0.03 (Sig)	44.8
PDI (≥ 4)	3.80 (± 1.86)	0.04 (Sig)	44.8
LDL	0.12 (± 0.04)	0.008 (Sig)	1.13
Smoker (Former)	-9.09 (± 3.47)	0.009 (Sig)	0.0001

Dependent variable: acute myocardial infarction vs chronic coronary heart disease
Note 1: Method of regression is forward stepwise additional method.
Note 2: Other independent variables included were age, sex, current smoking, diabetes, hypertension and HDL.
PI: plaque index
PDI: periodontal disease index
HDL: high density lipoprotein
LDL: low density lipoprotein
Sig: significant, P < *0.05*

Table 5 Results of multiple logistic regression analysis after adjusting for age, current smoking, diabetes, hypertension and LDL

Independent variable	Regression coefficient (± SE)	*P* value
PI (≥ 2)	2.98 (± 1.62)	0.07 (NS)
PDI (≥ 4)	3.34 (± 1.77)	0.06 (NS)

Note: The variables which were significant in univariate logistic regression analysis were adjusted. Former smoking was not adjusted since it contributed a negative risk.
PI: plaque index
PDI: periodontal disease index
NS: not significant, P > *0.05*

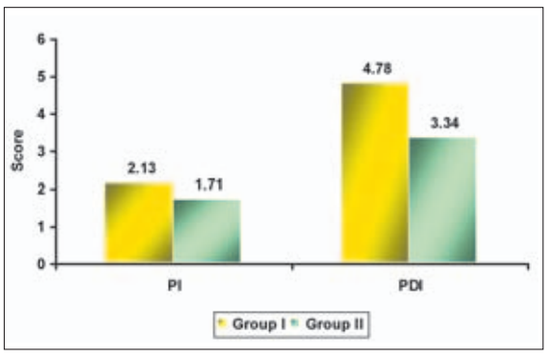

Fig 1 Comparison of mean plaque index (PI) score and mean periodontal disease index (PDI) score between group I and group II.

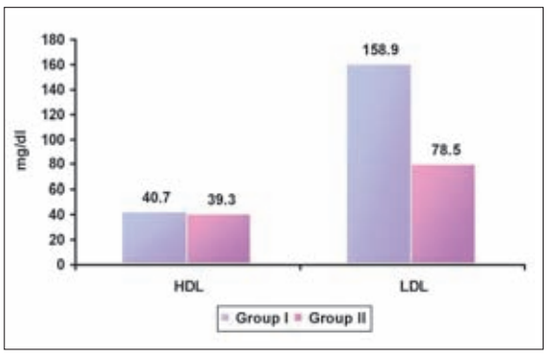

Fig 2 Comparison of mean lipid profile between group I and group II (HDL, high-density lipoprotein; LDL, low-density lipoprotein).

However, none of the other variables were significantly associated with AMI ($P > 0.05$).

As depicted in Table 4, results of multivariate logistic regression analysis (MLRA) showed that the factors such as PI ≥ 2 (OR = 44.8, $P = 0.03$), PDI ≥ 4 (OR = 44.8, $P = 0.04$) and LDL (OR = 1.13, $P = 0.008$) were significantly associated with AMI. Former smokers (OR = 0.0001, $P = 0.009$) had a significantly lower risk for AMI. However none of the other variables such as age, sex, current smoking, diabetes and hypertension were significantly associated with AMI ($P > 0.05$).

As depicted in Table 5, results of MLRA, after adjusting for age, current smoking, diabetes, hypertension and LDL showed that PI ≥ 2 ($P = 0.07$) and PDI ≥ 4 ($P = 0.06$) were not significantly associated with AMI.

■ Discussion

CHD is the major cause of morbidity and mortality worldwide. It is interesting to note that the classical risk factors of CHD can only account for one-half to two-thirds of the variation in the incidence of CHD. Thus it is likely that other, as yet unrecognised factors may also contribute to the pathogenesis of CHD. Recent evidence suggests a role for infectious agents in the pathogenesis of CHD, particularly periodontal disease.

Among the various parameters recorded, age is an important risk factor for AMI. Mean age in group I (54.5 ± 7.3) was significantly lower than the mean age in group II (57.7 ± 9.7) ($P = 0.04$) (Table 1).

Though the results of ULRA showed that lower age was significantly associated with AMI (Table 3), the results of MLRA failed to confirm this association (Table 4). It should be noted that group I patients also had higher PDI scores than group II (Fig 1). These findings are in accordance with the study conducted by Emingil et al[5], who did not find age a significant contributing factor to AMI.

Smoking is a known risk factor for both periodontal disease and CHD. The smoking status of the patients was recorded in the study according to the criteria established by the Center for Disease Control and Prevention as current smokers, former smokers and non-smokers.

The proportion of current smokers in group I (68.3%) was higher than in group II (5%). The proportion of former smokers was greater in group II (85%) than in group I (6.7%) (Table 2). Since group II patients were intensely educated about the hazardous effects of smoking, most of them had discontinued smoking.

The results of ULRA (Table 3) showed that current smoking was significantly associated with group I ($P = 0.03$), which also had higher PDI scores. This result is similar to that found in the study conducted by Buhlin et al[6].

Results of ULRA and MLRA showed that former smokers presented a negative risk for AMI ($P < 0.0001$). PDI scores were also relatively low in former smokers in contrast to the study conducted by Haber et al[7]. To minimise the effect of smoking as a risk factor for both periodontitis and CHD, the effect of smoking was later adjusted in the MLRA (Table 5).

The proportion of patients with diabetes and hypertension showed no significant differences between the two groups (Table 2). The lipid profile values are important because a relationship has been suggested between chronic periodontitis and hyperlipidemia[8]. Among the HDL and LDL values, mean LDL in group I (158.9 ± 27.7) was significantly higher than group II (78.5 ± 32.4) ($P < 0.0001$), while HDL values did not show any significant difference (Table 1 and Fig 2). Also, the results of ULRA (Table 3), showed that HDL ($P = 0.44$, OR = 1.02) did not significantly contribute towards protection against AMI, which was in accordance with the study conducted by Emingil et al[5], who also found no significant difference in HDL levels between the two groups.

The results of ULRA and MLRA (Tables 3 and 4) showed that LDL was significantly associated with AMI. It is important to note that higher PDI scores were also noted in group I. The lower level of LDL in group II might be due to the fact that the patients in group II had received dietary counselling and antihypercholesterolemia medications. This finding was in accordance with the study conducted by Katz et al[9] and Loesche et al[10], with respect to restriction in diet and medications contributing towards a decrease in LDL level in group II.

Plaque accumulation scores do not significantly contribute to a diagnosis of periodontitis, but do contribute to models of periodontitis-atherosclerosis syndrome (PAS). Plaque alone does not confer risk for PAS, but if severe disease is present, then the risk increases with increasing plaque[11]. Mean PI score in group I (2.13 ± 0.33) was significantly higher than in group II (1.71 ± 0.49) ($P < 0.0001$), as shown in Fig 1. Mean PDI score in group I (4.78 ± 0.83) was significantly higher than in group II (3.34 ± 1.13) ($P < 0.0001$) (Table 1).

Results of ULRA and MLRA without adjusting for confounders (Tables 3 and 4), showed that PI ≥ 2 was significantly associated with AMI. The results were consistent with other studies[12], where they found a significant association between high plaque scores and CHD risk.

The explanation offered by the author was that streptococci in supragingival plaque may be associated with risk of CHD, due to its thrombogenic potential. Also, the heat shock protein on the surface of *Chlamydia pneumoniae* and *Porphyromonas gingivalis* could elicit a hyperinflammatory response that in turn could contribute to atherosclerosis[13].

One reason for the high amount of plaque in group I patients might be that since the patients were hospitalised, they were unable to perform proper oral hygiene procedures for plaque control. So, the PI scores in group I may not be representative of a long-term measure of the presence of plaque. The results of MLRA, after adjusting for age, sex, smoking, diabetes, hypertension, LDL and HDL (Table 5), showed that a PI score ≥ 2 ($P = 0.07$) was not significant, which was similar to the study conducted by Morrison et al[14].

The mean PDI score in group I (4.78 ± 0.83) was significantly higher than that in group II (3.34 ± 1.13) ($P < 0.0001$) (Table 1). Results of ULRA and MLRA, without adjusting for confounders, showed that a PDI score ≥ 4 was significantly associated with AMI ($P < 0.0001$, OR = 16.71) (Table 3).

From the above results, it can be concluded that PDI scores were significantly decreased in group II. This could be because dental check-ups were emphasised soon after the patients had an episode of AMI, and also due to the differential changes in diet, smoking and oral hygiene among survivors of AMI, which could have affected the progression of periodontal disease[12].

The PDI score increase in group I was consistent with the periodontitis-atherosclerosis model proposed by Offenbacher et al[11], according to which there was a monotonic increasing gradient of risk for CVD as PDI scores increase, using a 3 mm attachment loss threshold. Also, the findings were similar to the Third National Health and Nutrition Examination Survey data (NHANES III, Arbes et al[15]), and other studies[12,16] that used clinical attachment loss as the periodontal exposure.

As shown in Table 5, results of MLRA, after adjusting for age, current smoking, diabetes, hypertension and LDL showed that PI ≥ 2 ($P = 0.07$) and PDI ≥ 4 ($P = 0.06$) were not significantly associated with AMI. Thus, the results of the present study can only indicate that there was a significant association between AMI and periodontal status when the confounders were not adjusted for.

Once the confounders were adjusted for there was no significant association between AMI and periodontal status. The results were in agreement with studies[17–19] in which there was no significant associ-

ation between periodontal disease and CHD. Thus, it can be concluded that confounders play a major role in eliciting the actual association between periodontal disease and CHD.

As emphasised by Beck et al[20], moderate associations which have been observed in longitudinal studies, might be because of a lack of control of confounding factors, residual confounding or overcontrolling of confounding factors.

Also there have been inconsistent results in different longitudinal studies due to different methods being adopted for measure of exposure and outcome.

However, the possibility of oral infections contributing to CVD risk cannot be ruled out owing to the numerous studies that have demonstrated an association even after adjusting for confounding factors. To help resolve potentially confounded associations, larger and better-controlled studies involving socially homogeneous populations are required that can establish causality and determine specific periodontal pathogens.

■ References

1. Mattila KJ, Nieminen MS, Valtonen VV, Rasi VP, Kesäniemi YA, Syrjälä SL, et al. Association between dental health and acute myocardial infarction. Br Med J 1989;298:779–781.
2. Beck JD, Danesh, Offenbacher S, Williams R, Gibbs P. Periodontitis: A risk factor for coronary heart disease? Ann Periodontol 1998;3:127–141.
3. Silness J, Loe H. Periodontal disease in pregnancy. II. Correlation between oral hygiene and periodontal condition. Acta Odontol Scand 1964;22:121–135.
4. Ramfjord SP. Indices for prevalence and incidence of periodontal disease. J Periodontol 1959;30:51–59.
5. Emingil G, Buduneli E, Aliyev A, Akilli A, Atilla G. Association between periodontal disease and acute myocardial infarction. J Periodontol 2000;71:1882–1886.
6. Buhlin K, Gustafsson A, Ahnve S, Janszky I, Tabrizi F, Klinge B. Oral health in women with coronary heart disease. J Periodontol 2005;76:544–550.
7. Haber J, Wattles J, Crowley M, Mandell R, Joshipura K, Kent RL. Evidence for cigarette smoking as a major risk factor for periodontitis. J Periodontol 1993;64:16–23.
8. Iacopino M, Cutler W. Periodontal disease: Links with serum lipids/triglyceride levels? Review and new data. J Int Acad Periodontol 2003;5:47–51.
9. Katz J, Chaushu G, Sharabi Y. On the association between hypercholesterolemia, cardiovascular disease and severe periodontal disease. J Clin Periodontol 2001;28:865–868.
10. Loesche WJ, Karapetoco F, Pohl A, Pohl C, Kocher T. Plasma lipid and blood glucose levels in patients with destructive periodontal disease. J Clin Periodontol 2000;27:537–541.
11. Offenbacher S, Madianos PN, Champagne CM, Southerland JH, Paquette DW, Williams RC, et al. Periodontitis-atherosclerosis syndrome: an expanded model of pathogenesis. J Periodontal Res 1999;34:346–352.
12. Hyman JJ, Winn DM, Reid BC. The role of cigarette smoking in the association between periodontal disease and cardiovascular disease. J Periodontol 2002;73:988–994.
13. Renvert S, Ohlsson O, Persson S, Lang NP, Persson GR. Analysis of periodontal risk profiles in adults with or without a history of myocardial infarction. J Clin Periodontol 2004;31:19–24.
14. Morrison HI, Ellison LF, Taylor GW. Periodontal disease and risk of fatal coronary heart and cerebrovascular diseases. J Cardiovasc Risk 1999;6:7–11.
15. Arbes Jr, Slade GD, Beck JD. Association between extent of periodontal attachment loss and self-reported history of heart attack: An analysis of NHANES III data. J Dent Res 1999;78:1777–1782.
16. Elter JR, Champagne CM, Offenbacher S, Beck JD. Relation of periodontal disease and tooth loss to prevalence of coronary heart disease. J Periodontol 2004;75:782–790.
17. Hujoel PP, Drangsholt M, Spiekerman C, DeRouen TA. Periodontal disease and coronary heart disease risk. J Am Med Assoc 2000;284:1406–1410.
18. Mattila KJ, Valtonen VV, Nieminen M, Huttunen JK. Dental infection and the risk of new coronary events: prospective study of patients with documented coronary artery disease. Clin Infect Dis 1995; 20:588–592.
19. Mattila KJ, Asikainen S, Wolf J, Valtonen V, Nieminen M. Age, dental infection and CHD. J Dent Res 2000;79: 756–760.
20. Beck JD, Eke P, Heiss G, Madianos P, Couper D, Lin D, et al. Periodontal disease and coronary heart disease: a reappraisal of the exposure. Circulation 2005; 112:19–24.