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Research Article

Periodontitis and Other Risk Factor for Coronary Artery Disease among Adults: A Case Control Study in Delhi, India

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ABSTRACT

Background: Periodontitis is an extension of inflammation to the supporting tissue of the tooth. Prevalence varies worldwide with a higher prevalence in Asian countries and in India as reported. Literature reports that the sub-gingival microflora and the continuous latent endotoxemia originating from the periodontal pockets is a risk factor for the damage to vascular endothelial integrity, platelet function and blood coagulation leading to periodontal disease playing a role in etiopathogenesis of coronary artery disease and cerebrovascular disease.

Aim: To study periodontitis and other risk factor that correlates with CAD among the adult urban population.

Settings & Design: Clinic based case control study carried out in medicine and dental outpatient departments (OPD) of Hamdard Institute of Medical Sciences & Research and associated HAH Centenary Hospital, New Delhi. Minimum sample size was calculated to be 140. A 1:3 case to control ratio was taken.

Methods & Materials: Periodontal Index (Russell Index) was utilized in our study to grade periodontal health status.

Statistical Analysis: The data was analysed using SPSS 21.0 version. Categorical variables were tested for significance using Chi square test and multiple logistic regression was used for predicting the probability of cases with cardiac problems having periodontitis.

Results: 30 (21.4%) participants were recruited as cases and 110 (78.6%) as controls. Among the cases the Mean Russell score for case was 3.98 ± 0.70 and control group was 3.11 ± 0.68 , respectively. Among the total subjects 76.4% showed a RI score of ≥ 3 indicative of established destructive and terminal periodontal disease and 23.5% constituted the beginning of destructive periodontal disease.

Conclusion: Severity of periodontitis was noted in cases as compared to controls. Findings suggest the relationship between CAD and periodontal disease.

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Introduction

Structures around teeth and gums can often get inflamed which finally leads to tooth loss and decay. This process is called periodontitis. The

bacteremia induced by the supra and subgingival microflora is the etiology of both reversible and irreversible damage to the surrounding soft and hard dental tissues namely gingivitis and periodontitis respectively [1, 2]. Recently, there has been a surge in studies done on

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periodontitis due to its probable correlation with CAD. Its prevalence varies in different regions of the world and a higher prevalence and severity of PD in Asian countries and India is reported [3, 4]. The presence of chronic inflammatory periodontal disease may significantly affect systemic inflammatory/immune conditions that have a high disease burden such as coronary artery disease (CAD) and CAD-related events such as angina, infarction, atherosclerosis, stroke. Endotoxins (lipopolysaccharides) from gram negative anaerobic organisms which play an important role in the etiopathogenesis of periodontal disease cause pro inflammatory cytokine release and complement activation. Periodontal disease may have an effect both on major blood vessels initiating atherosclerosis as well as indirect effects that stimulate changes in the cardiovascular system especially coronary or cerebrovascular arteries. It is stated that the subgingival microflora and the continuous latent bacteremia and endotoxemia originated from the periodontal pockets might be responsible for the damage of the vascular endothelial integrity, platelet function and, blood coagulation establishing a causal relationship between periodontitis and CAD [5].

Our study utilized the most widely used periodontal index (Russell Index) in epidemiological surveys worldwide. The Russell periodontal Index (1956) addresses both gingival soft and hard tissue destruction, with emphasis on marked gingival inflammation, which makes reversible marked inflammation equivalent to irreversible periodontal destruction in the calculation of the index [6]. Despite significant association between PD and coronary artery disease, there are so many Indian studies conducted on CAD but still, there is a paucity of recent studies focusing on the CAD with reference to periodontal disease in our city. Therefore, we conducted a study to highlight the importance of periodontitis and other risk factors for CAD among urban adult population of Delhi.

Objective

To study the periodontitis and other risk factor correlates of CAD among the adult urban population.

Methods

Data was collected through medical records of cardiac evaluation and by face-to-face interview method using pretested semi-structured questionnaire having questions pertaining to socio demo-graphic details, tobacco use and history of CAD. Periodontal disease was assessed by clinical examination using Russell Index and validated questionnaire for periodontal disease [7]. The semi-structured questionnaire included three sections as followings:

- i) Demographic profile: Age, sex, income and education status.
- ii) Russell Index: It was intended to estimate the severity of periodontal diseases by measuring the presence or absence of gingival inflammation, pocket formation and masticatory function. The scale of values ranges from 0-8 with increasing prevalence and severity of the disease. All the teeth presents were examined. All the gingival tissue circumscribing each tooth (i.e., all the tissue circumscribing a tooth is considered a scoring or gingival unit) was assessed for gingival inflammation and periodontal involvement. Scoring Criteria of Russell chose the scoring values (0,1,2,6,8) in order to relate the stages of the disease in an epidemiological survey to the clinical conditions observed. Scheme and distribution of population according to clinical condition and individual

PI Score is given in (Table 2) of Index was calculated using the formulae given below [8].

Calculation of the Index = sum of individual PI score/No. of teeth present

Based on the inclusion criterion for cases and assuming 10% refusal rate, 30 cases of CAD were recruited from the medicine OPD. In a routine OPD on weekdays, the dentist used to recruit the diagnosed CAD patients. Individuals with a medical indication for cardiac evaluation (coronary angiography or prior history of CAD, with ECG changes suggestive of CAD) were invited to participate in the study. After obtaining informed consent, data was collected by standardized in-person interview. This was followed by dental check-up. The whole procedure was completed in two hours. Hence two patients of CAD were recruited on daily basis. The intra-oral soft tissue was also examined for the presence or absence of stains, and premalignant lesions condition. Russell's periodontal index was used to estimate the presence or absence of gingival inflammation and its severity, loss of periodontal attachment, and mobility of teeth. All the study subjects were examined for gingival inflammation and periodontal involvement [9].

Controls recruited from dental OPD were matched with cases based on demographic characteristics. A total of 113 controls were approached of which 3 were excluded as on cardiac evaluation they were found to have signs of CAD. Hence 110 controls were recruited. Before conducting a dental check-up, another dentist who was not aware of the study was asked to encourage patients to participate in the survey. After informed consent from the patient, he/she was subjected to dental assessment and blood pressure checkup followed by an interview. Those who refused were treated as routine OPD patients. The presence of chronic periodontitis was determined by clinical examination that included visual and tactile inspection performed by a periodontist. The periodontist evaluated the amount of dental plaque, calculus, gingival bleeding, exudation, and signs of inflammation.

I Study Design and Study Population

The present study was a clinic-based case control study carried out in medicine and dental outpatient departments (OPD) of Hamdard Institute of Medical Sciences & Research and associated HAH Centenary Hospital, New Delhi. Minimum sample size was calculated to be 140, at 80% power, 95% confidence interval. Odds ratio of periodontal disease and CAD from literature was taken as 6.5 with 66% of controls having no periodontal disease [6]. The ratio of cases to controls was taken to be 1:3. Study population constituted all the adults aged above 18 years attending the OPD.

II Exclusion Criteria

Those using immunosuppressive drugs, had autoimmune or neoplastic diseases, history of infective endocarditis, pregnant or lactating, mentally challenged were excluded from the study. Besides above conditions if anyone who did not give consent for the study or was unable to respond to the questions (due to hearing problem or any other reason) was also excluded.

III Operational Definitions

Coronary artery disease was defined as:

- i) Definite CAD: Evidence of prior acute coronary syndrome (ACS), history of undergoing coronary angioplasty or CABG, more than 50% epicardial coronary stenosis by invasive coronary angiography, ECG with pathological Q waves (any of Minnesota code 1-1-1 to 1-1-7 or 1-2-1 to 1-2-5 or 1-2-7), imaging evidence of loss of viable myocardium that is thinned and has a motion abnormality, in the absence of a non-ischaemic cause, RAQ angina in addition to ECG changes (any of Minnesota codes 4-1-1, 4-1-2, 4-2 or 5-1, 5-2) or RAQ angina plus positive treadmill ECG (exercise-induced horizontal or down-sloping ST depression of ≥ 1 mm at 80 mms from J point) or inducible ischaemia on stress imaging [8].
- ii) Probable CAD based on: RAQ angina without significant ECG changes, ECG changes (any of Minnesota Code 4-1-1,4-1-2, 4-2 or 5-1, 5-2) without RAQ angina or positive treadmill ECG without RAQ angina [8].

IV Statistical Analysis

The data was analysed using SPSS 21.0 version. Chi square test was used for ascertaining significance. Multiple logistic regression was used for

predicting CAD. For the purpose of analysis, we have grouped 0, 1, 2 as category 1 and labelled RI less than 2 and 3, 4 as RI 3 and above.

Results

Of the 140 study participants, 30 (21.4%) were recruited as cases and 110 (78.6%) as controls. Males predominated the study population at 87% and females were 12.1%. Around less than half (45%) belonged to the age group of 40-59 years followed by 18 -39 and >60 years at 30% and 25.7% respectively. Literacy was observed as high as 77.1% of the study population. Almost half of the population were hypertensive and more than two third (67.1%) were non-diabetic. There is no significant difference was found among the cases and controls with respect to variable such as age, gender, literacy status.

Among the study populations, just more than half (57.8%) were smokers and 47.8% were SLT users. It is encouraging that only a few (8.5%) were using both forms of tobacco. Despite tobacco usage; a majority (86.4%) did not show the presence of premalignant lesions. Among the cases 73.3% were SLT users, 53.3% were smokers and only 16.6% were using both forms; whereas 43.5% were not using tobacco in any form in the control group (Table 1).

Table 1: Baseline demographic with periodontitis and other conventional risk factor among cases and control group.

	CAD present	CAD not present	Total	P value
Total	N=30(%)	N=110(%)	N=140	
Percentage N=140(%)	21.4%	78.6%	100.0%	
Sex				
Male	28(93.3%)	95(86.6%)	123	0.53
	20%	86.3%	87.8%	
Female	2(6.6%)	15(13.6%)	17	
	1.4%	10.7%	12.1%	
Age groups (years)				
18-39	5(16.6%)	37(33.6%)	42	0.35
	3.5%	26.4%	30%	
40-59	13(43.3%)	49(44.5%)	62	
	19.2%	35%	44.2%	
≥ 60	12(40%)	24(21.8%)	36	
	8.5%	17.1%	25.7%	
Literacy status				
Literate	23(76.6%)	85(77.2%)	108	0.99
	16.4%	60.7%	(77.1%)	
Non literate	7(23.3%)	25(22.7%)	32	
	5%	17.8%	22.8%	
Smokeless tobacco				
Users	22(73.3%)	49(44.5%)	71	
	15.7%	35%	50.7%	0.05
Non users	08(26.6%)	61(55.4%)	69	
	5.7%	43.5%	49.2%	
Smokeless tobacco frequency (times per day)				
Mean \pm SD	4.02 \pm 5.3	2.1 \pm 2.4	2.19 \pm 2.4	0.000001
Duration of SLT use in years				
Mean \pm SD	6.2 \pm 7.95	5.4 \pm 6.6	6.1 \pm 7.3	0.19

Quantity of SLT use (in pack years)				
Mean ±SD	1.14+ 1.43	1.09+ 1.02	1.09+_1.1	0.05
Smokers	16(53.3%)	44(40%)	60	0.03
	11.4%	31.4%	42.8%	
Mean ±SD	1.12+ 1.40	1.06+1.04	1.06±1.04	
Hypertension present				
Yes	21(70%)	44(40.1%)	71	0.012
	15%	31.4%	50.7%	
No	09(30%)	56(50.9%)	69	
	15.9%	40%	49.2%	
Diabetes				
Yes	16(53.3%)	30(27.2%)	46	0.007
	11.4%	21.4%	32.8%	
No	14(46.6%)	80(72.7%)	94	
	10%	57.1%	67.1%	
Russell index				
Mean RI				0.01
≤ 2	3(10%)	30(27.2%)	33	0.04
	2.1%	0.7%	(23.5%)	
≥ 3	27(90%)	80(72.7%)	107	
	19.2%	57.1%	(76.4%)	
Premalignant lesion				
Present	6(20%)	13(11.8%)	19	0.56
	4.2%	9.2%	13.5%	
Absent	24(80%)	97(88.1%)	121	
	17.1%	69.2%	86.4%	

Independent t-test was used; ^bOne way ANOVA was applied.

Table 2: Scheme of calculations and distribution of population (cases and controls) as per the Russell Index score.

Russell's Index Score	Cases	Control
Stages -0 Clinically normal periodontal tissues (0-0.2)	0	0
Stage -1 Simple gingivitis (0.3-0.9)	0	11(10%)
Stage-2 Beginning Destructive (1-1.9)	3(10%)	19 (17.2%)
Stage -3 Established destructive periodontal disease (2-4.9)	17(56%)	68(61.8%)
Stage-4 Terminal Periodontal Disease (5-8)	10(33.3%)	12(10.9%)

Among the total subjects, 76.4% showed a RI score of ≥3 indicating the presence of established destructive and terminal periodontal disease and 23.5% fell in the category of beginning destructive periodontal disease. It was observed that periodontitis was severe (in terms of RI) among cases than controls. 90% of cases showed a score of ≥3 as compared to 57.1% of control group. This was statistically highly significant (P < 0.04). The Mean Russell score for cases was 3.98 ± 0.70 and for control group, it was 3.11 ± 0.68 (Table 2).

Univariate analysis revealed CAD to be significantly associated with periodontitis frequency, quantity of risk factors such as SLT use, smoking and lifestyle disorders such as diabetes and hypertension. Variables significantly associated in univariate analysis were further analysed by applying regression model.

Table 3: Multinomial logistic regression by taking total Russell index and other risk factors as independent variable.

Independent variable	Logistic regression analysis Adj OR	95% CI		P value
SLT users	.389	.062	2.456	0.31
Non users	1			
Smokers	.065	.006	.677	0.02
Non users	1			
Russell Index ≤2	.075	.006	.991	0.05
≥3	1			
SLT packets quantity	3.258	1.189	8.929	0.02
SLT frequency	1.036	.790	1.359	0.80
Hypertension present	3.482	1.133	10.697	0.03
Absent	1			
Diabetes present	2.834	.782	10.272	0.11
Absent	1			

On regression analysis, the factors which were found to be significantly associated with CAD were Russell Index ≤2 (OR 0.75, CI: 0.006:0.991), smoking [Odds ratio (OR) 0.65, Confidence interval (CI): 0.006-0.677], Smokeless tobacco (SLT) use (OR 0.389, CI: 0.062-2.456), SLT quantity (OR 3.258, CI: 1.189-8.929), SLT frequency (OR 1.036, CI:

0.790-1.359), Hypertension (OR = 3.482 (95% CI: 1.133-10.697), Diabetes (OR=2.834, CI: 0.782-10.272) (Table 3).

Discussion

There has been a shift from viewing periodontitis as a localized oral health problem to establishing its connections with systemic diseases. Literature reports that people with periodontal diseases are twice as likely to suffer from coronary artery disease as those without periodontal diseases [10-14]. An increase in prevalence of CAD in past 2 decades has led to exploring periodontal disease as a possible risk factor. Epidemiologic studies across India indicate a prevalence of CAD between 7% and 13% in urban India [8, 15, 16]. Among Indians, more than 60% people with CAD have higher plasminogen activator inhibitor (PAI-1), C-reactive protein and homocysteine levels that cannot be attributed to conventional risk factors [6]. Traditional risk factors such as smoking, dyslipidemia, hypertension, and diabetes mellitus do not explain the presence of coronary atherosclerosis in a large number of patients. Localized infection resulting in a chronic inflammatory reaction has been suggested as a mechanism underlying CAD in these individuals. Detection of systemic inflammatory markers plays an increasingly important risk assessment for vascular events such as MI and cerebral infarction. Acute phase reactant proteins (C-Reactive protein and fibrinogen) are inflammatory markers produced by liver to produce which in turn induce production of tissue factor. Tissue factor activates the coagulation pathway and increases blood coagulability. CRP also stimulates the complement cascade further exacerbating inflammation. Elevations in serum CRP are well accepted risk factors for cardiovascular disease [17].

In a study done on subjects with different degrees of gingivitis and periodontitis and those having clinically normal periodontium, a positive correlation between moderate to severe degrees of inflammation in gingivitis and periodontitis, the active tissue destruction in acute gingival or periodontal lesion and the presence of CRP in serum was observed [18]. Recent studies have focused on periodontitis as a potential trigger for systemic inflammation. The periodontium, when affected by periodontitis, acts as a reservoir of endotoxins (LPS) from gram negative organisms. Endotoxin pass readily into the systemic circulation and precipitate many downstream processes linked with cardiovascular diseases. Oral organisms may be involved in coronary thrombogenesis. Platelets aggregation-associated protein (PAAP) are expressed on some strains of bacteria which cause aggregation of platelets. Platelets selectively bind some strains of *Streptococcus sanguinis*, a common component of supragingival plaque, and *Porphyromonas gingivalis*, a pathogen closely associated with periodontitis [19].

Thus, periodontal disease may have both direct pathogenic effects on major blood vessels (e.g., Atheroma formation) as well as indirect effects that stimulate changes in the CVS (e.g., Elevation of systemic inflammatory responses). In a study conducted by C M Ardilla *et al.* in 2015, a link between periodontopathogens such as *T. forsythia* and higher levels of serum total cholesterol and LDL was established. Chronic infection with these organisms was correlated with an increase in the atherogenicity of low-density lipoprotein that may subsequently increase the risk of atherosclerosis in patients with periodontal disease [20]. These reports are in conjunction with the multivariate analysis of our study which affirms periodontitis and smoking as conventional risk

factors for coronary artery disease. Clinical features of periodontitis among smokers and/or smokeless tobacco users assume significance in the light of research findings that indicate periodontitis independently as a risk factor for CAD/ cardiovascular disease [21].

According to the recent Global Adult Tobacco Survey (GATS, 2016-2017), Indian adult males are more likely to use tobacco (42.4%) as compared to their female peers (14.2%) [22]. Our study also reported similar results with the predominance of males over females. Despite the higher literacy rate higher tobacco usage was observed in both cases and controls. This is in contrast to study conducted in Delhi by M. Parashar *et al.*, which reports significantly higher prevalence of tobacco consumption as risk factor for CAD among the less educated, older age groups especially middle-aged males, and agricultural and labour workers [23]. Prevalence of SLT use is higher than smokers among the study groups which is in line with the GATS 2016-17 results. Our study has more SLT users in case group as compared to controls. When compared to smoking; chewing tobacco is a convenient substitute; SLT can be used simultaneously while working slowly releasing the tobacco products and absorption by the oral mucosal tissues [24]. Literature reports of studies wherein current use of spit tobacco was statistically significantly associated with death from coronary heart disease, stroke, and diseases of the respiratory, digestive, and genitourinary systems [25].

In our study none of the cases showed the presence of normal gingival tissues or simple gingivitis. Majority suffered from established destructive or terminal periodontal disease whereas almost half of the control group suffered from either of the same. Kamili *et al.* in their study also reported tobacco users to have 2.43 times risk for periodontal disease when compared with non-tobacco users with odds ratio (OR) 2.43 (95% confidence intervals) [8]. The observation of simple gingivitis and beginning of destructive periodontitis was greater in cases as compared to control which could be attributed to the varied significant risk factor present among the cases as compared to controls in the present study. Premalignant lesions were found to be present in around 13.5% of the population in our study. Similar results were reported by Thavarajah *et al.* where in the premalignant lesions such as oral submucous fibrosis (OSF), leukoplakia, and erythroplakia ranged between 2-10% [26]. Both CAD and oral malignancy can be easily avoided if detected early and patient being counselled for tobacco cessation in his own interest. It is pertinent to mention here that tobacco plays a key role in the etiopathogenesis of both atherosclerosis and oral malignancy. This concept of cardio-oncology is fast emerging in clinical cardiology [9].

Limitations

Increasing the sample size of the study may unravel better statistical correlation of CAD with other cardiovascular risk parameters. Better techniques of detecting silent CAD, evaluation of newer risk factors and genetic predisposition are the points that need to be emphasized more in planning future studies.

Conclusion

The RI Score were found to be more among the CAD patients than control group. Findings in the present study suggest the relationship between CAD and periodontal disease which is in line with most of the

studies conducted in other areas. It is recommended that due to common risk factors CAD as well as the periodontal disease among these patients can be managed jointly. The relationship between the periodontal and systemic disease is a two-way relationship. Hence, it is desirable that healthcare professionals and dentists promote self-care for systemic health conditions as well as oral health education for the management of both systemic health conditions and periodontal health, especially among patients with a long duration of systemic health conditions. Therefore, there is an immediate need to raise awareness among the general population about these risk factors, promote the correct diet and physical activity, and at the same time develop guidelines for screening and preventive therapeutic programmes to identify and manage individuals at high risk for future CAD.

Consent

Written informed consent was obtained from the respondents after explaining the nature and objectives of the study in their own local language.

Ethical Approval

Necessary permission to conduct the study was obtained from the concerned authority of the construction site. The study was approved by the Institutional Review Board and Institutional ethical committee.

Conflicts of Interest

None.

Funding

None.

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