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ASSESSMENT OF PERIODONTAL STATUS, C-REACTIVE PROTEIN AND FIBRINOGEN LEVELS IN PATIENTS WITH PERIODONTITIS AND MYOCARDIAL INFARCTION

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ABSTRACT

Aim: The aim of the study was to assess and compare the periodontal status, C-reactive protein and plasma fibrinogen levels, in periodontitis patients with and without myocardial infarction in association with the other confounding factors.

Materials and Methods: The study comprised of 86 subjects aged 30 years and above divided into 2 groups: MI+P: Patients with Myocardial Infarction with periodontitis and P:

periodontitis. Medical history was taken and all the confounding factors were recorded including the history of hypertension and diabetes. All the subjects underwent assessment and comparison of periodontal status such as Plaque index (PI), Periodontal index (Pi), Clinical attachment level (CAL) and Probing Pocket depth (PPD) along with the estimation of C-reactive protein and fibrinogen levels.

Results: The periodontal parameters were found to be increased in patients with myocardial infarction and periodontitis with more possibility of the presence of the various confounding factors associated with MI+P group. C- reactive protein and fibrinogen levels were also found to be elevated in these patients with significant p-value. Plaque index and fibrinogen level showed a significant odds ratio in comparison with the other confounding variables.

Conclusion: Our study confirms an increase in the severity of periodontal status in patients with myocardial infarction with periodontitis. Increased C- reactive protein and elevated fibrinogen levels were also observed to be increased indicating them as potential inflammatory markers for myocardial infarction (MI). In future, more prospective studies with periodontal intervention are needed to further authenticate the role of periodontitis with respect to the other confounding factors considering C- reactive protein and fibrinogen levels as markers of inflammation.

Keywords: myocardial infarction, c-reactive protein, fibrinogen, periodontitis, inflammation

Introduction

Periodontal diseases are the most common bacterial infections occurring in adults with poor oral health and mostly in those who delay seeking dental care. These chronic oral infections may also influence the overall health of the person leading to various systemic diseases.[1] The number of reports associated with oral infections and systemic diseases have been increasing steadily in the last few years. [2,3,4] Out of these, reports associating periodontitis with cardiovascular diseases have occupied a significant place.[3,4] Both, periodontitis and cardiovascular diseases like undesirable weeds share a common soil. These are more likely to occur in males who are old, smokers, socially isolated, have lower educational status, poor financial resources and are hypertensive. Even in this era of modern antibiotics, groups of bacteria can selectively colonize on injured or defective heart valves and cause life-threatening diseases.[5] More than 700 species of bacteria create an exquisite microbial ecological system in the form of biofilm in oral cavity. The bacteria form biofilm on the surface of the teeth and continuously shed virulent components and metabolites especially lipopolysaccharides. The host in turn responds by forming a dense infiltrate of inflammatory cells. The engagement between infection and immunity has a marked effect on the vascular endothelium which results in platelet aggregation and adhesion, cholesterol deposition and formation of lipid laden cells, both in the immediate area and in other cells distant from the periodontium.[6]

Cardiovascular disease is known to be a major cause of death in the world. There are a number of risk factors for this disease. Apart from the known risk factors such as smoking, serum cholesterol concentration, hypertension and diabetes, periodontitis may be one of the risks for the development of cardiovascular disease.[7] Various inflammatory markers have shown to be associated with cardiovascular diseases and oral diseases such as periodontitis.[8] Chronic bacterial infections in the form of gingivitis and periodontitis increases the systemic inflammatory markers such as plasma fibrinogen level and white blood cell count which are

consistent strong predictors of cardio vascular diseases.[9] Myocardial infarction and other types of tissue injury generate changes in plasma protein as a part of the acute-phase response.[10] Periodontitis also elicits a sufficient vascular challenge to trigger a mild systemic acute response with an increase in C-reactive protein levels, a marker of systemic inflammation.[11] Limited literature exists stating the role of periodontitis with respect to the other confounding factors considering C- reactive protein and fibrinogen levels as markers of inflammation in the progression of periodontitis and myocardial infarction. Hence in the present study, we aimed to assess and compare the periodontal status, C-reactive protein and plasma fibrinogen levels in patients with periodontitis and without myocardial infarction.

Materials and methods

Study design

The study population was recruited during the time period of January 2022 to November 2022. The study comprised of 86 subjects aged 30 years and above and divided into 2 groups: Group Myocardial Infarction with periodontitis (MI+P) consisted of 43 subjects (36 males and 7 females) suffering from myocardial infarction with stage II grade B periodontitis and Group periodontitis (P) - consisted of 43 subjects (37males and 6 females) with periodontitis only. In group MI+P patients, myocardial infarction was confirmed by a senior cardiologist by estimating an increase in serum creatinine phosphate kinase isoenzyme MB, and change in electrocardiogram. Patients with periodontitis in both the groups were diagnosed based on the following criteria: generalized interdental CAL ≥5mm with radiographic bone loss extending to middle third of the root and beyond, tooth loss due to periodontitis present ≤4 teeth, probing pocket depth (PPD) ≥6mm, vertical bone loss ≥3mm with class II/III furcation and moderate ridge defect with clinical attachment loss < 2mm over 5 years based on 2017 World workshop classification of Periodontal disease.[12] Subjects, apart from MI and diabetes having other systemic conditions such as steroids, antibiotics or anti-inflammatory drugs taken recently within 6 months of investigation or who have undergone any recent periodontal treatment within the 3 to 6 months, pregnant and lactating women were excluded from the study.(figure 1) Diabetes was included in this study since it is a major confounder for both MI and P. The participants were explained about the investigating procedures and a written informed consent was taken from them before the commencement of the investigation. The study was approved by "Institutional Ethical Committee" MAHER – Deemed to be University, Chennai (MADC/IEC-1/023/2021-SECTION A).

Periodontal Examination:

Thorough medical history was taken with appropriate dental and medical evaluation. Intra oral examination was carried out in artificial light using a mouth mirror. The subjects were seated comfortably in an upright position on a dental chair and clinical parameters were recorded by two trained investigators (MB and JM) using Williams graduated periodontal probe to the nearest of the millimetres. All the subjects underwent periodontal evaluation of Plaque index (PI) [13], Periodontal index (Pi) [14], Clinical attachment level (CAL) [15] and Probing Pocket depth (PPD) [16].

Molecular Analysis:

Estimation of plasma fibrinogen levels:

Estimation of plasma fibrinogen level was done by functional clotting assay using "Tulip fibrinogen kit." Blood samples were obtained by venipuncture of the cubital vein and

transferred to the sterile test tubes. The samples were then allowed to clot in order to separate the serum from the RBCs. Centrifugation was done for 3 to 5 minutes and separated serum was transferred to the clean test tubes with the help of micropipettes. For estimation of plasma fibrinogen levels, all reagents and samples were brought to room temperature. The thrombin reagent was reconstituted with 1mm of distilled water. After a waiting period of 5 minutes, the vial was swirled gently till the solution attained homogeneity and used for estimation. The fibrinogen calibrator stock solution was diluted with Oweren's buffer. 1:10 dilution of plasma specimen was prepared with Oweren's solution. 0.2ml of the plasma sample was then added to a test tube at 37ºC. To the same test tube, 0.1mL of prewarmed (37ºC for 1 minute) thrombin reagent was added and the stop watch was started simultaneously. The watch was stopped at the first appearance of the fiber web as the gel clot began to form. The time was recorded in seconds. The values were calculated from the time taken for known standards. The coagulation time was proportional to the fibrinogen concentration which allowed the estimation of plasma fibrinogen.

Estimation of C-reactive protein In Patient's Blood Serum:

Rhelax C-reactive protein slide test for detection of C-reactive protein is based on the principle of agglutination. The blood samples were collected, centrifuged for 15 minutes and separated serum was transferred to clean test tube with the help of micropipette. One drop of serum was placed on a glass slide using disposable pipette followed by one drop of Rhelax C-reactive protein latex reagent and care was taken not to touch the dropper tip to the liquid on the slide. Serum and Rhelax C-reactive protein latex reagent were then mixed uniformly over the entire circle marked on the slide with the help of the provided mixing stick. Stop watch was started immediately and the slide was rocked gently back and forth observing for agglutination. Agglutination occurred (within 2 minutes) was recorded a positive test result and indicated the presence of C- reactive protein in the specimen. If C - reactive protein concentration was greater than 0.6 mg/dl a miscible agglutination was observed. No agglutination was observed when the concentration was less than 0.6 mg/dl. If the sample showed no agglutination, the result was recorded as negative that is absence of C- reactive protein. Positive reaction was graded based on the agglutination as follows: 1+ or less: 25% less agglutination; 2+: 50% agglutination; 3+: 75% agglutination; 4+: complete agglutination.

Statistical Analysis:

Statistical Package for Social Science (SPSS, (IBM Corporation, Chicago, IL, USA) software program version 17) for Microsoft Windows was used to statistically analyse the obtained data. Normal distribution of data was observed. Descriptive statistics were presented with the aid of numbers and percentages. Chi-square statistical test was also done for the non-quantitative variables and p-value was derived. Student's 't' test was used to compare means of quantitative variables such as fibrinogen levels, serum cholesterol, number of teeth present, plaque index, periodontal index, clinical attachment level and probing pocket depth. Stepwise multivariate logistic regression analysis was carried out to assess the independent effect of each variable while controlling for the effects of other confounding factors with myocardial infarction. It is mainly used to analyse the binary response data based on the multiple logistic regression model. This method can simultaneously control for the potential

confounding effects of several covariates. In stepwise logistic regression analysis, we calculated Odds ratio to assess the strength of association between the variables. p value<0.05 was considered as a level of significance.

Results

Table I: Comparison of Mean and standard deviation of the quantitative variables between MI+P and P groups:

Variable	MI + P (No of participants: 43)		P (No of participants: 43)		P values
	Mean	SD	Mean	SD	
Age (years)	57.7674	10.7301	56.0465	9.6707	0.75 ^{NS}
Weight (kg)	61.16	5.93	59.93	3.89	0.51^{NS}
Number of teeth present	25.32	7.25	28.95	5.28	0.01*
Plaque index	2.60	0.26	1.44	0.65	0.001*
Periodontal index	6.48	0.67	2.85	2.54	0.001*
Probing Pocket depth	5.69	1.13/	3.74	1.54	0.001*
Clinical attachment level	6.21	1.28	3.81	1.59	0.001*
Total Cholesterol (mg/dl)	176.95	36.88	158.81	25.95	0.01*
Fibrinogen (mg/dl)	426.67	48.41	237.6	48.09	0.001*

NS- p value non-significant, *- p value significant

Mean age of periodontitis patients with myocardial infarction (MI+P) was 57.7 years and P group was 56.04 years. Similarly, mean weights of the groups MI+P and P were 61.16 kg and 59.93 kg respectively. They were found to be similar and hence statistically non-significant. The mean of 'number of teeth present' in groups MI+P and P were 25.32 and 28.95 respectively and was found to be significant with p=0.01. The mean plaque index in MI+P was 2.60 and P was 1.44 which was also significant at 0.1 % level (p=0.001). The mean periodontal index of MI+P was 6.48 and P was found to be 2.85 which was significant at p=0.001. Similarly, the mean pocket depths in MI+P and P were 5.69 and 8.74 respectively which indicated that there is an association at 0.1% level (p=0.001). Likewise, the mean clinical attachment level in MI+P was 6.21 and for P it was found to be 3.81 which was again significant at 0.1% level (p=0.001). Mean total cholesterol value for MI+P was 176.95 mg/dl and for P was 158.81 mg/dl. This was also significant at 1% level (p=0.01). Mean fibrinogen level for MI+P was found to be 426.67 mg/dl and for P it was 237.6 mg/dl which indicated a significant association at 0.1% level (p=0.001). (Table I)

Table II: Comparison of the non-quantitative variables among MI+P and P groups :

	MI+P	P	

		Number	%	Number	%	Chi-square value (x^2)	P value
Sex (Gender)	Males	36	83.7	37	80	5.45	0.62^{NS}
	Females	7	16.2	6	13.9		
Family history of cardiac diseases	Present	3	7	0	0	3.10	0.78^{NS}
	Absent	40	93	43	100		
Socio economic status	Medium/ rich	17	39.5	40	93	27.52	0.001*
	Poor	26	60.4	3	7		
Tobacco chewing habit	Present	9	20.9	0	0	10.052	0.002*
	Absent	34	79	43	100		
Smoking habit	Present	19	44.1	6	13.9	9.53	0.002*
	Absent	24	55.8	37	86		
History of alcohol consumption	Present	15	34.8	11	25.5	0.882	0.348^{NS}
	Absent	28	65.1	32	74.4		
Hypertension	Present	17	39.5	3	7	12.77	0.001*
	Absent	26	60.4	40	93		
Diabetes	Present	15	34.8	0	0	18.16	0.001*
	Absent	28	65.1	43	100		
Brushing technique	Finger	21	48.8	1	2.32	33.6	0.001*
	Brushing once	22	51.1	27	62.7		
	Brushing twice	0	0	15	34.8		
C- reactive protein	-ve	26	60.4	43	100	21.18	0.01*
	1 +	5	11.6	0	0		
	2 +	6	13.9	0	0		
	3 +	3	6.9	0	0		
	4 +	3	6.9	0	0		

NS- p value non-significant, *- p value significant

On comparing the study variables among the two groups, sex, family history of cardiac diseases and history of alcohol consumption were found to be insignificant. Rest all the variables such as socio-economic status, tobacco chewing, smoking, hypertension, diabetes, brushing technique and C- reactive protein were significant with p value <0.05 (Table II)

Table III: Results of step wise multivariable logistic regression analysis

Independent variable	Regression coefficient	Standard error	P value	Odds ratio
Fibrinogen	4.2391	1.21	0.0005*	69.3

Plaque index	3.8676	1.47	0.0086*	47.8

*- p value significant

Step wise multivariable logistic regression analysis was done to evaluate the independent effect of each variable while controlling the other confounding factors associated with myocardial infarction. The other confounding factors recorded in this study such as family history, socio economic status, total cholesterol, habits such as tobacco chewing, smoking, alcohol consumption, hypertension, diabetes, brushing technique, plaque index, periodontal index, probing pocket depth, clinical attachment level, fibrinogen level and C-reactive protein value were included in this analysis. Age, sex and weight were excluded as these variables were more or less similar in the study. The variables were recorded according to the following criteria: family history: present / absent; total cholesterol: >220mg/dl/<220mg/dl; brushing technique: finger / brush; plaque index: >0.9 / <0.9; C-reactive protein value: +ve / -ve; socio economic status: poor/rich or medium; hypertension: present / absent; type II diabetes mellitus: present / absent; smoking habit: present / absent; alcohol drinking habit: present/absent; tobacco chewing: present / absent; periodontal index: > 0.9 / <0.9; probing pocket depth: ≥ 5/<5; clinical attachment level: >3 / <3; plasma fibrinogen level: > 400 mg/dl/<400mg/dl. (Table III)

We found that fibrinogen level and plaque index were significant with P value 0.0005 and 0.0086 respectively and all other included variables became insignificant. The odds ratio was also calculated which was found to be 69.3 and 47.8 respectively after confounding or adjusting all the other variables. This indicated that chances of developing myocardial infarction was 69 times higher for the individuals who were having fibrinogen level more than 400 mg/dl provided if the other variables were similar. Similarly, chances of developing myocardial infarction were 47 times higher in patients with plaque index more than 0.9 keeping similarity for other variables. From the above analysis we concluded that more amount of plaque and elevated levels of fibrinogen were highly contributing to the development of myocardial infarction. (Table III)

Discussion

Periodontal disease has shown to be associated with increased risk of coronary heart disease. It is seen that patients with periodontitis are almost twice as likely to have a fatal heart attack and three times as likely to have a stroke as patients without periodontal disease even after adjusting for known cardiovascular risk factors such as blood lipids, cholesterol, body mass, diabetes and smoking. Cardiovascular diseases, including atherosclerosis and myocardial ischemia occur as a result of a complex set of genetic and environmental factors. In periodontitis, dental plaque microorganisms disseminate through the blood vessels and contribute towards the occurrence of atherosclerosis thereby posing a risk for myocardial ischemia and infarction.[17] The present study was planned to assess the periodontal status, fibrinogen level and C-reactive protein value in the patients suffering from myocardial infarction, so as to provide evidence indicating that periodontitis may be a risk factor for MI considering the above inflammatory markers.

Mean age and **weight** were similar in both, MI+P and P groups with p-values of 0.75 and 0.51 respectively. This was in accordance with the findings of the study done by Yagnik K et al, who also found an insignificant difference in age among the groups.[18] It is stated that both periodontitis and cardiovascular diseases progress as the age increases. Literature suggests,

that the patients have a prolonged exposure to the bacterial aetiology with increase in the age with more amount of periodontal destruction. In our study, the participants in both the groups were more than 55 years of age and hence were at risk for the above diseases. However, they did not show any significant difference as the adult patients with similar age group were selected in both the groups. Likewise, weight in both the groups was also found to be similar. (Table I)

In our study, **sex** (gender) showed statistically insignificant difference with higher prevalence of myocardial infarction seen in males in both the groups when compared to females. Study done by Leng Y et al found that the prevalence may arise from the expression of Y-encoded genes and the lack of cardiovascular protective effects of estrogen, leading to male-specific cardiovascular events.[19] Family history of cardiac diseases showed an insignificant difference. Wahrenberg et al identified **family history** as a significant risk factor for the development of myocardial infarction and peripheral vascular disease.[20] In contrast, our study showed no association between family history and myocardial infarction. One reason could be that for the question "Has a doctor ever told you that you had a heart attack"? it was not known, how subjects interpreted the meaning. While heart attack implies myocardial infarction or, at most some form of coronary heart disease, most of the subjects were from the sub-urban area without significant knowledge on heart diseases and hence it was likely that they interpreted the words more broadly to include other forms of cardiac ailments and hence were unable to justify the history of MI. We found a significant association of **socioeconomic status** in the form of income between the groups. The study participants were mainly from sub-urban population that belonged to low or middle socioeconomic backgrounds. This was in accordance with the study by Schultz M et al who reported that a lower socioeconomic status was associated with a higher risk of cardiac disorders.[21] De Mestral C et al echoed these findings claiming that in higher-income countries, socioeconomic status is a determinant of cardiovascular risk.[22] It is understood that subjects with low-income group with less knowledge of dietary habits are mostly under nourished and thus can be prone to the cardiac diseases such as MI. (Table II)

Our results showed a strong relation between **smoking habit and tobacco** with myocardial infarction. MI+P group was mainly chronic smoker. Our findings were consistent with of Silva H et al who showed that MI participants in his study were aged and were smokers.[23] It is shown that smoking has a deleterious effect on fibroblast function, chemotaxis and phagocytosis by neutrophils, immunoglobin production and peripheral vasoconstriction. Smoking tends to mask gingival inflammation by constricting the blood vessels of the gingiva as well as coronary arteries. These substances rapidly penetrate epithelium and affect fibroblasts, decreases the intestinal absorption of calcium thereby affecting osteoblastic activity, causing increased bone loss and producing endothelial irritation through noxious agents. These in turn stimulates the production of of pro-inflammatory cytokines which may affect the immune system. It may increase the arterial wall stiffness which may in turn effect the likelihood of atherosclerosis and myocardial infarction. Thus, smoking is increasingly accepted as a shared risk factor for both, periodontitis and MI. We found no association of **alcohol** between the groups since the participants in both groups were from sub-urban area from the same socioeconomic group and thus had the same frequency of alcohol intake. Ilic M et al also found a positive

correlation between alcohol consumption and cardiovascular disease.[24] He stated that the daily consumption of alcoholic beverages was the recognised risk factor for cardiovascular disease. However, his questionnaire did not ascertain how many alcoholic drinks were consumed daily hence could not associate the amount of daily alcohol consumption with likelihood of cardiovascular accidents. (Table II)

A significant association of **hypertension** was found between the groups. This was in accordance with the study done by Leong XF et al who stated that hypertension is one of the major risk factors for cardiovascular diseases.[25] Oxidative stress and endothelial dysfunction are among the critical components in the development of hypertension which plays a significant role in periodontitis. Inflammation has received much attention recently and may have a pivotal role in hypertension. In our study, the subjects due to improper diet, smoking and alcohol consumption having more severe periodontal inflammation were found to have a higher blood pressure and were mostly seen in MI+P group. The reason could be that hypertension mainly results in alterations in blood flow in the vessels leading to focal intimal thickenings and producing characteristic atheromatous plaque. It may further cause narrowing of the lumen, leading to insufficient supply of blood to the heart causing myocardial infarction. Thus persistent hypertension may be regarded as a potential risk factor for myocardial infarction.

Diabetes mellitus was also found to be strongly associated among the groups We found that most of the MI+P patients were diabetic as compared to P group. Liccardo D et al also reported a higher diabetic status in MI patients.[26] It is assumed that this association may be due to the fact that diabetes affects vessels of all size, from aorta to the smallest arterioles and capillaries. Hyperglycemia may itself be injurious to intima and de-arranged arterial wall metabolism may therefore set the stage for atherosclerosis and myocardial infarction. Diabetes induces platelet abnormalities. The platelets adhere to the endothelium lining of the blood vessels and causes accumulation of collagen and proteoglycans leading to the development of atheromatous plaque which might lead to myocardial infarction. Diabetes is considered to be a major risk for both MI and P. In our study subjects mostly consumed more starch intake in the form of rice and hence could be one reason for them to be a diabetic.

More number of subjects with myocardial infarction and periodontitis in our study showed **improper brushing habit**. Our findings were in accordance with de Oliveira C et al who reported that improper brushing habit could lead to series of cardiovascular events.[27] In our study, the subjects participated had an inadequate knowledge of maintaining proper oral hygiene. They cleaned their teeth with a finger or brushed with an improper technique. As a consequence, more amount of plaque was accumulated which could be a pre-disposing factor for atherosclerosis and myocardial infarction. Another reason could be that our documentation of periodontal and medical parameters were taken after the occurrence of myocardial infarction event in these individuals and it is possible that the oral hygiene practiced by these hospitalized patients even with the additional help could be deficient. (Table II)

We found a significant difference in the number of teeth present among the groups. Subjects with MI+P had **lesser number of teeth present** as compared to P. This was in accordance with Lee HJ et al who found a significant tooth loss in patients with MI.[28] Liljestrand et al and Joshy et al also considered tooth loss to be a simple and objective proxy

for the accumulated inflammatory burden of oral disease and was independently associated with cardiovascular events and mortality.[29,30] Cheng CL et al did a meta-analysis of 879,084 subjects found that an increase of 1 missing tooth was associated with a 1.5% increment in coronary heart disease risk and a 1.5% increment in stroke risk.[31] Two main pathways through which tooth loss can attribute to myocardial infarction are infection related mediators and other through diet. Since periodontal disease is one of the major determinants of tooth loss, it is possible that the relation between tooth loss and myocardial infarction was entirely a result of the association between periodontal inflammation in contributing towards associated cardiac events such as myocardial infarction. On the other hand, **diet** may be an additional potential mediator between the tooth loss and myocardial infarction. Tooth loss can lead to detrimental changes in diet, including reduced intake of provitamin A carotenoids and fibers. Edentulous participants had significantly lower fiber, fruits and vegetable intake with higher sweets and snacks consumption which would lead to obesity and many other health problems which in turn serve as pre-disposing factors for cardiovascular disease. (Table I)

When all the **periodontal parameters** such as PI, periodontal index, PPD and CAL were compared between the groups a significant difference was found. PI, PPD and CAL was seen to be significantly high in MI+P group. This clearly denotes that the periodontal parameters definitively showed a relative hike in the periodontitis patients with MI. These results were supported by World Workshop of Periodontology, 2017 which clearly indicates that CAL (severity) and PPD (complexity) are two important factors in determining the diagnosis of periodontitis.[12] Additionally, Arbes Jr SJ et al stated that according to NHANES III, patients with elevated 104 PPD results were found to have an increased risk for CAD (Odds ratio 3.8 compared to lower PPD levels).[32] Similarly, various other literature evidences suggests that periodontitis can also remain as a chronic infectio -inflammatory foci, whose severity (in the forms of clinical parameters) could denote the pathognomy towards the risk of systemic sequelae.[33,34,35] Periodontal destruction in our study was higher which could be due to the fact that the teeth with increase in probing pocket depth and attachment loss would increase the surface area for plaque accumulation. This coupled with the history of not having their teeth cleaned on a regular basis, led to a pattern of oral neglect by promoting bacterial overgrowth on the dentogingival surface which could have predisposed the subjects to myocardial infarction. During periodontitis, gram-negative micro-organisms such as *P.gingivalis* may contribute to lipopolysaccharide (LPS) mediated damage to the endothelium by priming macrophages and other inflammatory cells and generating inflammatory cytokines which may further worsens the state of cardiac events such as MI.[34] (Table I)

We found a higher **total cholesterol** levels in MI+P group which was found to be significant. This was in accordance with Yagnik et al and Tang et al, who also showed a higher significant TC level in patients with CAD and periodontitis.[18,36] Hypercholesterolemia shows a strong association with the development and progression of CHD which can also influence the underlying inflammatory mechanisms that affect the periodontal status of an individuals. Subjects in our study had a high average daily intake of sweets, snacks and saturated fatty diet with less consumption of fibrous food. This could increase the total cholesterol level. The periodontium has been described as a potential reservoir of endotoxin, cytokines and lipid mediators elsewhere in the body. The infections with gram negative

periodontal pathogens could trigger the systemic release of IL-1ß and TNF-α. The endotoxins released can induce changes in the lipid metabolism resulting in hypertriglyceridemia through increased hepatic lipoprotein production. The high levels of total cholesterol in turn get deposited in the smooth muscle cells of the intimal layer of aorta leading to MI through long term alterations in the fatty acid metabolism potentiating inflammatory cytokine production. (Table I)

In our study, the inflammatory markers such as **CRP** and **fibrinogen** levels were found to be higher in MI+P individuals as compared to P. Our findings were in consistence with Wojtkowska A et al who found a higher CRP and fibrinogen levels in the cardiovascular group.[37] Ndrepepa G et al reported that elevated CRP level increases the risk of myocardial infarction and contributes to an increased risk of complications and worsen the disease prognosis.[38] Likewise, Seringec et al found considerably higher levels of hsCRP, fibrinogen, and globulins among patients with chronic periodontitis, as well as a higher tendency of erythrocytes to aggregate than in people with healthy periodontium.[39] We determined the effects of fibrinogen and PI while controlling the other variables in multivariate analysis and found that PI and plasma fibrinogen levels were relatively higher with significant odds ratio after confounding or adjusting all the other variables. It is stated that fibrinogen participates in the thrombotic process. Being pro-inflammatory in nature, it increases the expression of adhesion molecules and stimulates production of inflammatory mediators via endothelial cells thus posing itself as a potential risk factor for MI. (Table I, II and III)

In our study, the increased CRP found in MI+P group could be due to two possible mechanisms. One pathway of model proposes that periodontal disease occurs as a joint response to local pathogens and to an underlying hyper inflammatory trait which causes elevation of systemic inflammatory mediators. Another mechanism could be an elevated systemic periodontal inflammatory response that potentiates an increase in C- Reactive protein which has a protective role to play by recognizing foreign pathogens and initiating their elimination probably by activating the classic pathway of complement. It is also known to induce IL-lα, IL-6, IL-18 and tumour necrosis factor-α, thus amplifying the inflammatory burden. On the other side, serum C-Reactive protein concentration could be related to the pathogenesis of myocardial infarction via the effects of inflammation on convention at risk factors. (Table II)

Overall, our study confirms the higher levels of fibrinogen and C-reactive protein and further supports the concept that periodontal infection has a significant role in clinically manifesting atherosclerosis and myocardial infarction after adjusting all the other confounding variables. Further, the estimation of CRP and fibrinogen may lead to early detection of the inflammatory diseases thereby preventing their further progression. These can further prove to be an important marker for chair-side diagnosis in periodontics. Also, in near future interventional clinical studies are needed to determine if the management of the oral infections in form of non-surgical therapy does reduce the overall systemic inflammatory and bacterial load thereby reducing the risk for MI. This will provide compelling scientific evidence coupled with improved health outcomes catalysing the reforms by collaborating both, dental and medical practice in order to maintain the overall health. Dentist will need to assume a larger responsibility for the overall health of the patients and eventually periodontal care may become a medical necessity.

Conclusion

The present study confirms a higher CRP and fibrinogen levels in MI with P. PI showed a sound association with the fibrinogen level with a significant odds ratio. Hence, we can infer that periodontal inflammation is a potential contributing factor to myocardial infarction. However more prospective studies in various populations are needed to confirm the association and to elucidate its nature.

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Figure 1: Study design flowchart