

## ORIGINAL ARTICLE

## PERIODONTITIS AND MYOCARDIAL INFARCTION RISK: A CASE-CONTROL STUDY

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**Objectives:** This study aimed to assess the association of periodontitis and Myocardial Infarction (MI) and contributes as a potential risk factor for its incidence.

**Methodology:** This multi-centre, case-control study enrolled 125 participants. Case group comprising of Acute Myocardial Infarction (AMI) = 55, control group consisting of non – AMI = 70. Both groups were assessed for presence of periodontitis along with specific risk factors that were recorded in a modified proforma comprising of questions pertaining to demographics, oral hygiene practices and oral eating habits. Chi-square test was used to assess association and p-value was considered significant at  $\leq 0.05$ .

**Results:** Periodontitis was found to be prevalent in 71% of Myocardial Infarction (MI) patients with an OR 4.125 (95% CI, 1.934 - 8.797) as compared to 37% in Control (non-Myocardial Infarct). Increasing age, male gender, illiteracy, unemployment/retirement, low socio-economic status, being overweight, no dental visits, and smoking (both duration & frequency) were found to be statistically significantly associated with occurrence of periodontitis and myocardial infarction in the study.

**Conclusion:** Periodontitis was found to be prevalent among the MI patients suggesting a causal link between these two conditions that can be reduced by adopting a healthy lifestyle, refraining from smoking, good oral hygiene and visiting a dentist for regular check-up.

**Keywords:** periodontitis, myocardial infarction, risk factors

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## INTRODUCTION

Periodontitis and cardiovascular diseases are two of the most chronic, prevalent and debilitating conditions that are of public health concern worldwide. Periodontitis is an oral infectious disease initiated and influenced by anaerobic bacteria and marked by gradually escalating, chronic, inflammation of the supporting structures of the tooth (periodontium) leading to its destruction.<sup>1</sup> It was declared by Global Burden of Disease study (GBD) as the 11<sup>th</sup> most prevalent oral disease in the world with a prevalence of 20 – 50% and the number is expected to rise in the years to come.<sup>2</sup> The prevalence of periodontitis in Pakistan presents no better picture than the rest of the world, with an occurrence of 53.3% in rural and 46.7% among the urban population.<sup>3</sup>

In the last two decades (2000 to 2019) more than 2 million deaths around the globe, have been attributed to ischemic heart diseases. Cardiovascular diseases have been predicted to be the foremost cause of mortality by year 2030.<sup>4</sup> According to Global Burden of Disease, less than 80% of deaths, observed in low- and middle-income countries, were due to acute myocardial infarction and other cardiovascular diseases (CVD), while prevalence of same was about 25% in the West.<sup>5</sup> Pakistan is currently facing a near

epidemic of CVDs, validated by about a quarter (25%) of its middle-aged adults exposed to CVD risk factors.<sup>6</sup> Cardiovascular diseases are a group of chronic and systemic inflammatory diseases with multiplex etiology. Myocardial infarction has been defined as the death of cardiac cells, largely due to disruption of the atherosclerotic plaque. This causes coronary artery spasm, micro dysfunction, and coronary embolism etc. leading to thrombosis and/or prolonged reduced myocardial perfusion also known as acute myocardial ischemia progressing to myocardial cell death.<sup>7</sup>

The consequences and untoward effects of periodontitis extend beyond the oral cavity. The inflammatory mediators and microbial toxins produced due to untreated periodontal diseases can disseminate into the systemic circulation, increasing the inflammatory burden and predisposing the body to systemic diseases.<sup>8</sup> This association has been verified and supported by a large body of research depicting a positive relationship between periodontitis and systemic conditions such as cardiovascular diseases, diabetes mellitus, metabolic syndromes, respiratory diseases, Alzheimer etc. and even adverse pregnancy outcomes, however local data in this regard is scant.<sup>9,10</sup> Periodontitis has been identified as an independent risk factor contributing to the initiation as well as

exacerbation of the cardiac diseases and its complications. Chronic inflammation enhances and hastens the process of atherosclerosis, accelerating the risk of plaque rupture leading to acute coronary syndromes.<sup>8</sup> Moreover a 19% increased risk of cardiovascular disease has been found to be associated with pre-existing periodontal diseases.<sup>9</sup> Both these conditions (Periodontitis & CVD) are linked via the chronic inflammatory disease pattern. Some risk factors shared between periodontitis and CVD, include a greater incidence in adult males, smokers, diabetics, and individuals with stresses and/ or a low socio-economic level.<sup>9,11</sup> Other than this, poor oral hygiene, accumulation of plaque and calculus, and deleterious oral eating habits predisposes to periodontal diseases.

Recent systematic review, meta-analysis and randomized clinical trials have concluded that periodontal treatment has beneficial effects by reducing the cardiac risk factors and enhancing endothelial function in patients with early post-infarct myocardial tissues. It is further recommended that with larger future trials, periodontal therapy may gain recognition as an advanced approach to improve cardiovascular outcomes.<sup>12</sup>

Hence, the object of this study was to find out whether periodontitis contributed as a potential risk factor for Myocardial Infarction (MI) incidence, by assessing selected demographic and oral health and hygiene risk factors association between the two conditions based on hypothesis that periodontitis is a risk factor having causative associated with MI.

## METHODOLOGY

This multi-centre case-control study was conducted from July 2020 to February 2021 at three institutes of Karachi. The cases were recruited from National Institute of Cardiovascular Diseases (NICVD) Karachi, whereas age-group and gender matched controls were selected from Ziauddin Dental Hospital and Bahria University Medical and Dental College (BUMDC) Karachi. The sample size (125) was calculated using Open Epi software version 3 keeping confidence interval of 95% and odds ratio of 3. The samples were allotted into case group (55) and control group (70) by consecutive sampling technique. The study was approved by the Ethical Review Committees of Ziauddin University and NICVD. Institutional permission was granted by Dental section of BUMDC. Inclusion criteria: Participants of both genders, aged between 25 to 70 years, admitted to the cardiac hospital (NICVD) within a week's duration with recent 1<sup>st</sup> Acute Myocardial Infarction (AMI) event: both ST- segment elevated Myocardial infarction (STEMI) and Non-ST segment elevated

Myocardial infarction (NSTEMI), having at least 20 teeth in their oral cavity so that presence or absence of periodontal diseases may be assessed, and provided written consent to participate in the study were recruited to the case group. The control group consisted of Non-myocardial infarction, age-group and gender matched individuals without any documented previous history of AMI or other cardiovascular pathologies, had a minimum of 20 teeth in their mouth and signed the consent form for participation were enrolled in the study. Exclusion criteria: participants presenting with a 2<sup>nd</sup> Myocardial Infarction or having any other cardiac pathology other than AMI, having lesser than 20 teeth, and not signing the consent form were excluded from the study. To minimize the influence of other disease conditions on the dental/ general body, both the case and control group participants with predisposing systemic illness such as diabetes, autoimmune diseases, other chronic inflammatory diseases, and cancers etc. were also exempted from the study.

An oral risk factor assessment proforma adapted from that of Ziauddin Dental hospital with some self-designed modifications was employed for data collection purpose. The proforma comprised of questions pertaining to demographic details, oral hygiene practices such as frequency, time and method of brushing, flossing, use of mouthwash, regular dental visits etc. and deleterious oral habits such as smoking, and consumption of pan, betel nuts etc. These details were duly filled for each participant by the researcher.

After this, examination of the oral cavity for the presence/absence of periodontal disease was carried out using William's periodontal probe and was classified according to the Periodontal Disease classification system of the American Academy of Periodontology by the principal investigator to eliminate any observational bias and ensuring inter-exam reliability.<sup>13</sup>

Myocardial infarct patients for case group were obtained from NICVD coming from all walks of life. After a brief interview to rule out the exclusion criteria, the purpose of the study was explained to all the participants. Upon signing the consent paper, the proforma was filled for every patient, who were then evaluated for periodontal disease. Similarly, controls were selected from the department of Periodontology at Ziauddin Dental hospital and BUMDC. The same procedure was employed for each control group participant by the principal investigator.

Research data was analyzed using Statistical Package of Social Sciences (SPSS) version 20. The quantitative

data was presented by means and Standard deviation and expressed as percentage and frequencies for categorical data. The relationship between categorical variables was tested by Chi Square. A p-value of < 0.05 was deemed significant.

**RESULTS**

A total of 125 participants were enrolled in this case-control study. Fifty-five of these were recruited to the case group (participants diagnosed with AMI) and 70 participants, age and gender matched to the control group (Non-AMI & Healthy individuals). The periodontal tissues of all the participants were examined to screen for the presence or absence of Periodontitis (Table 1).

The majority of participants i.e. 39 (71%) suffering from acute myocardial infarction (AMI) in case group were found positive for Periodontitis as opposed to only 26 (37%) of healthy/non-AMI participants of control group. Among the periodontitis participants, more than half i.e. 20 (51.28%) had a localized form of periodontitis whereas 19 (48.7%) were affected with generalized form of periodontal disease. The difference between the two groups was found to be highly statistically significant with the p-value of <0.001. Moreover, the Odds for an individual with periodontal disease suffering a myocardial infarction was 4.125 times higher than those without periodontal disease (OR: 4.125; 95% CI, 1.934 – 8.797) (Table 1).

**Table 1: Periodontitis status among healthy and myocardial infarction patients**

Periodontal Status	Case Group (55)	Control Group (70)	P-Value
Healthy	16 (29%)	44(62.8%)	<0.001
Periodontitis	39 (71%)	26(37%)	
Periodontally Healthy	16 (29%)	44 (62.8%)	<0.001
Localized Periodontal disease	20 (51.28%)	19 (73%)	
Generalized Periodontal disease	19 (48.7%)	7 (27%)	

Our study population was predominated by males in both case & control groups (80% and 74.3%) while the females’ representation was only 20% & 25.7%. The age range of participants was from age 25 to 65 years while majority fell between 35 years to 56 years of age. Punjabi (49%, 44.3%) and Urdu speaking (32.7%, 37.2%) ethnicity was found highest among the case and control group. The educational status of most of the participants in case group i.e. 45.4% (25) was uneducated or under matric, 13 (23.6%) were unemployed/retired and 13 (23.7%) participants belonged to unskilled and partly skilled occupational

classification. Majority of case group participants 21 (38%) belonged to middle and lower socioeconomic groups respectively. Meanwhile, the educational status of majority 30 (42.8%) of control group participants was intermediate (high school) and graduate. About 21% (15) of control group participants were skilled manual workers, while 20% (14) were unskilled. However, 48.6% (34) participants belonged to middle class status followed by lower and upper middle class. Body mass index (BMI) calculated for each participant revealed that most of the participants of case group were overweight (45.5%), 18% were obese, and none was underweight. The BMI of control revealed an equal predominance of normal as well as overweight participants.

The Chi-square results for age, education, occupation, socioeconomic status/position, and BMI was found to be highly statistically significant with p-values < 0.05. (Table 2).

**Table 2: Demographic Risk Factor Characteristics of Case and Control Group**

Parameters	Case Group (n = 55)	Control Group (n = 70)	P-value
<b>Age</b>			
20– 25	1(1.8%)	2 (2.8%)	0.002*
26– 35	8 (11.4%)	26 (37.1%)	
36– 45	15 (27.3%)	26(37.1%)	
46– 55	13 (23.6%)	10 (14.3%)	
56– 65	15 (27.3%)	6 (8.6%)	
>65	3 (5.45%)	0	
<b>Gender</b>			
Male	44 (80%)	52 (74.3%)	0.297
Female	11(20%)	18 (25.7%)	
<b>Ethnicity</b>			
Punjabi	27 (49%)	31 (44.3%)	0.193
Sindhi	5 (9%)	8 (11.4%)	
Balochi	3 (5.45%)	0	
Pathan	1 (1.8%)	5 (7.2%)	
Urdu speaking	18 (32.7%)	26 (37.2%)	
Others	1 (1.8%)	0	
<b>Education</b>			
Uneducated	16 (29%)	5 (7.14%)	0.005*
Under matric	9 (16.4%)	12 (17%)	
Matric	13 (23.6%)	10 (14.3%)	
Intermediate	6 (10.9%)	16 (22.8%)	
Graduate	9(16.4%)	14 ((20%)	
Master	2(3.6%)	13 (18.6%)	
<b>Occupation</b>			
Professional Class	0	13 (18.6%)	0.001*
Intermediate class	13 (23.6%)	4 (5.8%)	
Skilled manual	10 (18.2%)	9 (12.9%)	
Skilled non-manual	6 (10.9%)	15 (21.4%)	
Partly skilled	4 (7.3%)	6 (8.6%)	
Unskilled	9 (16.4%)	14 (20%)	
Unemployed/retired	13 (23.6%)	9 (12.9%)	
<b>Socioeconomic Status</b>			
Upper middle class	13 (23.6%)	18 (25.7%)	0.001*
Middle class	21 (38%)	34 (48.6%)	
Lower class	21 (38%)	18 (25.7%)	

BMI			
Underweight	0	8 (11.4%)	0.006*
Normal weight 19-24	20 (36%)	30 (42.8%)	
Overweight = 25 -29	25 (45.5%)	29 (41.4%)	
Obese = >30	10 (18%)	3 (4.3%)	

\*significant at <5%

Regular tooth brushing practice was reported by majority i.e. 87.3% (48) of case and 94.3% (66) control group participants while only 12.7% of case group and 5.7% of control group participants reported only occasional brushing of their teeth. Most of the participants in both groups brushed their teeth in the morning, while 34.5% and 42.8% of case and control group reported brushing twice daily. Use of mouth wash and flossing was rarely employed by participants in both the groups and the majority i.e. 90-100% of participants denied using these aids for better oral hygiene maintenance (p=0.026). None of the case group participants had ever visited a Dentist for either consultation or treatment of any dental ailment or complaint. 34.4% (24) control group participants however reported paying a visit to a dentist (p<0.001).

47.3% of cases and 14% controls were current smokers while the rest were non-smokers or had stopped smoking more than 10 years earlier (p<0.001).

23.6% cases reported consuming cigarettes for more than 25 years, 11% for past 15 years while 12.7% had been smoking for 5 years or less. One packet or more was reported by 29% cases. The difference was statistically significant (p<0.05) for the smoking behavior between the case and control group.

The consumption of gutka, naswar, pan, and betel nut among the case and control was almost minimal (Table 3).

**Table 3: Periodontitis Related Risk Factors Characteristics**

Characteristics	Case Group (n = 55)	Control Group (n = 70)	P value
<b>Frequency of Brushing</b>			
Once	30 (54.5%)	35 (50%)	0.146
Twice	14 (25.5%)	29 (41.4%)	
Thrice	4 (7.3%)	2 (2.9%)	
Occasionally	7 (12.7%)	4 (5.7%)	
<b>Time of Brushing</b>			
Morning	33 (60%)	33 (47%)	0.316
Evening	3 (5.45%)	7(10%)	
Both	19 (34.5%)	30 (42.8%)	
<b>Use mouthwash</b>			
Yes	3 (5%)	7 (10%)	0.352
No	52 (94.5%)	63 (90%)	
<b>Do you floss</b>			
Yes	0	6 (8.5%)	0.026*
No	55 (100%)	64 (91.4%)	
<b>Visit the dentist</b>			

Yes	0	24 (34.3%)	<0.001*
No	55 (100%)	46 (65.7%)	
<b>Do you smoke?</b>			
Yes	26 (47.3%)	10 (14%)	<0.001*
No	29 (52.7%)	60 (85.7%)	
<b>Duration of smoking</b>			
< 5 years	7 (12.7%)	7 (10%)	0.001*
< 15 years	6(11%)	2 (2.8%)	
>25 years	13 (23.6%)	1 (1.4%)	
<b>Number of cigarettes smoked</b>			
< 5 cigarettes	5 (9%)	4 (5.7%)	0.002*
5 -10 cigarettes	5 (9%)	4 (5.7%)	
1 packet	8 (14.5%)	1 (1.4%)	
> 1 packet	8 (14.5%)	1 (1.4%)	
<b>Do you consume gutka?</b>			
Yes	2 (3.6%)	2 (2.8%)	0.806
No	53 (96%)	68 (97%)	
<b>Do you consume naswar?</b>			
Yes	6 (10.9%)	1 (1.4%)	.036*
No	49 (89%)	69 (98/6%)	
<b>Do you consume pan?</b>			
Yes	11 (20%)	10 (14.3%)	0.396
No	44 (80%)	60 (85.7%)	
<b>Do you consume betel nut?</b>			
Yes	8 (14.5%)	14 (20%)	0.427
No	47 (85.5%)	56 (80%)	

\*significant at <5%

## DISCUSSION

Periodontitis is the most common disease of the oral cavity which affects the periodontium, whereas cardiovascular diseases (CVDs) are leading the boards for the most common cause of mortality world-wide. Both these chronic, inflammatory diseases are interlinked, and highly prevalent around the globe and sufferers are rendered to a life of disability.<sup>11</sup>

It was observed that the majority i.e. 71% (39) of Myocardial infarction patients (case group) were suffering from periodontitis in comparison to only 37% (26) non-myocardial infarction/healthy (control group) participants. Almost 50% of the participants of case group had a generalized form of periodontal disease which points to the severity of the disease and its related outcomes in MI participants in comparison to the more prevalent localized form of periodontitis in the control group. Our findings justify the fact that periodontitis may have a causal relationship and serves as a risk factor for triggering myocardial infarction episode by predisposing the body to increased chronic inflammatory loads.<sup>14</sup> The results were statistically significant having a p-value of <0.001. Moreover, the Odds Ratio (OR) was found to be 4.125 (95% C.I 1.934-8.797) which advocates a strong risk involvement of periodontitis for MI. Fatima et al also found statistically signified, higher prevalence (65.75%) of periodontitis among MI patients as compared to 21.9% in controls with the OR of 6.8.<sup>15</sup> Rydén et al. also reported 43% prevalence of periodontitis among MI participants but with a lesser

OR=1.49 which was also statistically proved.<sup>8</sup> In addition, a recent meta – analysis of 10 cohort studies encompassing 5,369,235 participants concluded that Periodontal Disease was modestly associated with MI.<sup>14</sup>

The demographic risk factor assessment showed a male predominance in both the case and control groups (80% and 74.5%) with an age range of 25 to 68 years. Most of the participants belonged to 36-65 years of age. Similar gender, age distribution and age range were observed in urban and rural areas of northern Punjab - Pakistan by Riffat Iqbal et al. (2015), and in Poland by Górska et al. (2017), who also reported a higher occurrence of periodontitis as well as MI in male population as compared to females.<sup>16-17</sup> This is attributed to ignorance of poor oral hygiene practices among males and psychosocial stresses experienced by men in our society which is the primary risk factor of periodontitis. Studies also found that men of middle age are 2-5 times at a higher risk of developing MI as compared to females who are protected against risk of Chronic heart diseases (CHD) owing to the higher estrogen levels.<sup>18-19</sup> Contrary to our findings, a recent global assessment of periodontal disease by Riccardo Nocini et al. reported a 13% increased risk of periodontal diseases incidence and prevalence in females of various part of world as compared to males owing to hormonal changes.<sup>20</sup> Lower education levels, and lower socioeconomic status observed in our study was also reported by many research strengthening the notion that these factors do have some role to play in periodontitis and CVDs occurrence.<sup>8,21</sup> Obesity owing to greater consumption of soft drinks and reduced intake of vitamin C and Calcium has been linked with periodontal diseases and considered as an important risk factor for its predisposition. Most of the participants of the present study were overweight having BMI (Body Mass index) in the range of 25 to 29 kg/cm<sup>2</sup>. Comparable results of  $28 \pm 4.3$  were also reported by B Wożakowska-Kapłon et al. in a similar case-control study.<sup>22</sup>

Oral hygiene habits were encouraging among the study population and both the case and control group participants reported tooth brushing with at least 50% participants brushing once daily. However, tooth brushing alone had no significant impact on the periodontal status of both the case and control group. Similar non-significant ( $p=0.714$ ) results were found between different groups of cigarettes and waterpipe (hookah) smokers having periodontitis; tooth brushing regularly or irregularly as reported by Bibars et al. 2015.<sup>23</sup>

This study found no significant association between case and control group with regards to tooth brushing

habits, its frequency and mouth wash usage. Cesar de Oliveira in a longitudinal cohort National population survey in Scotland extracted that people who never or rarely brushed their teeth had a hazard ratio of 1.7 with an increased risk of cardiovascular diseases.<sup>24</sup>

Flossing and visits to a Dentist, however, was observed only among the control group participants and had a strong significant ( $p\text{-value}\leq 0.05$ ) association with reduced periodontal disease prevalence. Bibars et al. on the contrary reported no significant difference ( $p\text{-value}=0.823$ ) regarding participants visiting the dentist or not in his study.<sup>23</sup>

Tobacco smoking has been reckoned to accelerate and intensify the risk of periodontal disease by 2-3 folds.<sup>23</sup> Smoking is also a chief risk factor and leading cause of cardiovascular diseases as well as CVD associated mortalities. Like periodontium, destructive effects of cigarette smoking, such as, altered vascularity of cardiovascular system, increased oxidative stresses, endothelial dysfunction, higher cholesterol concentration and lowered HDL (high-density lipoprotein) are produced which directly predispose the body to cardiovascular disease. Our study revealed that about 47.3% case group participants suffering from MI were found to be active smokers as compared to 14% non – MI participants. B Wożakowska-Kapłon et al. reported a much greater smoking prevalence of 85% among his case group (MI patients) participants.<sup>22</sup> Renata Górska et al. reported comparable results to our study, where 49.3% of MI patients were current smokers while also suffering from periodontal disease.<sup>16</sup> A large cohort study by Shin-Young Park et al. on 235,610 non- cardiac individuals, also found similar results, showing a lesser prevalence (21.8%) of current smoking habits in both males and females participants, akin to our study.<sup>25</sup> Therefore, dental diseases, especially periodontitis, should not be ignored, and every effort must be made to prevent and/or treat it. Physicians and Dentist should work hand in hand with each other and make appropriate referral if they suspect any possibility of periodontitis related oral inflammation. Awareness programs for general public should also be encouraged to educate them about the impact which a small, often ignored, oral disease can have on the body's systems, predisposing them to many systemic illnesses. This will in turn help in reducing or preventing many systemic ailments and improve the quality as well as life expectancy of our people.

## CONCLUSION

Hence Periodontitis has been observed to serve as a risk factor for initiating the first myocardial infarction episode and the severity level increases with the generalized form

of periodontitis. Moreover, risk factors such as age, educational level, socio-economic status, BMI index, use of dental floss, visit to dentist and the frequency & duration of smoking all have been found to be significantly associated with predisposition to periodontitis and Myocardial infarction.

### AUTHORS' CONTRIBUTION:

RB: Conceiving and designing the study, data collection, data analysis, formulation of result and writing the manuscript, and responsible for accuracy of results and integrity of research.

MH, ZR, TS, FS: Conceiving and designing the study, interpretation of data, critical review of manuscript, approval of final draft, and responsible for accuracy of results and integrity of research.

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