The Prevalence and Severity of Periodontitis in Patients Diagnosed with Atherosclerotic Coronary Artery Disease

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ABSTRACT

Background and aims: According to World Health Organization (WHO), estimating 17.5 million people died from cardiovascular diseases (CVDs), representing 31% of all global deaths. An estimated 7.4 million were due to coronary heart disease (CAD). Our aim of this study was to determine a possible relationship between periodontitis and atherosclerotic coronary artery disease patients.

Methodology: A cross-sectional study was done at the department of cardiology, King Khalid University Hospital in Riyadh, Saudi Arabia. Study population consisted of 100 patients who underwent angiography and have been diagnosed with coronary artery disease. Population was further categorized into low risk (40% patients) and high risk (60% patients) based on the angiography results. Patients were handed self-administered questionnaires to obtain socio-demographic data. Afterwards, periodontal charting was done by examining the patients to determine their periodontal attachment level.

Discussion: The small sample size of patients due to restricted exclusion criteria limited the chance of finding statistically significant relationship, also the CAD classification according to Risk stratification instable angina need a large number of subjects to determine statistical measures.

Results: 100 diagnosed patients with Atherosclerotic CAD, included in the study, 19 (55%) had high risk atherosclerotic CAD and 15 (45%) had low risk atherosclerotic CAD. Atherosclerosis patients with High Risk are 1.35 times more likely to have severe CAL comparing with Low Risk patients (OR=1.35, 95%CI (0.343 ,5.315, P-value=0.6)

Conclusions: With increasing prevalence of Atherosclerosis in Saudi Arabia, patients with Atherosclerotic CAD should be screened for periodontitis and preventive oral health care should become part of the regular care for improvement of overall quality of life in these patients.

Keywords: Atherosclerosis, Chronic Periodontitis, Coronary Artery Disease, Prevalence

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Introduction

Periodontitis is defined as an inflammatory disease of the supporting tissue of the teeth caused by specific micro-organisms, resulting in progressive destruction of the periodontal ligament and alveolar bone with increase probing depth formation, recession or both. It is classified according to the new classifications based on severity and complexity of management: Stage1: Initial Periodontitis,Stage II: Moderate Periodontitis, Stage III: Severe Periodontitis with potential for additional tooth loss, and Stage IV: Severe periodontitis with potential for loss of dentition. A case-control study that was carried out in 2010 showed that the concentrations of serum levels of C-reactive protein (hs-CRP) and interleukin-6 (IL-6) in the sera of periodontitis patients were significantly higher than those in control subjects. By contrast, the concentration of tumor necrosis factor-alpha (TNF-alpha) was significantly lower in periodontitis patients than in control subjects. Although periodontal infection does affect the concentration of hs-CRP and IL-6 in serum, a subgroup of patients exist who are highly susceptible to an increased risk of coronary heart disease (CHD) associated with periodontitis, suggesting that there may be subjects who have an elevated risk of CHD independent of susceptibility to periodontal tissue destruction per se (2).

Coronary heart disease (CHD) is defined by the National Heart, Lung, and Blood Institute as a disease in which a waxy substance called plaque builds up inside the coronary arteries. These arteries supply oxygen-rich blood to your heart muscle. When plaque builds up in the arteries, the condition is called atherosclerosis. The buildup of plaque occurs over many years.

And according to World Health Organization (WHO), an estimated 17.5 million people died from cardiovascular diseases (CVDs) in 2012, representing 31% of all global deaths. Of these deaths, an estimated 7.4 million were due to coronary heart disease (3).

Current evidence supports that inflammation is a major driving force underlying the initiation of coronary plaques, their unstable progression, and eventual disruption; patients with a more pronounced vascular inflammatory response have a poorer outcome(3). Recent studies suggest that, besides CRP, other inflammatory biomarkers such as cytokines [interleukin (IL)-1, IL-6, IL-8, monocyte chemoattractant protein-1 (MCP-1)], matrix metalloproteinases (MMPs), cellular adhesion molecules [intercellular adhesion molecule 1 (ICAM-1), and A2 phospholipases may have a potential role for the prediction of risk for developing coronary artery disease and may correlate with severity of CAD (3). A study was done to assess the relationship between periodontal status and C-reactive protein and interleuckin-6 levels among atherosclerotic patients. The results of this study showed that CRP and IL-6 are associated with periodontal diseases in atherosclerotic patients (5).

In a large case-control study of periodontal disease, verified by radiographic bone loss and with a careful consideration of potential confounders, the risk of a first myocardial infarction was significantly increased in patients with periodontal disease even after adjustment for confounding factors. These findings strengthen the possibility of an independent relationship between periodontal disease and myocardial infarction (6). Also, the results of another study showed that in people over 40 years, who had coronary artery disease proved by coronary angiography, gingival inflammation (periodontitis) has a significant relation as a risk factor (8).

At the Department of Cardiology, CSM Medical University, Lucknow, India, a study was done to evaluate the efficacy of non-surgical periodontal therapy on the levels of serum inflammatory markers in subjects with chronic periodontitis and known coronary artery disease. In this study, periodontal treatment resulted in a significant decrease in bleeding on probing (BOP) and probing depth (PD), and this treatment lowered the serum inflammatory markers (hsCRP and WBC counts) in patients with coronary artery disease. This may result in a decreased risk for coronary artery disease in the periodontally treated

patients (9). Also, according to the result of another study, non-surgical periodontal therapy lead to the improvement of periodontal health, with a significant decrease in the levels of LDL and CRP in patients with hyperlipidemia and chronic periodontitis. Therefore, local non-surgical periodontal therapy may be considered as an adjunct in the control of hyperlipidemia, along with standard care (10).

The previously mentioned studies highly suggest a link between periodontitis and atherosclerotic cardiovascular disease. The link is thought to be through by chronic inflammation and inflammatory mediators. However, the link is yet to be fully understood. And we could not find any published papers on the prevalence of periodontitis among patients diagnosed with atherosclerotic cardiovascular disease in Saudi Arabia.

Research Objectives

Primary Objective:

To determine the prevalence of periodontitis in patients who were diagnosed with atherosclerotic coronary artery disease in 2016-2017.

Secondary Objective:

To find the relationship between the severity of periodontitis and the severity of atherosclerotic CAD.

Research Methodology

Study design:

Cross-sectional.

Study Setting:

The study would be carried out at the department of cardiology, King Khalid University Hospital (KKUH) in Riyadh, Saudi Arabia.

Study Population:

The study population is going to be patients who were angiographically diagnosed with coronary artery disease, and has not yet been treated or has been recently treated (not longer than a week ago).

Inclusion Criteria:

1. Aged between 25-75 years old.
2. Non-smokers or quit smoking for at least 6 months.
3. Has not taken anti-biotic for at least 6 months.
4. Must has at least 10 teeth.
5. Angiographically diagnosed with coronary artery disease.

Exclusion Criteria:

1. Smokers.
2. Pregnant women.
3. Patients with systemic diseases rather than hypertension.

Sample Size:

To estimate the prevalence of periodontitis among patients who were diagnosed with coronary artery disease and achieve 95% confidence interval of 80% power is 96. And assuming a 5% error rate, the sample size would be 100 patients. The sample size was calculated using the following equation:

$$\mathrm{n} = \frac{2\,(\mathrm{p})\,(1-\mathrm{p})\,(\mathrm{Z}\beta\ +\ \mathrm{Z}\,\alpha\,2\,)2}{(p1\ -\ p2)\,2}$$

Data Collection Methods:

Self-administered questionnaires will be handed to patients to elicit socio-demographic variables. Such as, age, gender, education, occupation, marital status and economic status. Afterwards, patient's periodontium will be examined using periodontal examination kit which contains: mouth mirror, an explorer, and a UNC probe , according to the

periodontal examination (Gingival index by Lo e&Silness 1963, Plaque index by Silness&Loe 1967, and periodontal charting). Dental examination will be done by 4 examiners who have been calibrated.
Information regarding the severity of the patient's coronary artery disease would be obtained from the angiography report. Patients will be classified based on the vessels involved into two categories(4):

1. Left main or three-vessel disease (high risk).
2. Single-vessel or two-vessel disease (low risk).

Cardiac echo:

1. Ejection fraction more than or equal to 50%.
2. Ejection fraction between 41% and 49%
3. Ejection fraction less than or equal to 40%.

Data Analysis Plan:
Data will be analysed using Statistical Package for the Social Science (SPSS), version 21.

Infection Control Measures:
All instruments in each periodontal examination kit will be used only once on one patient. Afterwards, they will be taken back to Riyadh Colleges of Dentistry and Pharmacy to be disinfected and sterilized.

Ethical Consideration:

1. All participants will receive a written consent form, the informed consent will be clear and indicates the purpose of the study, why they were chosen, all potential risks and benefits and their right of the participant to withdraw at any time without any penalty or loss of benefit, why they were chosen, all potential risks and benefits and that they could refuse to participate, or could withdraw from the study at any point in time.
2. The informed consent will be clear and indicates the purpose of the study and the right of the participant to withdraw at any time without any obligation towards the study team.
3. No incentives or rewards will be given to participants.

Results:
A total of 100 (Male=60, Female=40) atherosclerosis patients participated in this study in which nearly half 49% of the participants had mild(stage1), 12% moderate(stage2) and 39%(stage 3-4) severe periodontitis. Among the study participants 60% had a high risk and 40% had low risk for the development myocardial infarction. In most of the study subjects (41%) 3 arteries affected with the atherosclerosis. The descriptive statistics of mean and standard deviation values for CAL (2.37±1.51mm), mean percentage of arteries blockade (67.60±22.46) and mean percentage of ejection fraction (45.31±13.03), as shown in (Table 1).

Table 1: Characteristics of the study participants

Variables		n	%
Gender	Male	60	60.0%
	Female	40	40.0%
Severity Periodontitis	Stage 1	49	49.0%
	Stage 2	12	12.0%
	Stage 3	39	39.0%
Risk of Myocardial infarction	Low risk	40	40.0%
	High risk	60	60.0%

Number of arteries affected	One	39	39.0%
	Two	19	19.0%
	Three	41	41.0%
	Four	1	1.0%
Age (years) mean±SD	55.82±8.68		
Clinical Attachment Level (mm)mean±SD	2.37±1.51		
Percentage of arteries Blockademean±SD	67.60±22.46		
Percentage ejection Fractionmean±SD	45.31±13.03		

Table 2 shows the frequency distribution and percentage obstruction of LAD, LM, LCX, and RCA in all subjects. It is evident that 91-100% blockage of coronary arteries was found with 7(10.9%) LAD artery followed by 2 (7.1%) LM, 2 (3.8%) LCX and 2 (3.4%) RCA. Half of the 29 (50%) RCA showed 71-90% of blockage followed by 24 (45.3%) LCX, 11 (39.3%) LM, and 25 (39.1%) LAD.

Table 2: Distribution of frequency and percentages obstruction of coronary arteries.

Percentage of obstruction	LAD		LM		LCX		RCA	
	n	%	n	%	n	%	n	%
0-50	12	18.8	7	25.0	9	17.0	9	15.5
51-70	20	31.3	8	28.6	18	34.0	18	31.0
71-90	25	39.1	11	39.3	24	45.3	29	50.0
91-100	7	10.9	2	7.1	2	3.8	2	3.4
Total	64	100.0	28	100.0	53	100.0	58	100.0
LAD= Left Anterior Descending Artery, LM= Left Main Artery, LCX= Left Circumflex Artery, RCA= Right Coronary Artery								

When severity of the periodontitis is compared across different obstructed cardiac arteries, it was observed that the stage1 periodontitis cases are associated with LAD (30) followed by RCA (25), LCX (19) and LM (5). Moderate(stage2) periodontitis was found to be associated with LAD (10), RCA (8), LCX (7), and LM (4). However, server(stage3) periodontitis was found to related with LCX (27), RCA (25), LAD (24) and LM (19), as shown in (Figure 1).

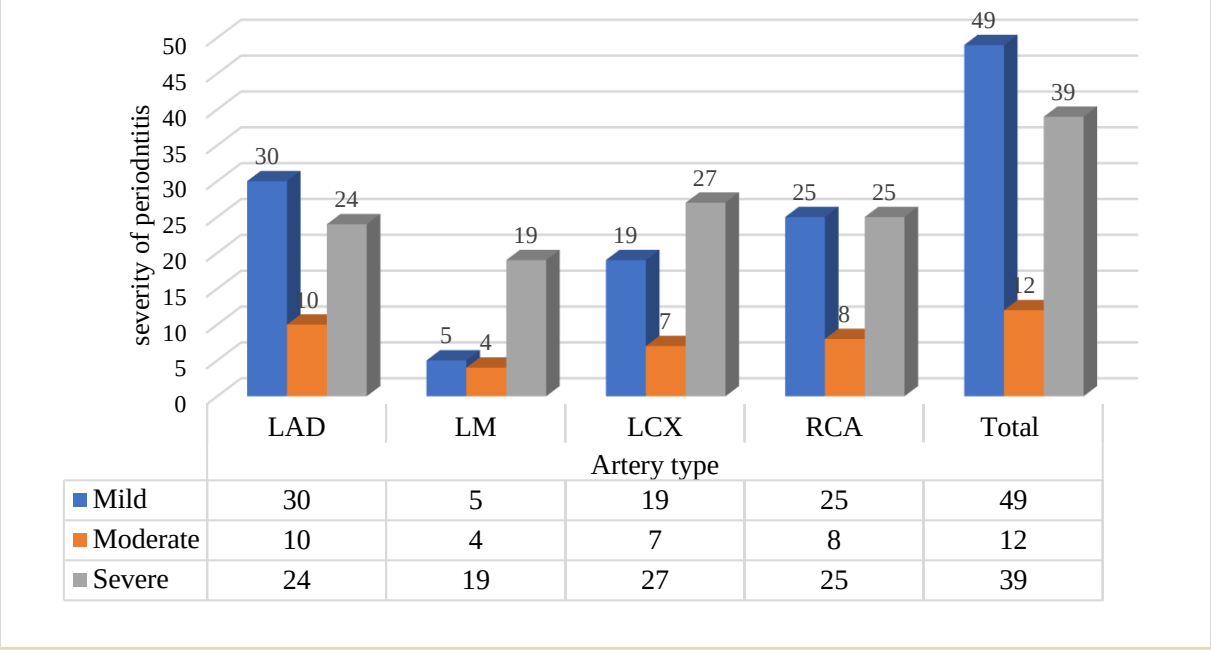

Fig 1: Severity of Periodontitis

A spearman's correlation coefficient was computed to assess the relationship between the severity of periodontitis and study variables (risk of atherosclerosis, Number of arteries affected, total artery obstruction, ejection fraction, LAD, LM, LCX and RCA). Severity of the periodontitis showed a significant positive correlation with the risk of atherosclerosis (r=0.705, p=0.000), number of arteries affected with obstruction (r=0.443, p=0.000), LM (r=0.402, p=0.000) and LCX (r=0.286, p=0.004). However, severity of the periodontitis showed a significant negative correlation with the ejection fraction of the arteries (r=**-0.494, p=0.000**). This is suggestive of the fact that as the severity of the periodontitis increases the risk of atherosclerosis increases, and the number of arteries affected with the obstruction also increases while decreasing the ejection fraction, as shown in (Table 3).

Table 3: Spearman's correlation coefficient between Severity Periodontitis and study variables

Variables	Correlation Coefficient	Sig. (2-tailed)
Risk atherosclerosis	**.705****	**0.000**
Number of arteries affected	**.443****	**0.000**
Total artery obstruction	0.056	0.578
Ejection fraction	**-.494****	**0.000**
LAD	0.014	0.894
LM	**.402****	**0.000**
LCX	**.286****	**0.004**
RCA	0.128	0.205
**. Correlation is significant at the 0.01 level (2-tailed).		

Odds of participants likely to have low risk of atherosclerosis is 5.37 times higher in (stage2) moderate periodontitis compared to the mild(stage1) periodontitis than in the individuals with high risk for atherosclerosis. Similarly, odds of participants likely to have low risk of atherosclerosis is 0.058 times in severe(stage3) periodontitis compared to the mild(stage1) periodontitis than the individuals with high risk for atherosclerosis (Table 4).

Table 4: Severity of periodontitis with risk for atherosclerosis

Severity of periodontitis[a]		B	Std. Error	Wald	df	Sig.	Exp(B)
Moderate	Intercept	5.041	3.148	2.564	1	.109	
	Age	-.076	.051	2.216	1	.137	.927
	[G=Male]	1.534	1.135	1.826	1	.177	4.637
	[G=Female]	0b	.	.	0	.	.
	[Low risk of atherosclerosis]	**1.681**	**.902**	**3.475**	**1**	**.062**	**5.373**
	[High risk of atherosclerosis]	0b	.	.	0	.	.
Severe	Intercept	6.239	3.219	3.757	1	.053	
	Age	-.085	.052	2.684	1	.101	.918
	[G=Male]	1.995	1.127	3.136	1	.077	7.353
	[G=Female]	0b	.	.	0	.	.
	[Low risk of atherosclerosis]	**-2.841**	**1.355**	**4.398**	**1**	**.036**	**.058**
	[High risk of atherosclerosis]	0b	.	.	0	.	.
a. The reference category is: Mild.							
b. This parameter is set to zero because it is redundant.							

Discussion:

The prevalence of Atherosclerosis is rapidly rising all over the globe at alarming rate. Atherosclerotic CAD is the critical form of Atherosclerotic. Those patients with high atherosclerotic CAD were likely to have severe clinical attachment loss compared to low grade Atherosclerotic CAD. 100% had a form of periodontal disease. The present study indeed shows that Saudi subjects with Atherosclerotic CAD have significantly increased prevalence of periodontitis.

According to the studies above, Current evidence supports that inflammation is a major driving force underlying the initiation of coronary plaques, their unstable progression, and eventual disruption; patients with a more pronounced vascular inflammatory response have a poorer outcome (3). Recent studies suggest that, besides CRP, other inflammatory biomarkers such as cytokines [interleukin (IL)-1, IL-6, IL-8, monocyte chemoattractant protein-1 (MCP-1)], matrix metalloproteinases (MMPs), cellular adhesion molecules [intercellular adhesion molecule 1 (ICAM-1), and A2 phospholipases may have a potential role for the prediction of risk for developing coronary artery disease and may correlate with severity of CAD (3).

The age of the subjects remain one of the confounding factor for both the atherosclerosis and chronic periodontitis, in this study the age had positive correlation with the severity of the atherosclerosis but no correlation between age and CAL.

Atherosclerosis is classed as a disease of aging, such that increasing age is an independent risk factor for the development of atherosclerosis. Atherosclerosis is also associated with premature biological aging, as atherosclerotic plaques show evidence of cellular senescence characterized by reduced cell proliferation, irreversible growth arrest and apoptosis, elevated DNA damage, epigenetic modifications, and telomere shortening and dysfunction (13,14,15).

Atherosclerotic carotid plaques obtained from men reveal a higher prevalence of PH than those from women. Local PH is significantly related to adverse cardiovascular outcome in men but not in women. This contributes to our understanding of sex differences in cardiovascular disease that can currently play a role in noninvasive imaging and help to target sex-specific therapies in the future, such as selecting patients for CEA based on plaque characteristics (16).

Aging is also a confounding factor for Clinical Attachment loss as mentioned in several studies including a recent study that was done in Paris, France that mentioned that the age and gender are powerful independent predictors of clinical attachment loss, as is the mean gingival bleeding index. To a lesser extent, the number of missing teeth was a good predictive variable (17).

Conclusion:

With increasing prevalence of Atherosclerosis in Saudi Arabia, patients with Atherosclerotic CAD should be screened for periodontitis and preventive oral health care should become part of the regular care for improvement of overall quality of life in these patients.

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