CHRONIC PERIODONTITIS A POSSIBLE THREAT TOWARDS CVD

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ABSTRACT

Background and Objective: Chronic periodontitis is a common oral health issue. The cause and affect relation of chronic periodontitis with cardiovascular disease has been a hot topic of research but there is scarcity of database in our population. The present study was designed to assess the association of mild to severe chronic periodontitis with cardiac disease in local males and females by estimation of pro-active inflammatory cytokine IL-6.

Methods: This was an analytical cross – sectional study conducted on 75 volunteers including 46 males and 29 females. A total of 55% patients were diagnosed with both cardiac and periodontal pathology, whereas 45% patients with only chronic periodontitis. Sandwich ELISA was used for the estimation of circulatory IL-6.

Results: Higher levels of circulatory IL-6 were found in both genders with advance state of chronic periodontitis. Although low IL-6 was observed in periodontitis alone in comparison with periodontitis associated heart disease. Highest serum IL-6 was estimated in cardiac patients with mild periodontitis in comparison with the severe one. Higher IL-6 was observed in males as compared to females with mild periodontitis alone and in those with cardiac pathology as well, except in the category of severe periodontitis.

Conclusion: In mild periodontitis with or without heart disease, males relatively exhibited increased serum IL-6 but in case of severe periodontitis, females displayed higher IL-6.

Keywords: Chronic Periodontitis, Cardiovascular Disease, Interleukin-6, Males, females.

INTRODUCTION

Prolonged inflammation of periodontal attachments including gingiva, cementum, bone of alveolus and periodontal ligaments is termed as chronic periodontitis. It involves accumulation of plaque (comprising of colonies of bacteria, which stick on the tooth surface as a film).[1,2] IL-6 being an acute phase reactant is also considered a pro-inflammatory cytokine, which is involved in the pathogenesis of coronary heart disease through autocrine, paracrine, and endocrine mechanisms.[3]

Circulatory IL-6 and tumor necrosis factor – alpha have been shown to be highly significantly associated with chronic periodontitis, as their concentration declined with periodontal treatment.[4] Positive affiliation of interleukin-6 in patients with unstable angina[5] has also been reported.

IL-6 being an acute phase reactant and inflammatory mediator acts as a possible contributor for cardiac pathology. A mediator IL-6 is released from Macrophages and T-cells.[6,7] Its raised serum level in males is positively associated with future risk of myocardial infarction. The role of this cytokine in early stages of atherogenesis is supported by research data.[8,9]

Elevated levels of serum IL-6 are seen in cases without periodontal therapy followed by reduced levels after treatment.[10-13]

A meta – analysis report showed that periodontal pathology may increase the risk of cardiovascular disease (CVD) by 20%. In the same report, even increased risk ratio between stroke and periodontal disease is documented. The cytokines and other pro-inflammatory mediators released in periodontal decay are considered to be involved in the pathogenesis of CVD.[14]

IL-6 is associated along with other serological factors (HDL, total cholesterol, haptoglobin, elastase, C-reactive protein, TNF-α receptor-1) with severe periodontitis in relation to cardiovascular disease. So IL-6 could be a potential risk factor of cardiac disease in patients with periodontitis along with other circulatory mediators.[15,16]

Below 60 years of age, chronic periodontitis would be considered as a potential threat for heart diseases, especially in males. A USA based study concludes that chronic periodontitis is a potential risk factor for coronary heart disease in younger males up to 35 years of

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age.[17]

Chronic periodontitis enhances the risk of coronary heart disease by elevating the serum concentration of CRP (C-reactive protein)[18] and IL-6 (Interleukin-6), which decrease in concentration after treatment.

PATIENTS AND METHODS

Study Groups: A total of 75 patients including 46 men and 29 women ranging between 30 – 70 years of age were taken for the estimation of Interleukin-6 in their sera after taking informed consent.

Among 46 men, 19 had chronic periodontitis alone (12 severe and 7 with mild state) and remaining 27 men had heart disease along with periodontitis having same ratio (12:7) of severe and mild cases. Out of 29 women, 15 had chronic periodontitis alone including 10 with severe and 5 with mild state, while remaining 14 had heart disease along with periodontitis including equal number of severe and mild cases.

Sample Collection and Storage: About 5 – 6 ml of blood was taken from antecubital vein of each category of patient and kept in sterile syringes in clotted state. Then the serum samples were vacunated for centrifugation at 3050 rpm for 7 – 8 minutes. Finally, the clear sera were stored at -20°C till their biochemical estimation.

Biochemical Assessment: Enzyme linked Immunoassay technique was used for biochemical assessment of Interleukin-6 on ELISA kits.

Bichromatic Reading and Calculations: Plate was read (at 450 nm against a set reference filter at 630 nm) to calculate the average of duplicate determinations. Optical density values were plotted against the corresponding IL-6 values and a calibration curve through the calibrator points was drawn by connecting the plotted points with straight line. The concentration for each control and sample was read by interpolation on the calibration curve.

RESULTS

It was noticed that serum level of IL-6 was higher with high state of chronic periodontitis in both genders. Females showed a relatively higher value of IL-6 in case of severe chronic periodontitis. In both genders, patients of chronic periodontitis alone showed significantly less IL-6 in comparison with those having heart disease along with chronic periodontitis. In both genders highest IL-6 level was found in cardiac patients with mild periodontitis rather than those with severe periodontitis (Figure 1).

DISCUSSION

In the present study, gender differences have been seen in patients with severe chronic periodontitis alone, whereas in other populations similar gender predilection has not been observed, though it is thought to be related to the conditions of oral hygiene. There is evidence in support of high occurrence rate of destructive periodontitis in men as compared to women.[20] The confounder of smoking needs to be ruled out.

In the sample population of Pakistan the association of IL-6 with respect to mild and severe chronic periodontitis with and without cardiac diseases has been observed whereas the same connection of IL-6 has been shown in Brazilian population above age 25 years, at gene level in moderate and severe periodontal patients.[21]

Current study concluded the positive correlation of circulatory IL-6 in periodontal patients with or without cardiac pathology; likewise a Chinese study reported the same association of gingival Crevicular IL-6 in chronic periodontitis.[22]

Positive association of Serum IL-6 genotypes with severe periodontitis leading to systemic inflammation

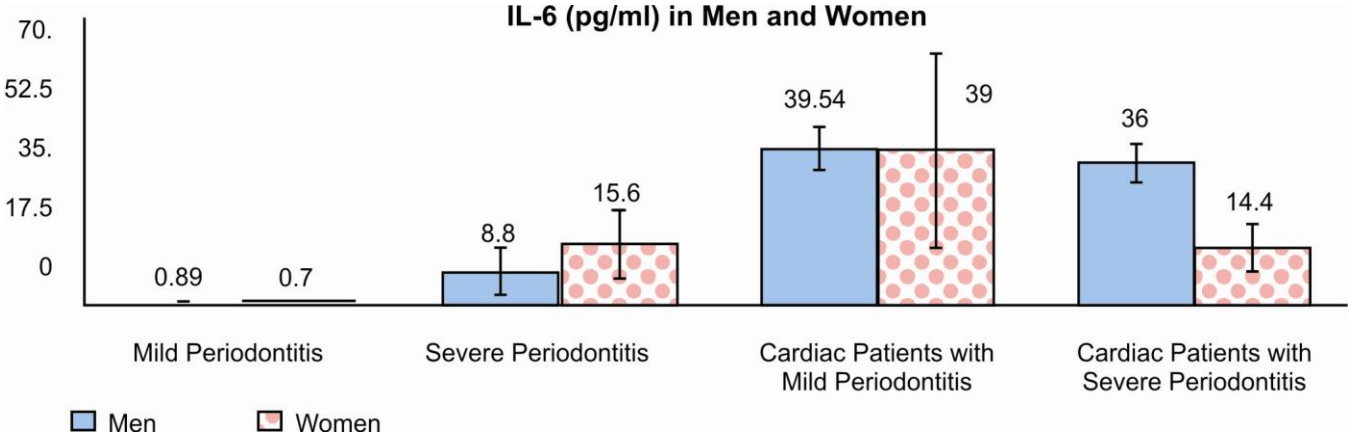

Figure 1: *Comparison of Interleukin-6 level in men and women in all groups (P = 0.005; ANOVA).*

has been reported.[23] IL-6 gene along with CD14 is strongly associated with periodontal pathology.[24]

At gene level, a significant association between IL-6 and chronic periodontitis was also found in German population.[25] Similarly at gene level, IL-6 association with cardiovascular disease is also reported by the bioscience researchers in Itlay.[26] In the local study of Pakistan, the level of IL-6 had been found to be significantly raised in cardiac patients with mild periodontitis, also the same positive linkage of IL-6 was observed in the study population of Brazil, with refractory arterial hypertensive patients having severe chronic periodontitis;[27] as the study revealed that level of marker reduces after periodontal therapy.

In the present study, the periodontal patients of ischemic heart disease, due to oxidative stress showed elevated levels of serum IL-6, likewise the same marker was found to be raised in the same regard along with C-reactive protein in a report conducted on the study population of UK.[28] The under said research on the sample population of Pakistan confirmed the positive association of serum IL-6 with chronic periodontitis, likewise another study in London had explained the same strong relationship of IL-6 at gene level with both types of periodontitis i.e. aggressive as well as chronic.[29]

The significantly raised level of mild periodontitis in cardiac patients indicated the proactive role of IL-6 in the present study. Similarly another study on the periodontal patients with metabolic syndrome, which includes risk of coronary heart disease, signifies the proactive role of IL-6.

It is ***concluded*** that in both genders, IL-6 is over expressed in heart patients along with early state of chronic periodontitis. However, men showed higher levels of IL-6 than women with mild chronic periodontitis alone as well as with heart disease, although significantly higher IL-6 was seen in women with severe periodontitis alone.

Limitations

Nutrition, smoking and BMI (Body Mass Index) are not included as research parameters, which may act as the confounders. A longitudinal interventional study is needed to reveal the effects on serum markers after clinical periodontal therapy / treatment.

Conflict of Interests: None.

ACKNOWLEDGEMENTS

The cooperation of the patients for the study is thankfully acknowledged. We are also grateful to the university authority for their support and facilitation for the project.

Author's Contribution

A.S. performed the research. A.M.C. supervised and S.M. improved the manuscript.

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