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Research Article

PLASMA FIBRINOGEN LEVELS IN CHRONIC PERIODONTITIS SUBJECTS: A PILOT STUDY

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ABSTRACT

Periodontitis is a chronic inflammatory condition of tooth supporting structures that may lead to tooth loss. Periodontitis has been considered as a risk factor for various systemic diseases that affect the human health. Cardiovascular Diseases is one of them. The various systemic inflammatory markers associated with Cardiovascular Diseases, actually increase the inflammatory activity in atherosclerotic lesions, potentially increasing the risk for cardiac or cerebrovascular events. Amongst the different inflammatory markers, plasma Fibrinogen is a classical positive acute-phase reactant considered to be an independent predictor of coronary heart disease. Various studies have shown that periodontitis is responsible for increase in systemic inflammatory markers. Very few studies have mentioned about the increase in Plasma fibrinogen levels in chronic periodontitis subjects. This pilot study was therefore planned to assess plasma fibrinogen levels in chronic periodontitis subjects.

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INTRODUCTION

Periodontitis is a chronic low grade inflammatory condition of tooth supporting structures that may lead to tooth loss. Chronic periodontitis, formerly known as "adult periodontitis" or "chronic adult periodontitis," is the most prevalent form of periodontitis. It is generally considered to be a slowly progressing disease. Chronic periodontitis has recently been defined as "an infectious disease resulting in inflammation within the supporting tissues of the teeth, progressive attachment loss, and bone loss."¹

The role of periodontal disease in the etiology of cardiovascular disease (CVD) has recently received considerable attention. Epidemiological studies have shown that there is elevation of the systemic inflammatory markers related to cardiovascular diseases in the peripheral blood of periodontitis patients. The inflammatory markers increase the inflammatory activity in atherosclerotic lesions, potentially increasing the risk for cardiac or cerebrovascular events²⁻⁶. Amongst the different inflammatory markers, one of the marker which acts as a risk factor for cardiovascular diseases is plasma Fibrinogen. Fibrinogen is a soluble plasma glycoprotein, synthesized by the liver that is converted by thrombin into fibrin during blood coagulation. Besides its role in blood coagulation, fibrinogen can also increase inflammatory response. It is increased in three different ways; i) by providing a framework for the accumulation of

inflammatory cells, ii) promoting the immuneresponse, and iii) aiding in bacterial colonization, adhesion and invasion. Higher levels of plasma Fibrinogen is associated with cardiovascular disease (>3.43 g/L). Fibrinogen levels may be elevated in any form of inflammation, as it is an acute phase protein. An elevated fibrinogen level may predispose to thrombosis and is an indicator of risk for coronary heart disease.

Many studies have mentioned about the increase of various inflammatory markers. The purpose of the present study was to investigate, plasma fibrinogen in Generalised Chronic Periodontitis subjects.

MATERIALS AND METHODS

Study design and experimental population

Participants were selected from the patients referred for the treatment of periodontitis in the Department of Periodontics in Bharati Vidyapeeth Deemed University Dental College and Hospital, Pune, India. The adult patients having generalized moderate to severe chronic periodontitis, with 5-8 mm probing pocket depth and less than 6 teeth missing were included in the study. Patients with known history of smoking, systemic diseases like Cardiovascular and Respiratory diseases, inflammatory conditions like Rheumatoid arthritis, acute infections like common cold, Sinusitis, patient taking systemic antibiotics, NSAIDs or statins and pregnant or lactating mothers were excluded.

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Study outline

A total of 25 subjects were enrolled into this study. Subjects who satisfied the inclusion criteria of the study were selected. On the day of first visit recording of age, gender, Body Mass Index (BMI), Plaque Index (PI) by Silness P. and Loe H. (1964), Gingival Index (GI) by Loe H. and Silness J. (1963) and Probing Pocket Depth (PPD) were completed. 4 ml of blood was collected from antecubital fossa, centrifuged and analysed for Fibrinogen with the lowest detection limit of 15 mg/dL. The blood was withdrawn without undue venous stasis and frothing, into a plastic syringe fitted with a short needle of 22 gauges. It was then emptied and stored into the plain and EDTA bulbs (2 ml in each). Plasma was obtained by centrifugation of blood for 15 mins at 2000 rpm on a laboratory centrifuge. If a delay in testing occurred, the samples were stored at 2–8°C for up to a week.

Statistical Analysis

Plasma fibrinogen level were found to be statistically significant in patients with chronic periodontitis. 96% subjects have increased levels of plasma fibrinogen levels.

RESULTS

25 subjects completed the study. Patients with generalized mild to moderate chronic periodontitis in the age group of 24–55 (38.97 ± 8.3) years which included 15 females and 10 males were analyzed in the study with the mean B.M.I of 21.75 ± 2.9 kg/m². Out of 25 subjects 24 subjects showed that subjects with periodontitis has increased plasma fibrinogen levels.

DISCUSSION

Cross-sectional and prospective studies have established that elevated peripheral blood levels of several systemic inflammatory markers including; fibrinogen; CRP and the cytokines IL-1 beta, IL-6, and tumor necrosis factor-alpha are associated with the risk of cardiovascular diseases and the severity of atherosclerosis^{7,8,9,10,11}. In addition, numbers of leukocytes are positively correlated with cardiovascular diseases^{10,11}. It has been proposed that these markers could be elevated due to undiagnosed chronic infectious processes; subsequently their proinflammatory properties may increase the existing inflammatory activity in plaque-associated lesions in coronary arteries and thus predispose for cardiac events^{12,13}. With the present study we observed a significant association for periodontitis with fibrinogen. Therefore we propose that periodontitis may be one such an undiagnosed chronic infectious process and the observed elevation of markers may explain at least in part the epidemiological association of periodontitis with cardiovascular diseases.

The observed associations are supported by a number of potential pathophysiologic links. Periodontal disease could result in repeated systematic exposures to bacteria, endotoxin lipopolysaccharide, and other bacterial products that may influence lipid metabolism and homeostasis. The loss of epithelial integrity within the periodontal pocket also creates an opportunity for direct bacterial translocation and bacteremia. Oral bacteria have been found circulating in the blood following tooth brushing, dental extraction, and periodontal surgery. The more severe the periodontal inflammation, the greater the hematogenous bacterial exposure in terms of

bacterial counts and duration. In addition, the lipopolysaccharide of dental plaque can penetrate the gingiva and elicit a systemic lipopolysaccharide-specific antibody response, Monocyte-derived cytokines, such as tumor necrosis factor and interleukins 1, 6, and 8, have powerful effects on hepatic protein synthesis (e.g., in up regulating fibrinogen synthesis), tissue catabolism, and lipid metabolism.

Sahingur¹⁴ has reported that periodontitis patients have significantly higher fibrinogen levels than healthy individuals. This is because a higher percentage of chronic periodontitis patients exhibit H1H2 or H2H2 genotypes associated with higher plasma fibrinogen levels than healthy individuals. The fibrinogen level was significantly higher in our study population and supported the above study.

Studies have shown that elevated levels of cytokines, C-reactive protein, and fibrinogen are associated with periodontal disease. The atherothrombogenesis caused by these factors may suggest the possible link between periodontal disease and CHD. In addition, periodontal pathogens themselves can cause platelet aggregation and thromboembolic events by expressing platelet aggregation-associated protein.¹⁵

The observation that cardiovascular risk factors might be influenced by periodontitis may have important clinical consequences. First, as inflammation plays an important role in the pathophysiology of various conditions (metabolic syndrome, BP, vascular health),¹⁶ the association of mild chronic inflammation with future serious events in observational studies¹⁷ may be influenced by an underlying severe periodontal infection. Second, periodontitis may increase the risk of future cardiovascular events because of the proatherogenic changes (increased cholesterol) and increased systolic BP induced in affected individuals. Cigarette smoking represents the major influential factor with regard to the association between periodontal infections and systemic inflammation, and this preliminary investigation raises the hypothesis of a possible interaction of smoking, periodontal infection, and systolic BP on systemic health. Third, if periodontitis were the major inflammatory stimulus in at least some patients with periodontitis, severe periodontal infections may represent a major etiologic factor for atherosclerosis, metabolic syndrome, and their sequelae. The significance of periodontitis as a cause of systemic inflammation and, potentially, disease has to be discussed in the context of the high prevalence of chronic periodontitis which affects in mild forms upto 40% and in more severe forms a good 10% of the adult population.

Periodontal diseases are bacterial infections in which certain bacteria play an important role in the development of the inflammatory process¹⁸. Increasing evidence suggests that inflammation in the vessel wall plays an essential role in the development of atherosclerosis.¹⁹ Periodontal infections may cause vascular events via lipopolysaccharides and inflammatory cytokines, contributing to the pathogenesis of cardiovascular disease²⁰. Periodontal pathogens themselves have been shown to increase platelet aggregation and thromboembolic events²¹. DeStefano *et al.*²² showed that subjects with periodontitis had a 25% increased risk of developing heart disease compared to those with little or no periodontal disease. In a 7-year CHD and also for further

coronary events. The study by Beck *et al*²³ confirmed the findings of these investigators,²⁴ indicating that periodontal disease may be a risk factor for CHD. Beck *et al*²³ reported that subjects with the most severe probing depths and bone loss at baseline had higher risk for developing CHD than those with minimal periodontal disease.

CONCLUSION

Taken together, our data provide evidence that periodontitis have plasma fibrinogen levels are elevated in the blood of moderate to severe periodontitis patients. We speculate that periodontitis, a common condition, may predispose affected patients to cardiovascular diseases by increasing levels of acute phase proteins and pro-inflammatory mediators, which may lead to increased inflammatory activity in atherosclerotic lesions and accelerated development of cardiovascular diseases. The current observations may explain the epidemiological links between periodontitis and cardiovascular diseases and fit the general hypothesis that obscure infectious processes contribute to the pathogenesis of cardiovascular diseases. Therefore periodontitis deserves serious consideration as a risk factor for cardiovascular diseases.

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