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Correlation between Signs of Anemia and Chronic Periodontitis

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I. Introduction

Periodontitis refers to an inflammatory disease of the supporting structures of the tooth caused by a group of specific microorganisms resulting in recession, pocket formation or both.[1] It represents a mixed type of infection of which the main etiologic factors are Gram negative bacteria. The inflammation of the gingiva begins as a response to colonization of Gram positive periopathogens, but as the disease progresses to deeper structures, pocket formation due to pathological deepening of gingival sulcus occurs. Such an area provides a favorable environment for Gram negative, anaerobic and more virulent microbes to colonize and flourish.

Periodontal tissue breakdown occurs as a complex interaction between endotoxins released by bacteria and host immune response. The bacterial products induce an immunoinflammatory response in the host tissue and periodontal diseases being chronic in nature act as a source of constant immunological challenge for the host. Albeit, the host response aims to waive off the microbial challenge, it invariably leads to production of tissue-degrading enzymes. Initially, the epithelial continuity of sulcular epithelium is broken down by tissue-degrading enzymes. This creates a pathway for periodontal pathogens to enter the connective tissue and finally systemic circulation. The systemic bacteremia resulting in persistent low grade systemic inflammation in chronic periodontitis patients has been speculated to be related to periodontal inflammation.[2]

The interrelationship between periodontal diseases and systemic conditions like atherosclerosis, cardiovascular diseases, diabetes mellitus and pregnancy is a well-established phenomenon. Studies indicate that the by-products of low-grade inflammatory process in host body contribute in aggravating the disease.

Anemia of chronic disease is the second most prevalent type of anemia after iron deficiency anemia and occurs in patients with acute or chronic immune activation.[3]'Anemia of Chronic Inflammation' is defined as anemia occurring in chronic infections, inflammatory conditions or a neoplastic disorder that is not caused by marrow deficiencies or other diseases and in the presence of adequate iron stores and vitamins.[4] Some diseases frequently associated with anemia of chronic inflammation are infections (fungal, bacterial, viral, parasitic), cancer, autoimmune diseases (vasculitis, SLE, Rheumatoid arthritis) and chronic rejection after solid organ transplant.[3]

Chronic periodontitis results in a low grade systemic inflammation and it is speculated that it may cause a depression in the no. of erythrocytes and consequently lowering of hemoglobin concentration.[5]
The aim of the present study is to assess whether patients with chronic periodontitis have an anemic status.

II. Materials and Method

Study population

This study was carried out in the Out Patient Department of Periodontology, Buddha Institute of Dental Sciences and Hospital, Patna. A total of 80 systemically healthy male subjects were selected for this study. Their age range was 25-60 years. 40 patients recruited were suffering from chronic periodontitis while rest 40 patients were volunteers who visited the dental hospital for regular dental checkups.

It was a cross sectional study and prior to commencement of sample collection; the study was approved by the Ethical Committee of the Institute. All patients received a verbal explanation about the nature of the study and informed written consent was obtained from them.

A detailed systemic and family history was recorded. Patients with a history of systemic diseases or conditions that could affect the periodontal health were excluded from the study. Following were the exclusion

criteria for the study: (1) female patients; (2) patients with history of previous periodontal therapy; (3) smokers or patients using tobacco in any form; (4) patients with history of diabetes, kidney failure, respiratory infections, any other fungal, bacterial, viral infections, cancer; (5) patients with history of hospitalization or intake of medications like antibiotics, iron supplements or vitamins in past 6 months.

Gingival and periodontal findings were recorded for each patient. The clinical parameters assessed were probing depth (PD), Gingival Index (GI) and Plaque Index (PI). The case group included patients with chronic periodontitis (Figure 1) with a probing depth of ≥ 6 mm in > 30% sites, GI≥2 and PI>2. The control group comprised of subjects with clinically healthy gingiva (Figure 2) with a probing depth ≤ 3 mm, GI≤1 and PI≤1.

Figure 1: Chronic Periodontitis

Figure 2: Clinically healthy gingiva

Blood parameters

Venous blood samples were obtained by venipuncture from the antecubital fossa and collected in test tubes containing EDTA and transported to clinical pathology laboratory. The samples were processed in an automated hematology analyzer within 4 hours of collection. The blood parameters analyzed were number of erythrocytes, hemoglobin concentration, mean corpuscular volume (MCV), hematocrit (PCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC).

Statistical analysis

Statistical analyses were performed. Mean value of all the parameters were calculated for both groups. To illustrate differences between groups, a Student t test with two-tailed P value was used, and was considered statistically significant if P value was<0.05.

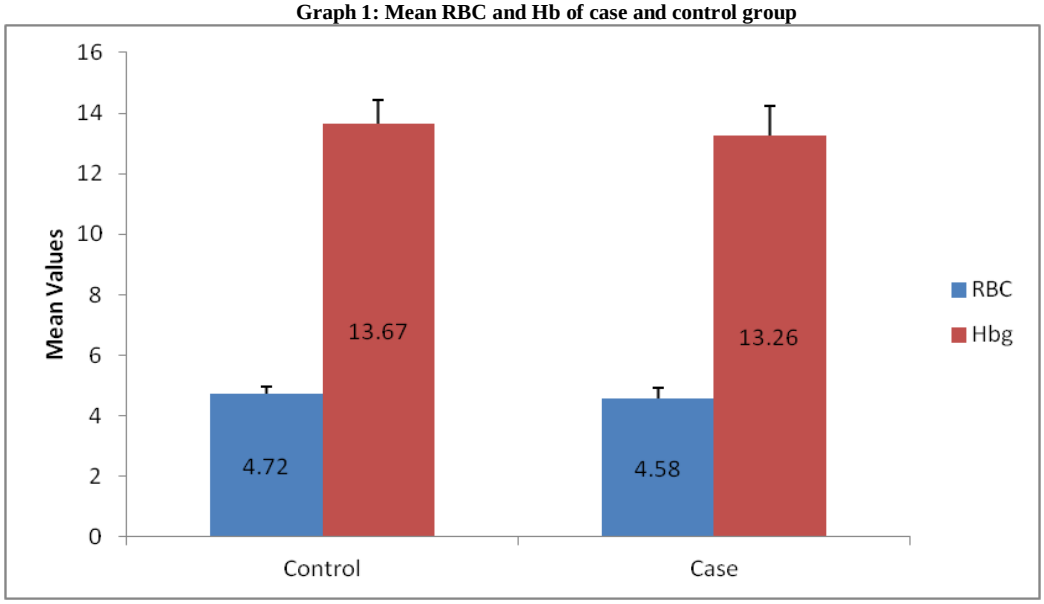
III. Results

Average age of subjects in control group was 31.92 ± 7.301 years whereas that in case groups was 39.25 ± 9.888.The mean number of erythrocytes in healthy controls were 4.72 million/mm^3 ± 0.253 and 4.58 million/ mm^3 ±0.354 for the case group. Mean RCB was significantly lower among cases as compare to controls (p-value = 0.042) (Table 1, Graph 1).

Table 1: Mean RBC and Hb of case and control group

	Group	N	Mean	t- Value	p- Value
RBC	Case	40	4.72	2.066	0.042
	Control	40	4.58		
Hb	Case	40	13.67	2.094	0.039
	Control	40	13.26		

Graph 1: Mean RBC and Hb of case and control group



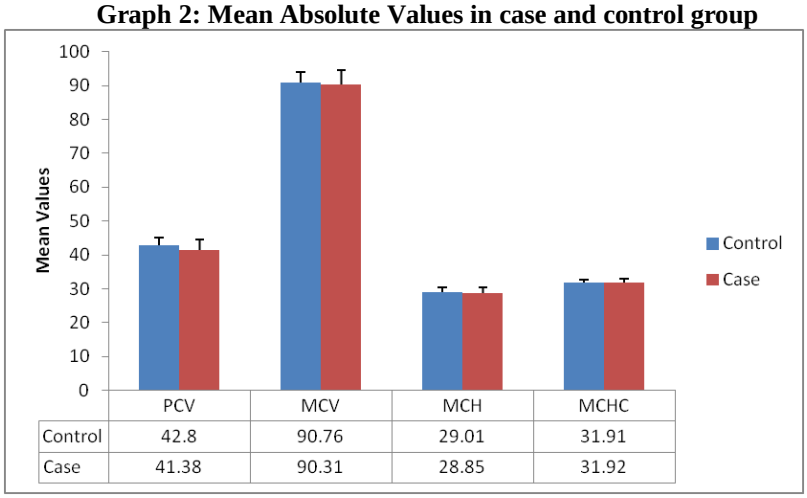
Mean Hemoglobin in control group was 13.67 ± 0.752 whereas in case group it was 13.26 ± 0.984. Mean hemoglobin was significantly lower in case group as compared to control group (p-value = 0.039) (Table 1, Graph 1).

Mean PCV in control group was 42.80 ± 2.265 and in case group 41.38 ± 3.176. Mean PCV was significantly lower in case groups as compared to control group (p-value 0.024) (Table 2, Graph 2). The difference between the values of MCV, MCH and MCHC were not statistically significant. (Table 2, Graph 2).

Table 2: Mean Absolute Values in case and control group

	Group	N	Mean	t-value	p-value
PCV	Control	40	42.80	2.302	0.024
	Case	40	41.38		
MCV	Control	40	90.76	0.541	0.590
	Case	40	90.31		
MCH	Control	40	29.01	0.519	0.605
	Case	40	28.85		
MCHC	Control	40	31.91	-0.054	0.957

Graph 2: Mean Absolute Values in case and control group



IV. Discussion

Anemia is a common hematological disorder. Worldwide, it is a public health problem of major concern. Globally anemia affects 1.62 billion people that is approximately 24.8% of the total population.[4] Alvarez-Uria et al in 2014 reported that majority of children below the age of 10 years from the rural background of India were affected by anemia followed by women and older adults.[6]The main types of anemia are nutritional anemia (iron deficiency anemia), blood loss anemia, aplastic anemia, megaloblastic anemia, hemolytic anemia and anemia of chronic disease.[7]Gokhale et al discussed the works of G.R. Lee and E. Beutler and concluded that anemia of chronic disease was the most common form of anemia observed in clinical medicine.[4] However, other studies noted that anemia of chronic disease was the second most prevalent form of anemia after iron deficiency anemia.[3,5]

Chronic periodontitis is an infectious disease of the tooth-supporting structures and is inflammatory in nature. It displays a complex interaction between bacterial products and host immune response. Many periodontal pathogens stimulate the production of interleukin-8, a proinflammatory chemokine that provides a signal for the recruitment of neutrophils.[1] Interleukin-1, interleukin-6 and TNF appear to have a central role in periodontal tissue destruction.[1]Kolte et al discussed Scannapieco's work stating that periodontitis is associated with an increased risk of systemic diseases like cardiovascular diseases, cerebrovascular ischemia and atherosclerosis as well as preterm low birth weight.[8] However, the interrelationship between periodontal diseases and anemia remains to be a lesser-documented phenomenon. It has been observed that periodontitis like any other chronic condition may tend towards anemia as the number of erythrocytes and levels of hemoglobin are lower in affected individuals despite presence of adequate iron and vitamin sources and absence of any other systemic chronic diseases.

The association between anemia and periodontitis has been studied since the early twentieth century but earlier anemia was considered a cause of periodontitis and not a consequence. Gokhale et al mentioned Lainson et al to be the first authors to implicate anemia as a systemic cause of periodontitis.[4] Similarly Chawla also suggested anemia as an important factor in the pathogenesis of periodontitis.[9] Epstein in 1935 was one of the earliest researchers to propose the concept that the depression in the number of erythrocytes is apparently secondary to the presence of periodontal diseases.[9]

Recently several studies have been undertaken to understand the interrelation and pathogenesis of chronic periodontitis and anemia. Gokhale et al in 2010 showed that patients with chronic periodontitis had lower values of hematocrit, no. of erythrocytes and hemoglobin when compared to healthy controls.[4]Shetty et al in 2014 demonstrated that there was an improvement in hemoglobin level for the test group after phase I periodontal therapy.[10]Pradeep et al concluded similar results that chronic periodontitis may tend towards anemia and non-surgical periodontal treatment could improve the anemic state of patients with chronic periodontitis.[11]Virdi et al observed a positive correlation between the hematological parameters and severity of chronic periodontitis as the test group expressed significantly lower mean values of erythrocytes and hemoglobin and significantly higher ESR.[12]

The present study depicts an association between chronic periodontitis and signs of anemia. Smokers were excluded from this study to eliminate confounding bias associated with nicotine consumption. Similarly, females were not included because anemia is more prevalent in India in female population because of poor nutrition, increased menstrual loss and high incidence of infections. They are also prone to hormonal fluctuations during puberty, through reproductive phase as well as during menopause.[4] The total number of erythrocytes and hemoglobin were significantly lower in the case group as compared to controls. Hematocrit refers to the percentage of blood that is cells and the remaining portion is plasma.[7]The hematocrit value in this study was significantly lower in patients with chronic periodontitis in comparison to healthy controls. The lower value of MCV suggests microcytosis and is most commonly caused by iron deficiency while increased values of MCV suggest macrocytosis caused by vitamin deficiency. Since the values of MCV in both groups were normal for this study, it suggests that the patients were not suffering from any iron or vitamin deficiency. Similarly normal values of MCH and MCHC in both groups while reduced mean hemoglobin values suggest an overall lowered levels of erythrocytes in case group.

Gokhale proposes Cartwright's work regarding possible processes involved in anemia of chronic disease: (1) shortened erythrocyte survival; (2) failure of bone marrow to increase RBC production to compensate for this increased demand and; (3) impaired release of iron from the reticuloendothelial system.[4] The anemia of chronic disease (ACD) is characterized by macrophage iron retention induced by cytokines and the master regulator hepcidin.

Weiss and Goodnough have proposed an elaborate explanation as to how chronic conditions cause depression of erythrocyte formation. Invasion of microorganisms leads to activation of T cells (CD3+) and monocytes. These cells induce immune effector mechanism, thereby leading to production of cytokines (interferon- γ from T cells and TNF-α, IL-1, IL-6 and IL-10 from monocytes and macrophages. IL-6 and

lipopolysaccharide (LPS) stimulate the expression of acute phase protein 'hepcidin' from liver which in turn inhibits absorption of iron in duodenum.

Interferon- γ and LPS stimulate the uptake of ferrous iron by macrophages. Activated macrophages phagocytose and degrade senescent erythrocytes. At the same time TNF-α, IL-1, IL-6 and IL-10 induce ferritin expression and stimulate the storage and retention of iron by macrophages. Additionally, TNF-α inhibits the production of erythropoietin in kidneys which is a crucial hormone required for erythropoiesis. All these mechanisms lead to a limited availability of iron and decreased biologic activity of erythropoietin resulting in inhibition of erythropoiesis and development of anemia.[3]

V. Conclusion

Periodontitis being a chronic inflammatory disease leads to elevation of cytokines. However severity of anemia depends upon the elevation of proinflammatory cytokines. Although the present study shows significant difference between the levels of RBCs and hemoglobin, but this difference is not as striking as that seen in other chronic conditions like rheumatoid arthritis, neoplasia or other parasitic infections. Since this study did not include any therapeutic intervention and measurements of hematologic or clinical parameters, it is beyond the scope of this study to comment whether anemia was a cause or consequence of periodontitis.

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