Association between Hemoglobin Level and Severity of Chronic Periodontitis

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Abstract. The aim of this study is to investigate the association between hemoglobin level and the severity of chronic periodontitis. Data were collected from 124 systemically healthy chronic periodontitis patients, referred to the Division of Periodontology, Faculty of Dentistry, King Abdulaziz University. Medical history, dental history, and periodontal parameters [such as bleeding on probing. Plus probing depth, clinical attachment loss and distance from cement-enamel junction to gingival margin, furcations, mobility and number of missing teeth] were recorded. Blood samples were collected to measure the hemoglobin level. The correlation between hemoglobin and the means of clinical attachment loss and bleeding on probing was insignificant. There was no significant difference in the mean hemoglobin level for individuals with different severity of periodontitis among male and females. The mean hemoglobin found to be insignificantly correlated with the number of missing teeth. No association between hemoglobin levels and periodontal status was found. Further longitudinal studies with larger sample size are needed to investigate this association, and the effect of periodontal treatment on hemoglobin level.

Keywords: Chronic periodontitis, Hemoglobin level, Systemic problems, Anemia.

Introduction

Periodontitis is a chronic infectious condition of the supporting tissues of the teeth that is caused by a complex mix of anaerobic, Gram-negative

bacteria. The clinical symptoms of this infection include swollen red gingiva, gingival bleeding and suppuration; formation of periodontal pocket; gingival recession, and loss of alveolar bone.

Periodontitis is considered one of the most common diseases of humans. Prevalence of periodontal diseases varies among different countries. In the US and Europe, moderate or severe forms of periodontal diseases affect 40% or 15%, respectively, of the adult population[1,2], whereas in Japan a prevalence of 23.4% was reported[3]. In Saudi Arabia, periodontal diseases were reported to affect about 68% of the studied population[4].

Epidemiologic studies suggested that periodontal deterioration increases the risk of systemic problems such as cardiovascular diseases[5], atherosclerosis[6], *diabetes mellitus*[7], and preterm low birth weight of infants[8]. These associations suggest that periodontal diseases have systemic effects. In addition, some studies had found that periodontal infection elicits systemic blood chemistry changes[9].

For thousands of years, blood has been regarded as the ultimate body fluid that could indicate disease process. In the past decade, there has been a renewed interest to study the association of periodontitis and changes in the cellular and molecular components of peripheral blood. For example the relationship of periodontitis with leukocytes[10-12], thrombocytes[13],   C-reactive   protein   (CRP)[14,15],   IL-6[16,17], fibrinogen[10,18]; erythrocyte sedimentation rate (ESR)[19], Von Willebrand factor[12], and red blood cells has been investigated[20]. Some studies found that the total numbers of leukocytes and plasma levels of C-reactive protein are consistently higher in periodontitis patients as compared to healthy ones. The aforementioned factors have also been found to have a strong association with cardiovascular diseases[21-24].

Anemia of chronic disease (ACD) has been described in the literature, and seems to be one of the most common forms of anemia observed in clinical medicine[25-27]. ACD is defined as the anemia occurring in chronic infections, chronic inflammatory processes or tumor formation that is not due to dysfunction of bone marrow cells or other diseases, and occurring despite the presence of adequate iron stores and vitamins[25-27]. A characteristic finding of the disorders associated with ACD was the increased production of the cytokines that mediate the immune or inflammatory response; such as tumor necrosis factor,

interleukin-1, and the interferon. All the processes involved in the development of ACD can be attributed to these cytokines, including shortened red cell survival, blunted erythropoietin response to anemia, impaired erythroid colony formation in response to erythropoietin, and abnormal mobilization of reticuloendothelial iron stores[28]. These cytokines are also released by periodontal tissues in response to bacterial infection, which suggests that periodontitis like other chronic disease may cause ACD.

There are only a few studies that investigated the red blood cell parameters, especially hemoglobin level, in relation to periodontitis.

The aim of the present study is to investigate the association between hemoglobin level and the severity of chronic periodontitis.

Materials and Methods

Study Design

This was a cross-sectional double-blind study. The examiners were not aware of the hemoglobin level of the patients and the laboratory technicians were not aware of the periodontal status of the patients. The study design was reviewed and approved by the Ethical Committee of the Faculty of Dentistry, King Abdulaziz University, Jeddah, Saudi Arabia.

Study Population

Data were collected from 124 systemically healthy patients with chronic periodontitis referred to the Division of Periodontology, Faculty of Dentistry, King Abdulaziz University. Patients were advised of their role in this study and asked to provide informed consent. Age and gender were recorded for all participants. Extensive medical and dental histories were recorded for each patient. Patients with aggressive periodontitis or any systemic disorder that may affect the periodontal tissue (such as diabetes, pregnancy and immunological disorders), anemic patient, and smokers were excluded from the study.

Periodontal Examination

Full mouth examinations (excluding third molars) were conducted for all patients. Six sites were examined for each tooth (mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual).

Plaque index (PI), bleeding index (BOP), and positive or negative suppuration were recorded for each site. Probing depths (PD) distance from the cementoenamel junction (CEJ) to gingival margin and clinical attachment loss (CAL) were recorded using a marked periodontal probe (UNC-15 (HU-Friedy), Chicago, IL, USA). Increased tooth mobility was assessed using an ordinal score: 1, horizontal displacement of 1 mm; 2, horizontal displacement > 1 mm; and 3, horizontal and vertical displacement > 1 mm. Furcations and the number of missing (NM) teeth were also recorded.

Blood Analysis

Under aseptic conditions, venous blood was drawn from ante-cubital fossa. The blood was taken into vacuum tubes and transported to a laboratory for processing within 4 hours after venepuncture, and hemoglobin (Hb) concentration was measured.

Statistical Analysis

Data were analyzed using statistical package for social sciences (SPSS, version 16). Means of continuous variables and frequency distributions of categorical variables were calculated. Bivariate Pearson correlation of Hb with age, CAL, PD, BOP, PI, and NM were calculated. Based on extent and severity of CAL, subjects were classified as having severe (CAL $\geq$ 5 mm at $\geq$ 30% of sites), moderate (CAL = 3-4 mm at $\geq$ 30% of sites) or mild (CAL < 3 mm). Mean Hb was compared among patients with mild, moderate and severe periodontitis using one way analysis of variance (ANOVA) statistical test. The number of missing teeth (NM) was classified into quartiles. Hb was calculated for each category and compared among the categories using ANOVA statistical test. Statistical significance was set at $p < 0.05$.

Results

Characteristics of the study sample are shown in Table 1. The mean age of the study sample was 34.2 ($\pm$ 13). Females constituted about 53% of the study sample. About 17% of the study sample had severe periodontitis, whereas more than 53% had mild periodontitis. The mean hemoglobin level was 12.8. On average, bleeding on probing was recorded on 57% of the examined sites. The mean plaque score was 74%. Clinical attachment loss (CAL) averaged 2.4 mm and mean probing

depth was 2.6 mm. More than 85% of the sample had no teeth with furcation involvement. About 6% of the patients had furcation of Grade I only, whereas Grade II or greater was detected in 10% of the subject. On average each patient had more than 5 missing teeth.

Table 1. Description of the study sample.

	N	%
Gender		
Females	65	52.4
Males	59	47.6
Prevalence of Periodontitis		
Mild	66	53.2
Moderate	37	29.8
Severe	21	16.9
Prevalence of Furcation		
No	105	85.4
Grade I	07	5.7
Grade II, III or IV	11	8.9
	Mean	**SD**
Age (years)	34.2	13.0
Hb (mmol/L)	12.8	2.0
BOP (%)	56.7	23.6
PI (%)	73.7	22.2
CAL (mm)	2.4	1.5
PD (mm)	2.6	0.6
Missing teeth (n)	5.5	3.7

Hb = hemoglobin level; BOP = bleeding on probing; PI = plaque index, CAL= clinical attachment level; PD= probing depth.

The correlations between hemoglobin level (Hb) and periodontal parameters are shown in Table 2. The CAL and plaque scores were positively and significantly associated with Hb. After adjusting for the age and gender, however, the correlation attenuated and became insignificant.

Table 2. Bivariate correlation of Hb and periodontal parameters.

	PCor	p - value	PCor	p - value
BOP	0.035	0.698	0.088	0.340
PI	0.188	0.037	0.177	0.054
mean CAL	0.248	0.005	0.039	0.670
mean PD	0.134	0.139	0.077	0.403

BOP = Bleeding on probing; PI = Plaque index; CAL = Clinical attachment level; PD = Probing depth.

H.A. Aljohani

Table 3 compares the mean Hb among subjects with varying severity of periodontitis in the total sample and stratified by gender status. The mean Hb level was significantly higher for subjects with severe as compared to mild periodontitis. However, when the sample was stratified by gender, the mean Hb level was not significantly different for individuals with different severity of periodontitis in the total sample as well as among males and females.

Table 3. **Mean (± SD) hemoglobin level (mmol/L) among patients with varying severity of periodontitis.**

	Total Sample		Male		Female	
	Mean	SD	Mean	SD	Mean	SD
Mild	12.5	1.9	14.5	1.2	11.4	1.2
Moderate	13.0	2.1	14.3	1.6	11.2	1.4
Severe	13.7	1.8	14.5	1.0	11.7	1.8
P-value*	0.043		0.758		0.750	

For the difference of the mean hemoglobin level among subjects with varying severity of periodontitis based one way ANOVA

Table 4 presents the means Hb across missing teeth categories. No significant differences in the mean Hb were found across the missing teeth categories in the total sample or after stratification with gender.

Table 4. **Mean (± SD) hemoglobin level (mmol/L) among patients with varying number of tooth loss.**

	Total Sample		Male		Female	
	Mean	SD	Mean	SD	Mean	SD
Mild	13.3	1.8	14.5	1.1	11.7	1.1
Moderate	12.8	2.1	14.5	1.2	11.3	1.5
Severe	12.5	2.0	14.2	1.6	11.3	1.3
P-value*	0.223		0.621		0.580	

For the difference of the mean hemoglobin level among subjects with varying number of tooth loss based one way ANOVA

Discussion

The current study investigates the correlation between hemoglobin level and the severity of periodontitis in systemically healthy patients with generalized chronic periodontitis.

A few early reports in the literature have investigated the bidirectional relationship between anemia and periodontitis. Goldstein[29], Siegel[30], Lainson *et al.*[31], and Chawala *et al.*[32] were among the first to

observe anemia in periodontitis. Most of these authors believed that anemia was one of the causes of periodontitis rather than being the consequences[29,31-32].

The hypothesis that infection will lead to anemia is possible. Strong evidence indicates that pathogenic bacteria or their products can stimulate cells such as fibroblasts, keratinocytes, and macrophages, which are present in periodontal tissue, to release a number of inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α); prostaglandin E_2; interleukins (IL-1β, IL-6, and IL-12); granulocyte colony-stimulating factor (G-CSF); and chemokines. These chemokines such as IL-8 can regulate T-cell function and induce secretion of interferon-inducible protein (IP)-10. And macrophages inflammatory protein (MIP)-1α, that are relevant to inflammatory process in periodontal diseases[33-38]. The elevation in cytokine and chemokine by cells within the gingival connective tissue in chronic periodontitis lesion may result in the increased level of these mediators in the blood circulation, where they can induce or perpetuate systemic effect[38,39].

Various studies have tried to evaluate the relationship between periodontitis and hemoglobin. Hutter *et al.*[2] and Thomas *et al.*[40] found that periodontitis patients have lower hematocrit, lower numbers of erythrocytes, lower hemoglobin levels and higher erythrocyte sedimentation rates when compared to healthy controls. Rai and Kharb[41] found an increased in hemoglobin and RBC levels in patients with severe periodontitis after scaling and root planning. Also, Agarwal *et al.*[42] demonstrated a significant improvement in hemoglobin value and erythrocyte count after periodontal treatment, including surgery in patient with generalized chronic periodontitis with anemia. On the other hands, Wakai *et al.*[3] failed to show any association between hemoglobin levels and periodontal status. Furthermore, Havemose-Poulsen *et al.*[43] failed to show any association between hemoglobin levels and periodontal status in patients with localized aggressive periodontitis, generalized aggressive periodontitis, juvenile idiopathic arthritis, and rheumatoid arthritis.

In the present study there is a positive and significant association between CAL and plaque scores with hemoglobin level. Also, the mean hemoglobin level was significantly higher for subjects with severe as compared to mild periodontitis. However, when the sample was

stratified by gender, both correlations attenuated and became insignificant. These results are in agreement with Wakai *et al.*[3] and Havemose-Poulsen *et al.*[43] studies. However, it differed from the Havemose-Poulsen *et al.* [43] study, as in the current study, it included chronic periodontitis patients only. This study cannot be compared to previous studies done by Hutter *et al.*[2] and Thomas *et al.*[40], as both of these studies compared hemoglobin level in periodontitis patients *vs.* healthy controls, while the current study compared hemoglobin level in patients with different severity of periodontitis.

The finding, which was observed in the present study, showed a higher level of hemoglobin in patients with severe chronic periodontitis as compared to moderate or mild periodontitis (even though it was not statistically significant). This may be attributed to the smaller sample size in severe periodontitis group as compared to mild ones. Also, this can be overcomed in further research by minimizing the difference in the sample size between different groups. Another possible hypothesis is that "as long as the patient is having periodontitis, the hemoglobin level will not differ among different severity". The addition of a control group without periodontitis will help to investigate the validity of this hypothesis.

Conclusion

No association between hemoglobin levels and periodontal status was found. Further longitudinal studies with larger sample size are needed to investigate the association between hemoglobin levels and different types of periodontitis, and the effect of periodontal treatment on hemoglobin level.

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العلاقة بين مستوى الهيموجلوبين و حِدة أمراض اللثة المزمنة

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المستخلص. إن الغرض من هذا البحث هو دراسة العلاقة بين مستوى الهيموجلوبين في الدم و حدة أمراض اللثة عند المرضى الذين يعانون من التهابات مزمنة في اللثة. لقد تم جمع معلومات البحث من ١٢٤ مريضٍ تم تحويلهم إلى عيادات علاج وجراحة اللثة بكلية طب الأسنان، جامعة الملك عبد العزيز. تم تعبئة التاريخ الصحي للمرضى و تاريخ علاج الأسنان واللثة، ثم قام مساعدو الباحث بعد التدريب الدقيق بالكشف على اللثة والأسنان لتشخيص أمراض اللثة. بعد ذلك قام فنيّو المعمل بجمع عينات دم من المرضى لمعرفة مستوى الهيموجلوبين في الدم. لم يكن هناك فرق هام في مستوى الهيموجلوبين في مختلف درجات حدة أمراض اللثة المزمنة في الذكور والإناث. مستوى حدة التهاب اللثة وفقدان الأنسجة المحيطة بالأسنان لم يكن مرتبطًا بمستوى الهيموجلوبين. لا توجد علاقة هامة بين مستوى الهيموجلوبين ودرجات حدة أمراض اللثة المزمنة. يجب القيام بأبحاث طويلة المدى على أعداد مرضى أكثر، لتأكيد هذه النتائج.