

Association of Chronic Periodontitis with Reduced Haemoglobin Level

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ABSTRACT

Introduction: Chronic periodontitis is an infectious disease of supporting tissues of tooth due to subgingival colonisation of pathogenic bacteria. Microorganisms or their by-products can invade periodontal tissues through ulcerated pocket epithelium and gain access to systemic circulation producing proinflammatory cytokines which can downregulate erythropoiesis in bone marrow thereby decreasing blood counts. Conversely, reduced oxygen-carrying capacity of blood in anaemic patients cause impaired oxygen supply to periodontal tissues leading to persistent pathogenic bacterial challenge.

Objective: To observe the association of chronic periodontitis with reduced level of haemoglobin.

Methods: This case-control study was conducted from 2015 May to 2016 May at UCMS after ethical approval. Sixty systemically healthy patients (controls=30 with healthy periodontium; cases=30 with chronic periodontitis) visiting Department of Periodontology and Oral Implantology, were included in study. The clinical parameters (gingival index, probing pocket depth, clinical attachment loss) and serum haemoglobin level of the participants were compared. Statistical analysis using student's unpaired t-test, analysis of variance, Pearson's correlation and Odd's ratio was performed.

Results: Statistically significant difference between cases and controls in haemoglobin level (11.64 ± 1.489 g/dl and 12.85 ± 1.360 g/dl respectively) was observed. The correlation analysis showed statistically moderate negative correlation of haemoglobin concentration with pocket depth ($r = -0.424$) and weak negative correlation with clinical attachment level ($r = -0.307$).

Conclusions: Chronic periodontitis patients had lower haemoglobin level compared to healthy controls. This suggests that chronic periodontitis like, any other long-standing conditions, may be associated with risk for anaemia. As these chronic conditions reinforce each other, meticulous management of either may assist treatment of other.

Keywords: Anaemia; chronic periodontitis; cytokines; haemoglobin; periodontium.

INTRODUCTION

Chronic periodontitis is an infectious disease of supporting tissues of tooth. However, the microorganisms/their by-products can invade periodontal tissues and gain access to systemic circulation producing proinflammatory cytokines.^{1,2}

Research has revealed that periodontitis increases the risk of various systemic problems and this long-standing

chronic inflammation can also lead to anaemia. Various studies³⁻⁷ have been conducted to clarify the relationship between reduced haemoglobin (Hb) level and chronic periodontitis and often, the association is bidirectional. The cytokines invading systemic circulation can downregulate erythropoiesis and decrease blood counts.⁸ Conversely, reduced oxygen-carrying capacity of blood in anaemic patients cause impaired oxygen supply to periodontal tissues leading to persistent pathogenic bacterial challenge.^{3,4}

To authors' best understanding, very limited number of studies have been carried out previously to observe the association between chronic periodontitis and reduced level of Hb. As these chronic conditions reinforce each other, meticulous management of either may assist treatment of other. Hence, this study was carried out to observe the association of chronic periodontitis with reduced level of haemoglobin.

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METHODS

This case-control study was conducted from May 16, 2015 to May 16, 2016. The study included 60 systemically healthy subjects visiting the Department of Periodontology and Oral Implantology, Universal College of Medical Sciences (UCMS), College of Dental Surgery, Siddharthanagar, Rupandehi, Nepal. The protocol of this study was approved by the Institutional Review Committee, UCMS (Ref. UCMS/IRC/016/15). The purpose of this research project was explained to the patients and informed consent forms were due signed.

Based on the study by Gokhale et al.,² sample size of 30 in each group was calculated using formula:

$$n=2SD^2(Z\alpha + Z\beta)^2 / d^2;$$

where $Z\alpha=1.96$ at 95% confidence interval; $Z\beta=0.84$ (at 80% power); standard deviation (SD) of haemoglobin level=1.525; and mean difference, $d=1.14$ (haemoglobin in control=13.28±1.29; haemoglobin in test=12.14±1.76). Hence, the participants were divided into controls: 30 periodontally healthy subjects and cases: 30 patients with chronic periodontitis. For inclusion in the study, participants had to be systemically healthy with following characteristics: (i) aged 30 to 60 years, (ii) probing depth ≤3 mm (controls) (iii) probing depth ≥5 mm in at least two teeth per quadrant and (iv) clinical attachment loss ≥2 mm at >30% sites (cases).⁹ Similarly, patients with history of known systemic diseases, severe trauma, or renal transplant, history of hospitalisation or who had taken systemic medications within previous six months, smokers, obese individuals, pregnant or lactating females were excluded in the study.

Under strict aseptic condition, periodontal examinations of the participants were done using mouth mirror and University of North Carolina-15 (UNC-15) probe. The

clinical parameters including gingival index (GI),¹⁰ probing pocket depth (PPD), and clinical attachment level (CAL) were recorded at the same visit. Based on their periodontal findings, they were categorised into case group and control group. A tourniquet and 3 ml syringe were used to withdraw venous blood from the cubital fossa. The collected blood was transferred into ethylenediaminetetraacetic acid (EDTA) containing vials. The sample was then sent to the Department of General Pathology for estimation of serum Hb level (cyanmethaemoglobin method). Data obtained by clinical examinations and laboratory tests were entered into Microsoft Excel Sheet 2013 and analysed using SPSS Statistics for Windows, version 16.0 (SPSS Inc., Chicago, Ill., USA). The student's unpaired t-test, one-way analysis of variance (ANOVA) test, Pearson's correlation and Odd's ratio were applied.

RESULTS

The patients with age 30-60 years were included in the study where mean age of control group and case group were 38.5 years and 40.2 years respectively. Similarly, control group included females 17 (56.7%) more than males 13 (43.3%) while cases had higher proportion of males 16 (53.3%) than females 14 (46.7%).

On comparing Hb concentration in the study population, cases showed lower Hb level as compared to controls which was statistically significant ($P < 0.05$, Table 1).

Age wise comparison of Hb concentration in the subjects showed that cases had lower values of Hb as compared to controls in all age groups (Table 2). It was statistically significant in 30 to 40 and 41 to 50 years age-group ($P < 0.05$). Similarly, genderwise comparison of Hb concentration in study groups demonstrated that cases had lower Hb level as compared to controls in both males and females which was statistically significant ($P < 0.05$).

Table 1: Comparison of Hb concentration in study groups.

Hb concentration (g/dl) Mean ± S.D.			
Controls	Cases	t-value	p-value
12.85 ± 1.36	11.64±1.49	3.29†	<0.001*

*Statistically significant ($p < 0.05$), †unpaired t-test

Table 2: Age wise and gender wise comparison of Hb concentration in study groups.

		Control	Cases	p-value
Age groups (years)	30-40	12.75±1.47	11.14±1.95	0.047*
	41-50	13.10±0.70	11.43±1.21	0.006*
	51-60	13.60±0.99	12.53±1.17	0.317
Sex	Female	11.96±0.82	11.07±1.44	0.049*
	Male	14.02±0.98	12.14±1.39	<0.001*

*Statistically significant ($p < 0.05$)

Table 3: Comparison of Hb concentration among various categories of periodontitis (Mean \pm S.D.)

Mild Periodontitis	Moderate Periodontitis	Severe Periodontitis	F- statistic	p- value
11.60 \pm 2.08	12.02 \pm 1.58	11.04 \pm 0.56	1.230	0.308

* Statistically significant (p <0.05), †One-way ANOVA

Table 4: Pearson's correlation among various study parameters in Cases group.

Mild Periodontitis		Hb Concentration	Age	Gingival Index Score	Probing Pocket Depth	Clinical Attachment Level
Hb Concentration	Pearson Correlation	1	0.297	-0.149	-0.424*	-0.307*
	p-value	-	0.111	0.430	.019	0.047
Age	Pearson Correlation	0.297	1	0.180	.046	0.138
	p-value	0.111	-	0.342	0.808	0.466
Gingival Index Score	Pearson Correlation	-0.149	0.18	1	0.169	0.164
	p-value	0.430	0.342	-	.371	0.386
Probing Pocket Depth	Pearson Correlation	-0.424*	0.046	0.169	1	0.867**
	p-value	0.019	0.808	0.371	-	0.000
Clinical Attachment Level	Pearson Correlation	-0.307*	0.138	0.164	0.867**	1
	p-value	0.047	0.466	0.386	0.000	-

* Statistically significant (p <0.05)

Table 5: Association between chronic periodontitis and Hb level in males and females.

		Cases	Controls	Total	Odd's Ratio	P-value
Males	Anaemic	11	1	12	26.4	0.0033*
	Non-Anaemic	5	12	17	Ref.	
	Total	16	13	29		
Females	Anaemic	11	7	18	5.24	0.083
	Non-Anaemic	3	10	13	Ref.	
	Total	14	17	31		

* Statistically significant (p <0.05); 95% confidence interval

Comparison of Hb concentration among various CAL groups in cases was done in order to assess if the level of Hb varies with the severity of periodontitis (Table 3). The P value, corresponding to F-statistic of one-way ANOVA was applied among various CAL groups, and was found to be >0.05 suggesting that the values of Hb does not differ among the different severity of periodontitis.

The correlation matrix of various demographic, haematological, and periodontal parameters among cases showed statistically significant moderate negative correlation of Hb concentration with probing pocket depth (r=-0.424) and statistically significant weak negative correlation of Hb concentration with clinical attachment level (r=-0.307). The analysis also showed weak negative correlation between Hb concentration and GI score (r=-0.149) which was statistically insignificant (Table 4).

On applying Yates corrected Chi-square test to assess the association between chronic periodontitis and the anaemic condition in male patients, it was observed that male patients who were anaemic have 26.4 times more chances to

have chronic periodontitis in comparison to the males who were not suffering from anaemia (Table 5). The association was statistically significant (P <0.05). Similarly, the female patients who were anaemic have 5.24 times more chance to have chronic periodontitis in comparison to those females who were not suffering from anaemia. However, this association was not statistically significant (P=0.083)

DISCUSSION

Earlier paradigms have maintained that periodontitis is an oral disease and that the tissue destruction remains localised within the periodontium, limiting its effects to oral tissues supporting the teeth only. However, recent studies have proved that periodontitis also affects the systemic health. Periodontal deterioration increases the risk of various systemic problems and this long-standing chronic inflammation can also lead to anaemia.^{5,6,11,12}

The present study showed that patients with periodontitis showed lower Hb level as compared to controls. In correspondence to the results of current study, several

authors^{1,2,12,13} have also deduced that periodontitis patients have lower Hb levels, lower haematocrit, lower number of erythrocytes when compared to healthy controls. A 10-week intervention study by Rai et al.¹⁴ found an increase in Hb and red blood cell (RBC) levels after scaling and root planing in the patients with severe periodontitis. Similarly, several studies^{15,16} also showed a significant improvement in Hb value and erythrocyte counts after non-surgical periodontal therapy. This supports the hypothesis that periodontitis may be a contributing factor for the reduced erythrocyte counts.^{9,17} On contrary to this, few studies¹⁸⁻²⁰ found no change in Hb and erythrocyte values in patients with and without periodontal diseases.

In the present study, age wise comparison of Hb concentration in the subjects showed that cases had lower values of Hb as compared to controls in all age groups, which was statistically significant in 30-40 years and 41-50 years age groups. On contrary to current result, Hawkins et al.²¹ in their study showed higher values of Hb tending to occur among the younger men. After the fifth decade, there was progressive and marked decrease in the level of Hb. Moreover, genderwise comparison of Hb concentration in study groups demonstrated that cases had lower Hb level as compared to controls in both males and females, which was statistically significant. This finding was in accordance with the result obtained in previous studies.^{22,23} When the haematological variables between the two study groups were compared separately in men and women, it was observed that, irrespective of gender, the patients with periodontitis had significantly lower Hb concentrations and lower erythrocyte counts.²³

Clinical attachment loss provides a reliable indicator of the degree of periodontal tissue destruction. Therefore, in the present study, Hb concentration was compared amongst various CAL groups (mild periodontitis, moderate periodontitis and severe periodontitis). This was done to assess if Hb concentration varies with the severity of periodontitis. However, it was found that the level of Hb does not differ among the different severity of periodontitis. This result was in accordance with previous studies²⁴⁻²⁶ where haematological and biochemical parameters were not affected by the severity of periodontitis. On contrary to the present study, the study by Khan et al.¹¹ showed a substantial decrease in red blood cell parameters with increase in the severity of periodontal destruction.

Pearson correlation analysis showed weak negative correlation between Hb concentration and GI score which was statistically insignificant. This result was in accordance to a study carried out by Ali¹² which showed a weak negative but statistically insignificant correlation between Hb level and GI. The result of present study was also in

correspondence to an interventional study performed by Patel et al.²⁷ where the GI score in anaemic patients dropped after periodontal treatment. It strongly suggested that gingivitis is closely linked with the severity of anaemia and the oxygen content in the blood. This is also in accordance with the study by Nair et al.⁵ and it can be interpreted that in the presence of gingivitis, the Hb% and the RBC count tends to decrease.

The analysis from present study also showed statistically moderate negative correlation of Hb concentration with probing pocket depth and statistically weak negative correlation of Hb concentration with clinical attachment level. This significant relationship may indicate the beginning of subclinical or clinically evident anaemic status. This result was in correspondence with the study conducted by Nair et al.⁵ which showed negative correlation between the CAL and Hb%. In accordance to the current study, a weak negative but insignificant correlation were found between Hb level and PPD in the previous studies.^{4,12} This negative correlation suggests that anaemic status may be considered a risk factor for the periodontal diseases. This may be caused by the impaired oxygen supply to the periodontal tissues as a result of the reduced oxygen-carrying capacity of blood in anaemic patients leading to a persistent sub-gingival gram-negative anaerobic bacterial challenge to the host.³

Conversely, some authors^{1,2} reported that depression in the number of erythrocytes is apparently secondary to the presence of periodontal disease. The inflamed and ulcerated epithelium, in periodontitis, acts as an easy portal of entry for the oral microorganisms to enter the connective tissue and thus into the systemic circulation producing proinflammatory cytokines. The elevated levels of proinflammatory cytokines from local chronic disease process, may downregulate erythropoiesis in bone marrow leading to low erythrocyte count and ultimately low Hb level.²⁸ The same inflammatory cytokines have been found to play a central role in the pathogenesis of anaemia of chronic disease (ACD).^{29,30} Hence, periodontitis, being a chronic disease, may lead to decreased erythrocyte count consequently lowering the Hb levels in a substantial number of patients. There have been conflicting findings as far as the Hb levels are concerned in periodontitis patients. On contrary to the present study, Wakai et al.²⁰ did not observe any relationship between increased Community Periodontal Index of Treatment Needs scores and Hb levels. Accordingly, the study by Havemose-Poulsen et al.¹⁹ did not show any association between Hb levels and periodontal status. The changes in Hb and RBC values were not as high as observed in anaemia due to other inflammatory conditions like rheumatoid arthritis and multiple myeloma. This may be due to the reason that other diseases are more severe

inflammatory conditions than periodontitis. Therefore, anaemia resulting from periodontitis (low-grade chronic infection) is relatively mild. This also might be the reason why some of the studies failed to find any relation between haematocrit indices and periodontal status.¹⁸⁻²⁰

It was observed that male patients who were anaemic were 26.4 times more likely to have chronic periodontitis in comparison to the males who were not suffering from anaemia. The association was statistically significant. In correspondence to the results of the present study, several studies^{1,2,11,27} also showed that male patients with chronic periodontitis have lower Hb level along with other red cell parameters when compared to healthy controls. Similarly, female patients who were anaemic have 5.24 times more chance of developing chronic periodontitis than the females who were not suffering from anaemia. However, the association was not statistically significant. Females are prone to hormonal imbalance during puberty, during the reproductive phase, and toward menopausal age. The microbial flora and the host immune response are altered leading to exaggerated response of the periodontal tissues to local factors. Therefore, to eliminate the bias, comparison of Hb concentration between the two study groups was performed separately between males and females.²²

It would be prudent that longitudinal studies with greater sample size, and determining the effect of interventional

therapeutics on the haematological parameters would have helped to arrive at a definitive conclusion. Within the limitations of the present study, it can be stated that chronic periodontal diseases are associated with alterations in the Hb concentration.

CONCLUSIONS

Like any other chronic condition, chronic periodontitis can also lead to signs of anaemia. Being a low-grade infection, the signs may not be as severe as seen in other systemic conditions, but they definitely cannot be ignored. As these chronic conditions reinforce each other, meticulous management of either may assist treatment of other. The present study has paved the path for future studies in order to further validate the association between periodontal disease and anaemia.

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Conflict of Interest: None.

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