Effect of Scaling and Root Planing on Erythrocyte Count, Hemoglobin and Hematocrit in Patients with Chronic Periodontal Disease

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Introduction

Despite substantial improvement in the oral health status of populations across the world, periodontal disease still remains a significant social burden. Periodontal diseases are the end result of the host response to complex actions of a group of periodontal bacteria, predominantly gram–negative anaerobes. Accumulating evidence on the role of periodontal diseases on general health has related chronic periodontal inflammation to various systemic diseases, diabetes mellitus being the most consistent.[1] On the other hand, the aggravating effect of periodontal diseases on cardiovascular diseases, pre–term and/or low birth weight, stroke, pneumonia and anemia has been clinically observed.[2–15]

The association between anemia and periodontal disease has been explored since the 20th century. Available literature indicates a 2–way relationship with some reports suggesting anemia to be a cause of destructive periodontal disease, whereas others suggest it is a consequence of it. Siegel et al reported depression in the number of erythrocytes apparently secondary to the presence of periodontal disease.[8] Various authors in the literature have substantiated these findings.[9–13,15] However, little was known at that time about the reasons for the hematological alterations. Lainson was one of the first authors to implicate anemia as a systemic cause of periodontitis.[16]

Abstract

Purpose: Anemia of chronic disease, a cytokine–mediated anemia, is a frequent complication of many chronic inflammatory conditions. The present clinical trial was aimed to evaluate the effect of chronic periodontal disease on erythrocyte count, hemoglobin and hematocrit and the changes produced in these parameters after the provision of periodontal therapy.

Methods: 40 systemically healthy non–smoker male subjects in the age group of 25 to 50 years suffering with chronic periodontal disease were selected and categorized into 2 groups. Group A was categorized as chronic generalized gingivitis, and Group B was categorized as chronic generalized periodontitis on the basis of clinical findings. The clinical parameters Gingival Index (GI), Probing Pocket Depth (PPD) and Relative Attachment Level (RAL) and laboratory blood investigations viz erythrocyte count (EC), hemoglobin (Hb), hematocrit (HCT) and red cell indices (MCV, MCH, MCHC) were recorded at baseline. Complete oral prophylaxis was performed for all patients. Patients were recalled after 3 weeks and 3 months. The clinical and hematological parameters were re–evaluated to analyze the changes after provision of phase I therapy.

Results: The mean values of EC, Hb and HCT were significantly lower in Group B in comparison to Group A, and showed a significantly greater increase at 3 months of observation. However, the values of MCV, MCH and MCHC showed a non significant change during the same observation period in both the groups.

Conclusion: Lower values of EC, Hb and HCT in Group B showed that mild anemia is associated with chronic generalized periodontitis, which tends to improve after provision of periodontal therapy. Minimal changes in MCV, MCH and MCHC indicated that the lower values are not due to any vitamin and mineral deficiencies, but secondary to the chronic inflammatory changes associated with chronic periodontal disease.

Keywords: Chronic periodontal disease, periodontitis, anemia, erythrocyte count, hemoglobin, hematocrit, inflammation, cytokines

This study supports the NDHRA priority area, **Health Services Research:** Evaluate strategies that position and gain recognition of dental hygienists as a primary care providers in the health care delivery system.

Mechanical debridement has been the cornerstone for professional plaque control and prevention of periodontal disease for centuries.[17] It aims not only to preserve periodontal tissues, but also to limit the oral source of inflammation contributing to overall systemic well–being.

Periodontal medicine defines a rapidly emerging branch of periodontology focusing on establishing a strong inter–relationship between periodontal disease and systemic health and offering new insights of the oral cavity as one system interconnected with the whole human body.[18] Most of the studies undertaken in the past to clarify the association between periodontal diseases and the lowered hematological parameters were either cross–sectional or longitudinal, and described only the co–existence of the 2. Thus, the present interventional trial was carried out to discover if the improvement in periodontal status after periodontal therapy could result in any alteration of the lowered hematological parameters.

Methods and Materials

Subject Selection

The study was carried out as a parallel, 2 group clinical interventional trial. The study design was approved by the Medical Ethical Committee of National Dental College & Hospital, Derabassi.

The study population consisted of 40 systemically healthy non–smoker male subjects suffering with chronic periodontal disease in the age group 25 to 50 years visiting the Department of Periodontology and Oral Implantology, National Dental College and Hospital, Derabassi (Punjab). The criteria for inclusion were:

1. Suffering with generalized chronic periodontal disease
2. No history of antibiotic intake for the last 3 months prior and during the course of the study
3. No history of blood loss in the recent past. No history of any minor or major trauma, any oral or general surgical procedure, which could have resulted in blood loss
4. No history of any periodontal treatment at least 6 months before the commencement of the study
5. No history of blood transfusion and/or donation 3 months prior and during the course of the study
6. Patients showing cooperation for the treatment

The study subjects were categorized into 2 groups of 20 patients each. Group A (Chronic Generalized Gingivitis, n=20) was described as showing clinical signs of gingivitis. Changes in color, contour, consistency, texture and bleeding on probing and probing pocket depth ≤3 mm. Group B (Chronic Generalized Periodontitis, n=20) was described as having probing pocket depth ≥5 mm and clinical attachment loss ≥3 mm. The selected subjects were verbally informed about the study protocol and asked for their voluntary participation.

Study Method

The gingival and periodontal status was evaluated for each patient using the following clinical parameters:

- Gingival Index – Loe and Silness,[19] 1963
- Probing Pocket Depth – William's Periodontal Probe (Hu Friedy, Chicago, Ill.)
- Relative Attachment Level (only for Group B) – CPITN probe with customized acrylic stent (Hu Friedy, Chicago, Ill.)

Collection of Blood Sample

After recording the clinical parameters, 5 ml of venous blood was drawn under aseptic conditions, from the ante cubital fossa. The drawn blood was transferred immediately to EDTA containing vacutainers to be transported to the medical laboratory. The estimation of the following hematological parameters was done using fully automated cell analyzer–Sysmex K21 analyzer:

- Total erythrocyte count (EC)
- Hemoglobin level (Hb)
- Hematocrit (HCT)
- Mean Corpuscular Volume (MCV)
- Mean Corpuscular Hemoglobin (MCH)
- Mean Corpuscular Hemoglobin Concentration (MCHC)

Thorough full mouth scaling and root planing was performed for all the patients using hand and ultrasonic instruments.

The patients were given oral hygiene instructions and instructed to brush twice daily and use mouth rinse with 0.12% Chlorhexidine digluconate twice daily for plaque control. The patients were advised not to take any iron or vitamin supplements, and were asked not to make any modifications in their diet during the course of study. The patients were recalled after 3 weeks and 3 months for reevaluation of all the clinical and hematological parameters. Oral hygiene instructions were reinforced at each follow up visit.

Statistical Evaluation

The data obtained was compiled and analyzed using SPSS Inc., version 15.0 for Windows. Mean and standard deviation for all parameters were calculated. The statistical significance of differences in independent variables for the intra–group measurements were analyzed by using student t–test (2 tailed, paired) and for inter–group measurements over time were tested according to student t–test (2 tailed, independent). The data was found to be normally distributed as analyzed with one sample Kolmogorov–Smirnov test and hence paired t–test was applied. A 2 tailed probability value (p–value) <0.05 was considered as statistically significant and p–value≤0.01 considered as highly significant. A p–value>0.05 was considered as non–significant

Results

The study population consisted of 20 males with a mean age of 27.6 years (age range: 25 years to 43 years) for Group A, and a mean age of 36.5 years (age range: 28 years to 50 years) for Group B. In Group A, all the 20 patients completed the follow up at 3 weeks and 3 months. In Group B, 17 patients completed the study, however, 3 patients did not return at the 3 month follow up due to unknown reasons. Data from these patients was excluded.

Baseline data of the total study population has been summarized in Table I. Data analysis revealed that the values of clinical parameters viz. GI and PPD were higher in Group B in comparison to Group A. In Group A, at baseline, 35% and 25% of subjects were below laboratory reference range (Figure 1) for erythrocyte count and hematocrit, respectively, whereas in Group B 75% of subjects were below reference range for erythrocyte count and hemoglobin, and 55% for hematocrit (Table II and III). The values of red cell indices viz. MCV, MCH and MCHC were comparable in both the groups and were within the normal reference range.

Analysis Of Clinical Parameters

The clinical and hematological parameters at 3 weeks and 3 months of observation for Group A and Group B have been summarized in Table I.

Gingival Index (GI)

In Group A, the mean reduction in GI from baseline to 3 months was 0.24±0.29, which was statistically significant. In Group B, a statistical significant reduction of 0.32±0.18 in GI was observed from baseline to 3 months. When Group A and Group B were compared for change in GI at different periods of observation, a statistically non–significant difference was observed between the 2 groups.

Table I: Showing mean values of clinical parameters and hematological values at baseline, 21 days and 3 months in Group A and Group B

Clinical Parameters	Group A	Group B
Gingival Index		
GI1	1.64±0.23	2.30±0.24
GI2	1.40±0.24	2.04±0.27
GI3	1.40±0.35	1.99±0.32
Probing Pocket Depth (in mm)		
PPD1	2.36±0.29	4.94±0.39
PPD2	2.11±0.27	4.64±0.29
PPD3	2.10±0.30	4.48±0.32
Relative Attachment Level (in mm)		
RAL1	–	9.07±0.76
RAL2		8.60±0.44
RAL3		7.88±0.78
Hematological Parameters	Group A	Group B
Erythrocyte Count (X 10^6/µL)		
EC1	4.60±0.42	4.06±0.61
EC2	4.61±0.34	4.15±0.55
EC3	4.70±0.40	4.28±0.46
Hemoglobin (g/dl)		
Hb1	14.29±0.65	12.77±2.02
Hb2	14.43±0.65	12.87±1.93
Hb3	14.60±0.81	13.08±1.95
Hematocrit (%)		
HCT1	42.72±3.29	39.34±5.10
HCT2	42.58±3.19	39.73±5.00
HCT3	43.23±3.14	39.75±4.89
Mean Corpuscular Volume (fl)		
MCV1	92.99±7.37	93.83±6.55
MCV2	92.57±6.25	93.77±6.67
MCV3	92.46±7.14	92.75±8.02
Mean Corpuscular Hemoglobin (pg)		
MCH1	31.38±2.22	30.93±3.46
MCH2	31.51±1.68	31.09±3.20
MCH3	31.21±1.79	30.82±3.65
Mean Corpuscular Hemoglobin Concentration (g/dl)		
MCHC1	33.42±1.47	32.66±1.96
MCHC2	33.88±2.72	32.31±2.60
MCHC3	33.74±2.58	33.40±2.06

Probing Pocket Depth (PPD)

In Group A, the mean reduction in pocket depth from baseline to 3 months was observed to be 0.25±0.27 mm, which was statistically significant, whereas, in Group B, the mean reduction in pocket depth from baseline to 3 months was 0.43±0.22 mm, which was also statistically significant. When Group A and Group B were compared for change in pocket depth a significantly greater reduction was present in Group A when compared to Group B from baseline to 3 months.

Table II: Table showing descriptive analysis showing distribution of hematological parameters based upon laboratory reference range for Group A

Group A	Baseline			3 months		
	Normal	Abnormal	% below reference	Normal	Abnormal	% below reference
Erythrocyte count	13	7	35%	15	5	25%
Hemoglobin	20	–	–	20	–	–
Hematocrit	15	5	25%	17	3	15%

Table III: Table showing descriptive analysis showing distribution of hematological parameters based upon laboratory reference range for Group B

Group B	Baseline			3 months		
	Normal	Abnormal	% below reference	Normal	Abnormal	% below reference
Erythrocyte count	5	15	75%	6	11	65%
Hemoglobin	5	15	75%	14	3	18%
Hematocrit	9	11	55%	9	8	47%

Relative Attachment Level (RAL)

In Group B, a mean gain in RAL from baseline to 3 weeks and baseline to 3 months was observed at 0.47±0.44 mm and 1.14±0.76 mm, respectively, which was statistically significant at both periods of observation.

Analysis of Hematological Parameters

Erythrocyte Count (EC)

In Group A, an increase of 0.09±0.22 $X10^6$/µL was noted in EC from baseline to 3 months, which was not statistically significant. In Group B, the increase in EC from baseline to 3 months was observed to be 0.30±0.39 $X10^6$/µL, which was statistically significant. When Group A and Group B were compared for change in EC, a statistically significant difference in improvement was observed for Group B in comparison to Group A at 3 weeks to 3 months of observation.

Hemoglobin (Hb)

In Group A, an increase of 0.31±0.57 gm/dl was observed in Hb concentration from baseline to 3 months, which was statistically significant. In Group B, an increase of 0.53+0.69 gm/dl was recorded, which was statistically significant. When Group A and Group B were compared for change in Hb concentration, a statistically significant difference in improvement was observed for Group B in comparison to Group A during the observation period of 3 weeks to 3 months.

Hematocrit (HCT)

Figure 1: Normal hematological values (for adult males)

COMPONENT	REFERENCE VALUES (in conventional units)
Erythrocyte count	4.5–6.5 X 106/µL
Hemoglobin	11.5–16.5 g/dl
Hematocrit	40–54%
MCV	77–93fl
MCH	27–32 pg
MCHC	30–35 g/dl

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In Group A, the mean change in HCT from baseline to 3 months was observed to be 0.46±1.72, which was not statistically significant. In Group B, an increase of 0.52±1.01 was observed in HCT from baseline to 3 months was statistically significant. When Group A and Group B were compared for change in HCT at different periods of observation, a statistically non–significant change was observed.

Red Cell Indices: Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC)

In Group B, a statistically significant difference in improvement was observed between mean values of MCHC at 3 weeks to 3 months interval. However, a non–significant change was observed in MCV, MCH at different periods of observation. In Group A, a statistically non–significant change was observed in

MCV, MCH and MCHC at different periods of observation.

A significant difference in improvement was observed with respect to MCHC in Group B when compared to Group A between 3 weeks and 3 months of observation.

The results of descriptive analysis showing distribution of hematological parameters based upon laboratory reference range for Groups A and B have been tabulated in Table II and III, respectively.

Discussion

The mouth is the mirror of health and disease, as a sentinel or early warning system, as an assessable model for the study of other tissues or organs and as a potential source of pathology affecting other systems and organs. The concept of periodontal diseases as localized entities affecting only the teeth and supporting apparatus has been revised, as it has been seen that rather being confined to the periodontium, periodontal diseases have wide ranging systemic effects. Periodontal disease has a potential relationship with several systemic conditions like cardiovascular diseases, diabetes mellitus, adverse pregnancy outcomes, obesity and stroke.[1–6] One of the lesser–documented associations has been the inter–relationship between periodontal disease and anemia.

Anemia of chronic disease (ACD) is an immune driven process in which cytokines result in decreased erythropoietin production, impaired proliferation of erythroid progenitor cells and disturbed iron homeostasis.[20,21] This normocytic and normochromic anemia has been described in many chronic diseases like rheumatoid arthritis, renal failure, bacterial and parasitic infections, and chronic periodontitis, among others.

An interventional study was planned to measure the effects of scaling and root planing on EC, Hb and HCT in patients with chronic periodontal disease. This study design was preferred over cross–sectional and longitudinal study, as it could clearly delineate that resolution of periodontal inflammation could influence general health by improving metabolic control and endothelial function.

The study population consisted of 40 adult males of Asian Indian origin and excluded females, tobacco smokers and chewers, patients on antibiotics and with recent history of blood loss, as these characteristics can act as possible confounding factors that could alter the hematological factors. Females were excluded as they undergo physiological blood loss and cyclic hormonal imbalance, which is responsible for an altered and exaggerated response to local factors. Gokhale et al reported that in India, anemia is more prevalent in females due to poor nutrition, increased menstrual losses, high incidence of tropical and intestinal infections and other miscellaneous factors.[13] Erdemir et al suggested that smokers with chronic periodontitis had lower number of erythrocytes, lower value of Hb, HCT and iron as compared to nonsmokers with chronic periodontitis.[22]

Clinical parameters GI, PPD and RAL were included in the study for the assessment of the inflammatory state of the gingival tissues, the progression of the periodontal disease and the therapeutic effect of the treatment i.e. scaling and root planing. The hematological parameters total EC, Hb, HCT, MCV, MCH and MCHC were selected for evaluation, as these are indicative of the anemic state of the patient and also the type of anemia based on morphology of the cell.[9,15]

The baseline analysis of the hematological parameters of the total study population revealed that in Group A, 35% and 25% of the subjects had values of EC and HCT below the normal laboratory reference range, while the values of all other hematological parameters were within normal laboratory reference range (Figure 1). In Group B, the values of EC, Hb and HCT were below the laboratory reference range in 75% and 55% of subjects, respectively, and were lower as compared to Group A, whereas the values of the red cell indices viz. MCV, MCH and MCHC were within the normal reference range. These findings were similar to as reported by Erdemir who stated some differences between the "healthy" and "periodontitis" groups in the erythrocytes, Hb, and hematocrit values in the peripheral blood, though they were within the reference range for a given parameter in the groups.[22] Similar findings have been reported by Hutter et al,[15] Yamamotu et al,[20] Gokhale et al,[13] Lainson et al,[16] Thomas[12] and Loos.[23] However, Salvi[24] and Zeibolz[25] observed a lack of correlation between anemia and periodontitis.

The subgingival organisms and their products have the potential to enter the blood stream and affect distant sites through the ulceration in the pocket epithelium, and thus evoke low grade systemic inflammation.[9,15,20] Pro–inflammatory cytokines such as TNF–α, IL–1β, INF–γ and PGE_2 are found in high concentrations in inflamed periodontal tissues, and have been related to the suppression of erythropoeisis.[20,22,25–31] Johnson et al exposed mice to a single intravenous dose of TNF–α, which resulted in suppression of spleen and mar-

row erythroid colony forming units (CFU–E).[26] Also, Faquin et al reported that IL–1 (α or β), TNF–α and TGF–β inhibited production of erythropoeitin hormone which is responsible for the regulation of erythropoeisis.[26] Also, periodontal inflammation often results in bleeding from gingiva. Therefore, direct loss of blood might also be responsible for the reduction in number of erythrocytes, but this has not been substantiated with evidence. These are a few plausible mechanisms explaining for decreased values of hematological parameters in patients with periodontitis.[13,20,26]

A significant improvement in the clinical parameters was evident by reduction in the scores of GI, decrease in the PPD in both groups and gain of attachment in the chronic generalized periodontitis patients at the 3 month follow up after phase I therapy from the baseline. This could be attributed to effective mechanical debridement, which was aimed at reduction in the bacterial load, as a result of which the local inflammation decreased significantly.

After 3 months of the periodontal therapy, there was a reduction in percentage of subjects who were below reference range of normal hematological values. In Group A, 25% and 15% of subjects were below reference range for EC and HCT, respectively, whereas in Group B, EC, Hb and HCT were below the reference range in 65%, 18% and 47% of subjects, respectively. A statistically significant improvement of 0.31 million/mm3 was noted in the patients with chronic generalized periodontitis with respect to the EC at the end of the 3 month follow up after the phase I therapy. The results are in accordance with the results of previous studies carried out by Rai[32] and Aggarwal et al,[9] who showed a significant improvement of 0.1 and 0.22 million/mm3, respectively, in EC after the periodontal therapy.

Both groups showed a statistically significant improvement in the Hb concentration at the end of the 3 month follow up after phase I therapy. This rise suggested that the anemia present was secondary to periodontal disease as it improved subsequent to periodontal therapy. The results of the present investigation are favorably comparable to the study carried out by Rai et al, who found a statistically significant increase in the mean hemoglobin level of 14.5 mg/dl at baseline to 15 mg/dl at 10 weeks after scaling and root planing.[32] The findings are also in agreement with the study by Aggrawal, which showed a mean increase in mean Hb value by 0.95g/dl at the end of a 1 year follow up.[9] The variation in the results could possibly be attributed to the longer period of study, where follow up continued for a period of 1 year and surgical treatment was carried out wherever necessary. However, studies by Wakai et al[33] and Havemose–poulsen et al[34] failed to show any association between Hb levels and periodontal status.

A statistically significant improvement was observed in the HCT of patients with chronic generalized periodontitis at the end of the 3 month follow up after phase I therapy with respect to baseline. A similar trend for improvement of HCT was observed in chronic generalized gingivitis patients as well, but the difference observed was statistically non–significant with respect to baseline.

A significant improvement was seen in mean corpuscular Hb concentration in patients with chronic generalized periodontitis at the end of 3 months after the periodontal therapy. Mean corpuscular volume and mean corpuscular Hb followed a statistically non significant rise after the periodontal therapy in both groups. The small increment of change in mean corpuscular Hb and mean corpuscular Hb concentration values compared to increase in Hb levels implied that anemia associated with periodontitis is of normochromic type.[2,30,32] MCV levels are the main determinants of certain types of anemia. A depressed level of MCV (microcytosis) relates anemia to iron deficiency and elevated level of MCV (macrocytosis) relates anemia to vitamin deficiency. In our study, MCV levels were between the reference values as mostly seen in ACD and called as normocytosis. This indicated that anemia due to chronic periodontitis is not due to vitamin or mineral deficiencies, but secondary to the inflammatory changes present in periodontitis.

It was observed that the values of EC, Hb and HCT in patients with chronic generalized gingivitis were higher than the chronic periodontitis patients and were within the laboratory reference range. Also, the changes observed in this study with respect to EC, Hb and HCT are statistically significant in the chronic periodontitis patients as compared to chronic gingivitis patients. The difference could be attributed to the amount of inflammatory response elicited by the periodontitis in comparison to gingivitis. It is important to note that the difference in the hematological parameters in chronic periodontitis was not as striking as observed in anemia due to other inflammatory conditions like rheumatoid arthritis, bacterial and parasitic infections and multiple myeloma. This could be due to the reason that the other diseases are more severe inflammatory conditions than periodontitis as observed by the more severe immune response evoked by them.

Within the limitations of the present study, it can be stated that chronic periodontal diseases lead to alteration in the hematological parameters EC, Hb and HCT, which showed an improvement after the provision of periodontal therapy. The present interventional study has paved the path for future studies, with a larger study population for a longer period of time to further validate the association between periodontal disease and anemia.

Conclusion

The following conclusions were arrived at from this study:

1. Chronic generalized periodontitis being a more chronic and long standing infection resulted in greater depression in the values of hematological parameters in comparison to chronic generalized gingivitis.
2. A highly significant improvement was observed with respect to Hb concentration, EC and HCT in the patients with chronic generalized periodontitis at the end of the 3 month follow up after phase I therapy with respect to baseline. The improvement observed in the patients with chronic periodontitis was significantly greater than chronic generalized gingivitis patients.
3. Non significant changes in the values of MCV, MCH and MCHC indicated that the decreased red cell counts are not due to any vitamin or mineral deficiency, but secondary to the inflammatory changes induced by periodontal diseases.

The emerging field of periodontal medicine offers new insights into the concept of the oral cavity as 1 system interconnected with the whole human body.[32] If this notion is believed to be accurate, we need to assume a larger responsibility apart from diagnosing and treating the periodontal infections, and also educate the public about the importance of oral health in the overall systemic well being. With the resurgence of emphasis on significance of oral disease related to systemic health, the medical professionals also need to familiarize themselves with the oral cavity and the oral–systemic relationships to treat or reduce the morbidity of the underlying medical condition. Oral health care professionals must reach out to the medical community and the general public to improve patient care through education and communication about the perio–systemic link.

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References

1. Soskolne W, Klinger A. The relationship between periodontal diseases and diabetes: An overview. *Ann Periodontol*. 2001;6:91–98.

2. Beck J, Offenbacher S. Association between periodontal diseases and cardiovascular diseases: a state of the science review. *Ann Periodontol*. 2000;6:9–15.

3. Montebugnoli L, Servidio D, Miaton RA, et al. Poor oral health is associated with coronary heart disease and elevated systemic inflammatory and haemostatic factors. *J Clin Periodontol*. 2004;31:25–29.

4. Joshipura KJ, Wand HC, Merchant TA, Rimm AB. Periodontal Disease and Biomarkers Related to Cardiovascular Disease. *J Dent Res*. 2004;83(2):151–155.

5. Agueda A, Manau C, Guerrero A, Echeverria J. Periodontal disease as a risk factor for adverse pregnancy outcomes: a prospective cohort study. *J Clin Periodontol*. 2008;35:16–22.

6. Scannapieco FA, Bush RB, Paju S. Associations between periodontal disease and risk for atherosclerosis, cardiovascular disease and stroke– a systematic review. *Ann Periodontol*. 2003;8:38–53.

7. Scannapieco FA. Role of oral bacteria in respiratory infection. *J Periodontol*. 1999;70:793–802.

8. Siegel EH. Total erythrocyte, leucocyte and differential white cell counts of blood in chronic periodontal disease. *J Dent Res*. 1945;24:270–271.

9. Agarwal N, Kumar V, Gujjari AS. Effect of periodontal therapy on hemoglobin and erythrocyte levels in chronic generalized periodontitis patients: An interventional study. *J Indian Soc Periodontol*. 2009;13:6–11.

10. Kazarian DMC, Janus CE, Abbott DM, Waldrop TCR. Association between anemia and Periodontitis; A NHANES III Review. IADR [Internet]. 2002. Available from: http://iadr.confex.com/iadr/2002SanDiego/techprogram/abstract_12468.htm

11. Chawla TN, Kapoor KK, Teotia SPS, Singh NK. Anemia and periodontal disease – A correlative study. *JIDA*. 1971;67–78.

12. Thomas B, Ramesh A, Ritesh K. Relationship between periodontitis and erythrocyte count. *JISP*. 2006;10(2):288–291.

13. Gokhale RS, Sumanth S, Padhya MA. Evaluation of blood parameters in patients with chronic periodontitis for signs of anemia. *J Periodontol*. 2010;81(8):1202–1206.

14. Gorustovich AA, Steimetz T, Giglio MJ, Guglielmotti MB. A histomorphometric study of alveolar bone modeling and remodeling under experimental anemia and polycythemia in rats. *Arch Oral Biol*. 2006;51(3):246–251.

15. Hutter JW, van der Velden U, Varoufaki A, Huffels RA, Hoek FJ, Loos BG. Lower numbers of erythrocytes and lower levels of hemoglobin in periodontitis patients compared to control subjects. *J Clin Periodontol*. 2001;28:930–936.

16. Lainson PA, Brady PP, Fraligh CM. Anemia, Systemic cause of Periodontal Disease? *J Periodontol*. 1968:35–38.

17. Greenstein G. Periodontal response to mechanical non–surgical therapy: a review. *J Periodontol*. 1992;63(2):118–130.

18. Williams RC, Offenbacher S. Periodontal Medicine: the emergence of a new branch of periodontology. *Periodontol 2000*. 2000;23:9–12.

19. Loe H, Silness J. Periodontal Disease in Pregnancy, I, Prevalence and Severity. *Acta Odontol Scand*. 1963;21:533–551.

20. Yamamoto T, Tsuneishi M, Furuta M. Relationship Between Decrease of Erythrocyte Count and Progression of Periodontal Disease in a Rural Japanese Population. *J Periodontol*. 2011;82(1):106–113.

21. Nissenson AR, Goodnough LT, Dubois RW. Anemia: Not just an innocent bystander? *Arch Intern Med*. 163(12):1400–1404.

22. Erdemir OE, Nalcaci R, Caglayan O. Evaluation of Systemic Markers Related To Anemia of Chronic Disease in the Peripheral Blood of Smokers and Non–Smokers with Chronic Periodontitis. *Eur J Dent*. 2008;2:102–109.

23. Loos B. Systemic markers of inflammation in periodontitis. *J Periodontol*. 2005;76:2106–2115.

24. Salvi GE, Lawrence HP, Offenbacher S, Beck JD. Influence of risk factors on the pathogenesis of periodontitis. *Periodontol 2000*. 1997;14:173–201.

25. Ziebolz D, Jager G, Hornecker E, Mausberg R. Periodontal findings and blood analysis of blood donors: a pilot study. *J Contem Dent Pract*. 2007;8(5):43–50.

26. Dosumu EB, Arowojolu MO, Akande OO, Akingbola TS. Hematological values in juvenile periodontitis patients in Ibandan, Nigeria. *Afri J Biomed Res*. 2002(5);141–143.

27. Craig RG, Yip JK, So MK, Boylan JR, Socransky SS, Haffajee JG. Relationship of destructive periodontal disease to the acute–phase response. *J Periodontol*. 2003;74:1007–1016.

28. Aiuto FD, Parkar M, Andreou G, et al. Periodontitis and Systemic Inflammation: Control of the Local Infection is Associated with a reduction in Serum Inflammatory Markers. *J Dent Res*. 2004;83(2):156–160.

29. Lu YS, Eng LH. Dramatic recovery from severe anemia by resolution of severe periodontitis. *J Dent Sci*. 2010;5(1):41–46.

30. Nemeth E, Rivera S, Gabayan V, et al. IL–6 mediates hypoferremia of inflammation by inducing the synthesis of the iron regulatory hormone hepcidin. *J Clin Invest*. 2004;113:1271–1276.

31. Shi D, Meng H, Xu Li, et al. Systemic inflammation markers in patients with aggressive periodontitis: A pilot Study. *J Periodontol*. 2008;79:2340–2346.

32. Rai B, Kharb S. Effect of Scaling and Root Planing in Periodontitis on Peripheral Blood. *Internet J Dent Sci*. 2008;6(1).

33. Wakai K, Kawamura T, Umemura O, et al. Associations of medical status and physical fitness with periodontal disease. *J Clin Periodontol*. 1999;26:664–672.

34. Havemose–poulsen A, Westergaard J, Stoltze K, et al. Periodontal and hematological characteristics associated with aggressive periodontitis, juvenile idiopathic arthritis, and rheumatoid arthritis. *J Periodontal*. 2006;77:280–288.

35. Newman M, Takei H, Klokkevold P, Carranza F. Carranza. Clinical Periodontology, 10th ed. W.B.Saunders. 2006:312–329 p.