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Estimation and Correlation of Hemoglobin, Neutrophils and Platelets in Healthy, Gingivitis, Chronic Periodontitis and Localized Aggressive Periodontitis Patients- A Clinico- Pathological Study

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KEYWORDS

Chronic Periodontitis, Localized Aggressive Periodontits, Hemoglobin, Neutrophils counts, Platelets Counts.

Abstract

Objectives: Periodontitis is a chronic inflammatory disease caused by bacterial infection of the supporting tissues around the teeth and which may alter the host response and in turn alter haematological parameters like Haemoglobin, Neutrophils, Platelets or vice-versa. These blood parameters might be the practical marker of general health status. The aim of the present study was to estimate and co-relate the hemoglobin, neutrophil, platelet counts in Healthy, Gingivitis, Chronic Periodontitis and Localized Aggressive Periodontitis patients.

Materials and Methods: A total of 80 subjects of both genders with age range of 20-50 years were included in the study and were divided into 4 groups. Blood sample were collected for hematological analysis to evaluate the Hemoglobin, Neutrophils, platelet counts.

Results: statistical analysis was done to comparison of blood parameters which showed no statistical significance in the mean value of haemoglobin percentage and platelets . The mean value of neutrophil countwerefound to be statistically significant.

Conclusion: The findings of the clinical trial suggests relationship between the haematological parameters and periodontal diseases.

Introduction

Periodontal inflammation can deteriorate systemic conditions through the pathology caused by leukocytes. Leukocytes, before all Polymorphonuclear Leukocytes are the major systemic cells of phagocytosis and the first cells of host defence mechanism against infective agents.[1]The number of leukocytes in the blood is often an indicator of disease.[2]

Recent researches have shown that inflammation plays a key role in ischemic heart disease (IHD) and leukocyte count is a marker of inflammation. Leukocytes are involved in the pathogenesis of atherosclerosis due to proteolytic and oxidative vascular damage, abnormal leukocyte aggregation and adhesion, release of cytokines and chemokines.[3,4] Correlation of leukocyte counts with coronary artery disease has been consistently shown to be an independent risk factor and prognostic indicator.[4]

Decreased haemoglobin levels have shown to be associated with an increased risk of coronary atherosclerosis due to increase in blood flow and shear stress resulting in endothelial damage and vessel wall thickness. Studies have shown that 1 g/dl decrease in haemoglobin level is an independent, statistically

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significant risk factor for the development of cardiac morbidity and mortality especially in patients with chronic renal failure. Anaemia is an independent risk factor for cardiovascular disease outcomes in the general population. Recent researches suggested that decrease haemoglobin is an independent predictor of increased morbidity and mortality in patients presenting with acute myocardial infarction. There is a need for studies to establish the association of haemoglobin with cardiovascular diseases in native population.[5]

Platelets and leukocytes activated during bacteremia can go onto excite other cells, enhancing the likelihood of atheroma plaque formation. Activated platelets release pro-inflammatory mediators, exposing pro-inflammatory receptors and resulting in the platelets' binding to leukocytes and endothelial cells.[6] It has been proposed that activated platelets regulate chemokine release by the monocytes in inflammatory lesions.[7] These functions make platelets important components of the thrombotic and inflammatory processes, and platelet activation has been implicated in atherosclerosis and coronary artery disease.[6]

The present study was conducted to estimate and co-relate the Hemoglobin, Neutrophil counts and Platelet countsin healthy, gingivitis, chronic periodontitis, and Localized aggressive periodontitis patients and with the hypothesis that, these markers will be probably altered and are more sensitive to stimulation by periodontal pathogens or exaggerated host response. Also it would explain how periodontitis is the link to the development of anaemia, atherosclerosis and cardiovascular diseases.

Material and Methods

80 subjects (40 males and 40 females) were selected from the Department of Periodontics, A.J. institute of dental sciences, Mangalore, during the period of 2016-2019. Ethical clearance was obtained and an informed consent was obtained from every patient. Written informed consent was taken from all the participants before starting the study and complete case history of the participants was taken and after comparing with indices and radiographs, the participants were be divided into four groups.

Group I: Control group consists of 20 subjects with Healthy Periodontium.

Group II: Gingivitis group consists of 20 subjects with moderate to severe Gingivitis, according to Loe and Silness gingival index.

Group III: Periodontitis group consists of 20 subjects with moderate to severe form of Chronic periodontitis (CP).

Group IV: Periodontitis group consists of 20 subjects withLocalized Aggressive Periodontitis (LAP).

SCREENING EXAMINATION INCLUDES:

- Complete medical and dental case history of the subjects was recorded.Plaque index (PI) was recorded according to criteria given by silness and loe (1964). Gingival index (GI) was recorded according to criteria given by Löe and Silness(1963). Calculus index – simplified (CI-S) was recorded according to criteria given by green and vermillion(1964). Full mouth periodontal examination was recorded which included the determination of probing pocket depth and clinical attachment level using William graduated periodontal probe and radiographs (Orthopantomogram-OPG).

INCLUSION CRITERIA: Age limit range of 20-50 years

INCLUSION CRITERIA FOR GROUP I: Systemically healthy individuals with Absence of any periodontal disease.

INCLUSION CRITERIA FOR GROUP II: Patients who were diagnosed with moderate to severe gingivitis having gingival index score of (>1.1)&Bleeding on probing was present.

INCLUSION CRITERIA FOR GROUP III: At least 3 sites with probing depth more than or equal to 5mm and atleast 3 sites with attachment loss more than or equal to 5mm.Radiographically, horizontal and/or vertical bone loss was assessed.

INCLUSION CRITERIA FOR GROUP IV: Patients less than 35 years of age with Systemically healthy individuals, either showed circumpubertal onset with periodontal damage being localized to permanent first molars and incisors& also showed radiographically, either showed "arc-shaped loss of alveolar bone extending from the distal surface of the second premolar to the mesial surface of the second molar or involving central incisiors

EXCLUSION CRITERIA: Patients with any systemic diseases which were known to affect any of the considered parameters in any way; Pregnant and lactating females;Patients who had undergone periodontal therapy in the previous 6 months; Use of any anti-inflammatory drugs and antibiotic medications in the previous 3 months; Any other infections (e.g. Common cold, influenza, any other ENT infections etc.) which may affect any of the considered study

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parameters; Subjects with history of tobacco chewing, alcohol consumption and smoking.

Haematological Parameters Which Were Evaluated Were: Haemoglobin % ; Neutrophil count ; Platelet count .

Collection of Blood

In aseptic conditions, 6 ml of venous blood was drawn in a disposable syringe by venipuncture from the antecubital fossa and was transferred to 2 separate vials, one of which contained anticoagulant and transported to the laboratory. The peripheral blood samples were collected by venipuncture in the antecubital fossa at the clinico-pathological laboratory of the institution. The samples were analysed for the following: haemoglobin percentage (Hb%, gm%) by cyan meth haemoglobin method and Total leukocyte count (TLC, cells/ cubic mm) in which, neutrophil count and platelet count were analysis using haematological automated analyser(sysmex-XN– 1000) in the institution which used the principle of volume, conductivity, scatter (VCS) and fluorescence, and neutrophil chemotaxis assay was done.

Results

The statistical analysis was performed using SPSS version 20 and statistical significance was defined as p value < 0.001. The comparison of all the groups with each other and clinical and haematological parameters was performed using One Way ANOVAandPOSTHOC TUKEY Test.One way ANOVA test was used for comparison of the gingival score in three groups only with elimination of the healthy group, as the score was 0 in HEALTHY group and CAL comparison in the group III and group IV were done using INDEPENDENT T test, as CAL was 0 in healthy and gingivitis group.

TABLE 1: AGE DISTRIBUTION USING ONE WAY ANOVA TEST FOR ALL THE 4 GROUPS

		N	Mean	Std. Deviation	Statistics/ mean squares	df2(welch) / F(Anova)	p value
AGE	GROUP I	20	29.8	40.305	70.316	37.501	≤0.001
	GROUP II	20	27.6	1.847			
	GROUP III	20	43.6	4.477			
	GROUP IV	20	29.6	3.604			
	Total	80	32.65	20.993			

TABLE 2: GENDER DISTRIBUTION

GENDER * GROUP Crosstabulation							
			GROUP				Total
			GROUP I	GROUP II	GROUP III	GROUP IV	
GENDER	FEMALE	Count	10	10	10	10	40
		% within GROUP	50.0%	50.0%	50.0%	50.0%	50.0%
	MALE	Count	10	10	10	10	40
		% within GROUP	50.0%	50.0%	50.0%	50.0%	50.0%
Total		Count	20	20	20	20	80
		% within GROUP	100.0%	100.0%	100.0%	100.0%	100.0%

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TABLE 3: GENDER DISTRIBUTION USING CHI – SQUARE TEST

Chi-Square Test

	Value	Df	p value
Pearson Chi-Square	.000	3	1.000
N of Valid Cases	80		

P value OF 1 INDICATES NO DIFFERENCE OF GENDER DISTRIBUTION

TABLE 4: PERCENTAGE OF VARIOUS PLAQUE SCORES BETWEEN THE GROUPS USING ONE WAY ANOVA TEST

		N	Mean	Std. Deviation	Statistics/ mean squares	df2(welch) / F(Anova)	p value
PLAQUE INDEX	GROUP I	20	0.2065	0.083305	205.428	35.316	**<0.001**
	GROUP II	20	0.439	0.242051			
	GROUP III	20	2.271	0.376925			
	GROUP IV	20	1	0.381134			
	Total	80	0.979125	0.855848			

TABLE 5: PERCENTAGE OF VARIOUS CALCULUS SCORES BETWEEN THE GROUPS USING ONE WAY ANOVA TEST

		N	Mean	Std. Deviation	Statistics/ mean squares	df2(welch) / F(Anova)	p value
CALCULUS SCORE	GROUP I	20	0.045	0.060481	160.346	36.085	**<0.001**
	GROUP II	20	0.097	0.122993			
	GROUP III	20	1.805	0.457079			
	GROUP IV	20	1.133	0.323112			
	Total	80	0.77	0.795088			

TABLE - 6: ONE WAY ANOVA FOR COMPARISON OF THE GINGIVAL SCORE IN THREE GROUPS ONLY WITH ELEMINATION OF THE HEALTHY GROUP

	GROUPS	N	Mean	Std. Deviation	Welch Statistics (*)/F (ANOVA)	P VALUE
GINGIVAL SCORE	GROUP II	20	0.4945	0.346706	**145.176**	**<0.001**
	GROUP III	20	2.1015	0.396886		
	GROUP IV	20	2.425	0.405067		
	Total	60	1.673667	0.931136		

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TABLE 7: PERCENTAGE OF VARIOUS PERIODONTAL POCKET DEPTH SCORES BETWEEN THE GROUPS USING ONE WAY ANOVA TEST

		N	Mean	Std. Deviation	Statistics/ mean squares	df2(welch) / F(Anova)	p value
PERIODONTAL POCKET DEPTH	GROUP I	20	2.65	0.489361	13.307	41.134	**≤0.001**
	GROUP II	20	3.15	0.587143			
	GROUP III	20	3.469	0.302844			
	GROUP IV	20	3.28	0.363969			
	Total	80	3.13725	0.536276			

TABLE 8: PERCENTAGE OF VARIOUS CLINICAL ATTACHMENT LOSS SCORES BETWEEN GROUP III AND GROUP IV USING INDEPENDENT T TEST

	GROUP	N	Mean	Std. Deviation	t	Df	P VALUE
CLINICAL ATTACHMENT LOSS	GROUP III	20	3.246	1.474729	0.639	38	0.527
	GROUP IV	20	2.97	1.248797			

TABLE 9: PERCENTAGE OF VARIOUS HAEMOGLOBIN PERCENTAGES (gm/dl) SCORES BETWEEN THE GROUPS USING ONE WAY ANOVA TEST

		N	Mean	Std. Deviation	Statistics/ mean squares	df2(welch) / F(Anova)	p value
HAEMOGLOBIN PERCENTAGE(gm/dl)	GROUP I	20	13.85	1.631112	0.382	0.126	0.944
	GROUP II	20	13.85	1.631112			
	GROUP III	20	13.795	2.166607			
	GROUP IV	20	13.56	1.446011			
	Total	80	13.76375	1.710596			

TABLE 10: PERCENTAGE OF VARIOUS NEUTROPHIL COUNT(%) SCORES BETWEEN THE GROUPS USING ONE WAY ANOVA TEST

		N	Mean	Std. Deviation	Statistics/ mean squares	df2(welch) / F(Anova)	p value
NEUTROPHIL COUNT(%)	GROUP I	20	58.15	8.677102	981.913	14.917	<0.001
	GROUP II	20	62.13	8.923364			
	GROUP III	20	71.29	8.149453			
	GROUP IV	20	72.535	6.478489			
	Total	80	66.02625	10.03065			

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TABLE 11: PERCENTAGE OF VARIOUS PLATELET COUNT (10^3) SCORES BETWEEN THE GROUPS USING ONE WAY ANOVA TEST

		N	Mean	Std. Deviation	Statistics/ mean squares	df2(welch) / F(Anova)	p value
PLATELET COUNT (10^3)	GROUP I	20	267.45	57.32224	6879.7	2.594	0.059
	GROUP II	20	272.7	56.86281			
	GROUP III	20	282.5	50.53451			
	GROUP IV	20	309.15	39.18818			
	Total	80	282.95	53.03495			

Discussion

Gingivitis and various forms of Periodontitis is a chronic inflammatory disease mainly due to bacterial infection and altered host response. It is one of the most common oral diseases of humans. Prevalence of periodontal diseases varies among different countries and increases concomitantly with age. Epidemiologic studies have suggested that chronic periodontitis increases the risk of systemic problems such as cardiovascular diseases, atherosclerosis, anaemia, diabetes mellitus and pre-term low birth weight of infants.[8] In addition, some studies had found that periodontal infection even elicits systemic hematologic changes. Periodontitis is a chronic inflammatory disease which leads to the production of cytokines, most characteristically tumour necrosis factor- alpha (TNF-α), IL-1 and IL-6.[9] Such inflammatory cytokines decrease the erythropoietin production leading to the development of anaemia.[10]

The various risk factors for cardiovascular diseases include genetic, biomedical, behavioural and lifestyle characteristics. Those firmly established include low density lipoprotein (LDL),blood pressure, smoking, dietary habits, physical inactivity. Similarly periodontal diseases are highly prevalent and can affect up to 90% of the worldwide population. Gingivitis, the milder form of periodontal disease is caused by the bacterial biofilm (dental plaque). The association of coronary heart disease and periodontal disease may be due to an underlying response trait, which places an individual at high risk for developing both periodontal disease and atherosclerosis.[11]

The link between periodontitis and atherosclerosis have been predicted based on the inflammatory mechanisms initiated by bacteria associated with periodontal lesions like periodontopathic bacteria like porphyromonas gingivalis and their by products reach systemic circulation. The adaptive immune response to the presence of these bacteria exacerbates the expression of pro inflammatory cells which in turn up regulate the endothelial cell activation, promote infiltration of activated leucocytes and influence the propagation of atherosclerotic lesions.[12]

In the present study 80 patients were included (40 males and 40 females) where, all the 4 groups contained 20 patients as per the inclusion criteria. All the 4 groups were demographically similar with respect to age and sex distribution at the time of sampling. Measurement of clinical parameters and its comparison with each other and each blood parameters, in each group were done. Blood samples were collected to estimate and compare haemoglobin, neutrophils and platelets counts in healthy, gingivitis, chronic periodontitis and localized aggressive periodontitis patients.

A tendency towards anaemia in patients with chronic periodontitis was also reported in the study done by **Santosh HN [4]**, whereas a reverse relationship was presented in data obtained during the third National Health And Nutrition Examination Survey (NHANES III), which suggested that individuals with anaemia may be more likely to have periodontal disease.[10]

Chawla et al. [13] suggested that anaemia is an important factor in the aetiology or pathogenesis of periodontal disease. Until then, **Lainson et al. [14]** implicated anaemia as a cause of periodontitis. **Seigel [15]** reported a depression in the number of erythrocytes apparently secondary to the presence of periodontal disease.

Dijk et-al [16] showed that in patients which manifest arterial disease, increasing haemoglobin levels were associated with reduced severity of atherosclerosis. Another study by **Sarnak et-al. [17]**showed that decreased haemoglobin level is an independent risk factor for IHD in general population. In a study by **Zeidman et-al [18]**concluded that anaemia was significantly correlated with advanced IHD, congestive heart failure, arrhythmias and higher mortality rates. Lower

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haemoglobin is also associated with adverse cardiovascular outcomes in patients with ischemic symptoms as it is indicated in a study by **Arant et-al.**[19]

In this present study **HAEMOGLOBIN LEVELS**were estimated in healthy, gingivitis, chronic periodontitis, and Localized Aggressive Periodontits patients. Comparison of HAEMOGLOBIN PERCENTAGE (gm/dl) showed the higher mean value in HEALTHY and GINGIVITIS GROUP followed by CHRONIC PERIODONTITIS GROUP and least in LOCALIZED AGGRESSIVE PERIODONTITIS GROUP and the results showed no statistically significant difference between all the 4 groups. The correlation between haemoglobin percentage (gm/dl) & the clinical parameters like plaque index, gingival index, calculus index, periodontal pocket depth and clinical attachment loss showed no statistically significant difference. In our study, there was no correlation found between anaemia and gingivitis, chronic periodontitis and Localized Aggressive periodontitis, which is in contrast with the study done by **Hutter et al.** [20]that evaluated the blood parameters in patients with chronic periodontitis and concluded that these patients showed signs of anaemia. Another study by **Pradeep and Anuj**[21] demonstrated that chronic periodontitis may tend towards anaemia and provides evidence that non-surgical periodontal therapy can improve the anaemic status of patients with chronic periodontitis, and that improvement in hematologic parameters was greater in female subjects.

The leukocyte count has been demonstrated in several epidemiological studies to be an independant predictor of future coronary heart disease. The majority of studies have shown a dose-response effect, insofar as increasing levels of leukocyte counts are associated with graded increase in cardiovascular risk. [22,23] According to a meta-analysis by **Wheeler et al** [24]neutrophil counts are much stronger predictors of IHD than other components.

In this present study neutrophil count(%) were estimated in Healthy, Gingivitis, Chronic Periodontitis, And Localized Aggressive Periodontits patients. Comparison of Neutrophil Count(%) showed higher mean value in Localized Aggressive Periodontitis group (72.535) is highest followed by chronic periodontitis group (71.29), gingivitis group (62.13) and least in heathy group (58.15). The results were statistically Significant with a test value of 14.917 and p value of <0.001. The correlation between Neutrophil Count(%) & the clinical parameters like plaque index, gingival index, calculus index, periodontal pocket depth and clinical attachment loss showed no statistically significant difference in all the groups. The correlation between the parameters Neutrophil count(%) & calculus score showed a good negative correlation, and is significant with a P value of 0.042 in gingivitis group. The results of our study were similar with the study done by **Frederiksson** [25] , where significantly higher leukocyte counts were reported in non-smoking periodontitis patients compared to non-smoking healthy controls . Also another study done by **Wakai et al.** [26] reported an independent association between WBC count and periodontal disease severity defined by the CPITN (community periodontal index for treatment needs) after adjustment for smoking and other periodontal risk factors.

The mechanism linking periodontal disease to atherosclerosis and coronary artery disease is not yet clearly understood. It has been hypothesized that platelets and leukocytes may be more sensitive to stimulation by periodontal pathogens [27] and that activated platelets and leukocytes might contribute to increased atherothrombotic activity. Studies done by **Monteiro et al.**[28] **and Buhlin et al.**[29], have shown that patients with periodontitis have elevated levels of WBCs and C-reactive protein compared to controls. Periodontitis has also been shown to be associated with an increase in plasma fibrinogen and an increase in platelet activation, which might contribute to a pro-coagulant state and thus an increased risk for atherosclerosis and cardiovascular disease in a study done by **Sahingur et al.**[30]

In this present study **PLATELET COUNT (10^3)** were estimated in healthy, gingivitis, chronic periodontitis, and Localized Aggressive Periodontits patients. Comparison of PLATELET COUNT (10^3)showed the higher mean value in Localized Aggressive Periodontitis group (309.15) followed by chronic periodontitisgroup (282.5), gingivitis group (272.7) and least in healthy group(267.45). The results showed no statistically significant difference between all the 4 groups with a test value of 2.594 and p value of 0.059.The correlation between PLATELET COUNT (10^3)& the clinical parameters like plaque index, gingival index, calculus index, periodontal pocket depth and clinical attachment loss showed no statistically significant difference in all the groups. The correlation between the platelet count (10^3) & plaque index showed a good positive correlation, and is significant

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with a p value of 0.024 in group II. The results of our study were in contrast with the study done by **Al-Rasheed [31], Papapanagiotou et al.[32], Wakai et al. [9]** Increase in neutrophil count, as seen in this study could indicate the fact that neutrophil count can be taken as reliable biomarker for detection of periodontal disease and cardiovascular diseases . Within the limitations of this study, which was relatively small sample size, it can be speculated that periodontal disease may predispose the patients to the risk of cardiovascular diseases.

Conclusion

Conventional periodontal diagnosis methods provide limited information about patient sites and risk of future periodontal breakdown, but haematological parameters like haemoglobin, neutrophils, platelets studied in this study give good information on not only assessment of status of the disease but can also predict the future risk of anaemia,atherosclerosis and other cardiovascular diseases in periodontitis patients. The positive correlation with these inflammatory markers in periodontal disease might be a possible causal pathway in linking the connection between periodontitis and risk for anaemia and cardiovascular diseases in these patients. Non-surgical therapy may avoid the risk of systemic disease in periodontitis patients but was not integrated in this study and the sample size was relatively small to determine the effect of periodontitis with cardiovascular diseases, which were the limitations of this study. Hence, further research to study the cellular and molecular mechanisms of these markers to elicit the risk for anaemia, atherosclerosis and cardiovascular diseases are needed to establish and confirm a definite link.

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