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## **Comparison of hematological parameters in anemia of chronic disease and chronic periodontitis**

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**Abstract**--Background: Periodontitis is a localized, chronic inflammatory reaction, induced by bacteria, and effect healthy periodontium. The third highest prevalence of periodontal disease in the world is in Asia.6 Infections, malignant cells, and autoimmune dysregulation these all factors lead to the activate the immune system and start production of cytokines. Chronic periodontitis can be a

cause of anemia of chronic diseases. **Materials and Methods:** The study population consisted of 160 individuals between the age groups of 20-70 years, Hemoglobin concentration, Erythrocyte count, Mean corpuscular volume, Mean corpuscular hemoglobin, Mean corpuscular hemoglobin concentration was measured using an automated hematology analyser. ESR was estimated using Westergren's method. Serum ferritin was measured on ELISA kit by a semi automated analyser on LISA SCAN. Student's "t" test was used for comparing the mean Hb, erythrocyte count, MCV, MCH, MCHC, ESR, and ferritin between the two groups. **Results:** The comparison of blood parameters was done among study and control males. Mean value of hemoglobin, RBC, MCH, MCHC, ESR and Serum Ferritin were statistically significant ( $P < 0.001$ ) whereas mean value of MCV was statistically insignificant. The comparison of blood parameters was done among study and control females. Mean value of hemoglobin, RBC, MCHC, ESR and Serum Ferritin were statistically significant ( $P < 0.001$ ) whereas mean value of MCV and MCH were statistically insignificant. **Conclusions:** These results show that Periodontitis could be a possible risk factor for ACD. The present study showed that periodontal inflammation results in a decrease in a number of red blood cells and levels of Hb and increased serum ferritin. Oral prophylaxis would be an improvement in health of the patient.

**Keywords**---hematological parameters, anemia, chronic disease.

## Introduction

Periodontium is one of the most sensitive tissues of oral regions that may be affected very early by systemic disorders like endocrine, hematologic, immunologic and mucocutaneous disorders.<sup>1</sup> In recent years periodontitis is considered as one of the most common but serious oral health problems in the world. Periodontitis starts with microbial dental plaque but in advance stage it is synchronized with multiple factors.<sup>2,3</sup> Periodontitis is a localized, chronic inflammatory reaction, induced by bacteria, and affects healthy periodontium. Initially, the microorganisms present on the tooth surface form a microbial bio-film, which evokes an inflammatory reaction and leads to the destruction of the periodontal ligament and alveolar bone.<sup>3,4,5</sup> The third highest prevalence of periodontal disease in the world is in Asia.<sup>6</sup>

Infections, malignant cells, and autoimmune dysregulation these all factors lead to the activation of the immune system and start production of cytokines. Notably tumor necrosis factor-alpha (TNF- $\alpha$ ) and interleukin-1 (IL-1) and IL-6 (IL-6) [5] and other inflammatory cytokines initiate suppression of the bone marrow and depress erythropoiesis and leading to the development of anemia.<sup>6</sup> Hutter in 2001, who used first the term Anemia of chronic disease to describe the anemia observed in periodontitis.<sup>7</sup> Chronic periodontitis can be a cause of anemia of chronic diseases. (Shin-YuLu) ACD is the most common form of anemia observed in clinical medicine.<sup>8</sup> ACD is defined as "anemia occurring in chronic infections,

inflammatory conditions, or a neoplastic disorder which is not caused by marrow deficiencies or other diseases and occurring despite the presence of adequate iron stores and vitamins".<sup>9</sup> ACD is considered as most frequent cause of anemia in rheumatoid arthritis (RA), which shows a pattern of hard and soft tissue destruction caused by an inflammatory process. this similar process is seen in chronic periodontitis also.<sup>10</sup>

These types of anemia are not only important for oral and dental health, but also because they may be recognized by oral examination before more pronounced systemic manifestations occurs by anemia are observed clinically. Because some oral findings may have observed together with several systemic manifestations of the primary disease leading to anemia.<sup>1</sup> The recent observational studies evaluating the relationship of periodontitis and anemia of chronic diseases have shown varying results. Hence an attempt is made in the present study to evaluate the prevalence of Anemia of chronic disease in patients with periodontal disease.

## **Material and Methods**

### **Source of data**

The study population consisted of 160 individuals between the age groups of 20-70 years, selected from the outpatient department of Vyas dental college and hospital, Jodhpur, Rajasthan and blood investigations were done and measured in Dr. S.N. Medical college and associated hospital, Jodhpur, Rajasthan. Institutional ethical committee clearance was obtained. Patients diagnosed with chronic periodontitis were included in the present study. Patients have been excluded from the study with known systemic diseases, tobacco users, person who have undergone periodontal therapy 6 months prior to the study, Person < 20 teeth, diagnosed anemic patients, Immuno-compromised patients, pregnant women, patient undergoing any antibiotic treatment.

### **Study design**

In the present study, 160 patients fulfilling the above criteria were included. All patients were informed about the study and informed consent was obtained. Clinical parameters recorded were Gingival index [ Loe and Silness (1963)], Probing pocket depth (PD) and Clinical attachment loss (CAL).

### **Hematological investigations**

5 ml of venous blood was drawn from the ante-cubital fossa and collected in 2 vials, one with Ethylene diamine tetra acetic acid (EDTA) as an anticoagulant and one without anticoagulant. 2.5 ml of blood without anticoagulant was used to estimate the serum ferritin levels and 2.5 ml of anticoagulated blood was used for other parameters. Hemoglobin concentration, Erythrocyte count, Mean corpuscular volume, Mean corpuscular hemoglobin, Mean corpuscular hemoglobin concentration was measured using an automated hematology analyser. ESR was estimated using Westergren's method. Serum ferritin was measured on ELISA kit by a semi automated analyser on LISA SCAN.

Patients with hemoglobin concentration <13 gm/dl for males, < 12 gm/dl for females and serum ferritin levels above 30ng/ml<sup>12</sup> were diagnosed as having Anemia of chronic disease.

### Statistical Analysis

Students “t” test was used for comparing the mean Hb, erythrocyte count, MCV, MCH, MCHC, ESR, and ferritin between the two groups.

### Results

160 individuals (study males-40, study females-40, control males-40, control females-40) between the age groups of 20-70 years, were analysed for blood parameters:- Hb, RBC count, MCV, MCH, MCHC, ESR and ferritin levels. The comparison of blood parameters was done among study and control males. Mean value of hemoglobin, RBC, MCH, MCHC, ESR and Serum Ferritin were stastically significant(P<0.001) whereas mean value of MCV was stastically insignificant(P=0.31) (Table -1) The comparison of blood parameters was done among study and control females. Mean value of hemoglobin, RBC, MCHC, ESR and Serum Ferritin were stastically significant.(P<.001) whereas mean value of MCV and MCH was Mean value of RBC were stastically insignificant. (Table -2)

Table 1: Comparison of blood paramters among males in study group and controls

Variable	groups	N	Mean	Std. D	t value	p value
Hemoglobin	study males	40	11.18	1.19	-13.855	.001
	Control males	40	14.95	1.25		
RBC	study males	40	4.18	.67	-7.513	.001
	Control males	40	5.17	.49		
MCV	study males	40	80.42	10.55	-1.016	.31
	Control males	40	99.75	119.90		
MCH	study males	40	27.32	4.02	-2.263	.03
	Control males	40	29.06	2.75		
MCHC	study males	40	33.99	1.91	-5.127	.001
	Control males	40	36.02	1.62		
ESR	study males	40	13.33	3.32	12.027	.001
	Control	40	5.13	2.75		

	males					
S.Ferritin	study males	40	79.16	31.94	10.502	.001
	Control males	40	25.92	2.77		
*Student t test						

\*\* p value < 0.05 is statistically significant

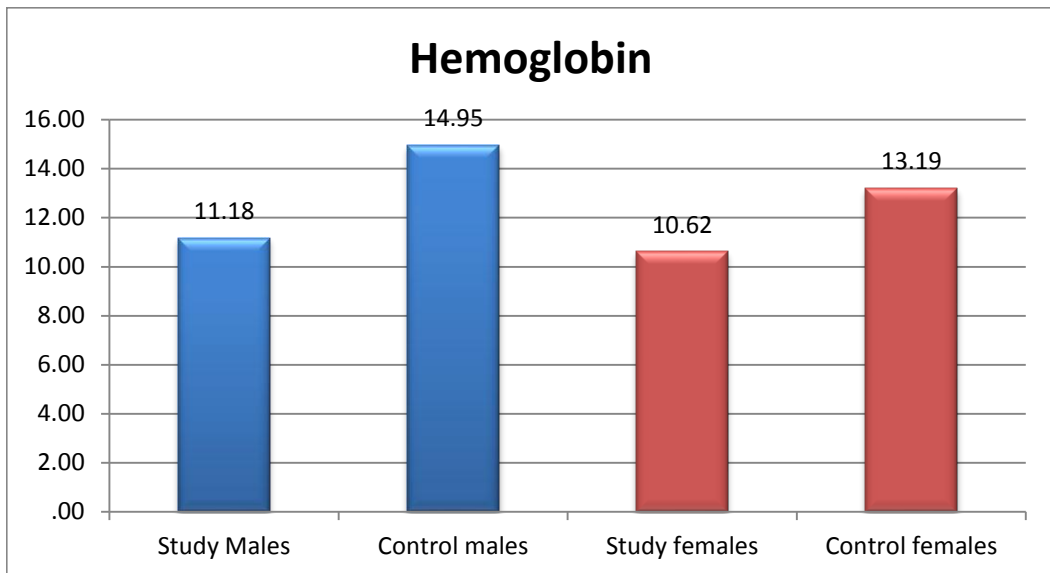
Table 2: comparison of blood parameters among females in study group and controls

Variable	Groups	N	Mean	Std. Deviation	t value	p value
Hemoglobin	Study female	40	10.62	1.66	-8.485	.001
	Control females	40	13.19	.96		
RBC	Study female	40	4.09	.70	-6.181	.001
	Control females	40	4.88	.40		
MCV	Study female	40	77.77	7.83	.342	.73
	Control females	40	77.27	4.74		
MCH	Study female	40	26.19	3.39	-1.709	.09
	Control females	40	27.26	2.05		
MCHC	Study female	40	33.54	2.04	-4.531	.001
	Control females	40	35.29	1.35		
ESR	Study female	40	15.78	4.23	9.339	.001
	Control females	40	7.40	3.77		
S.Ferritin	Study female	40	47.03	14.37	10.161	.001
	Control females	40	22.67	4.84		

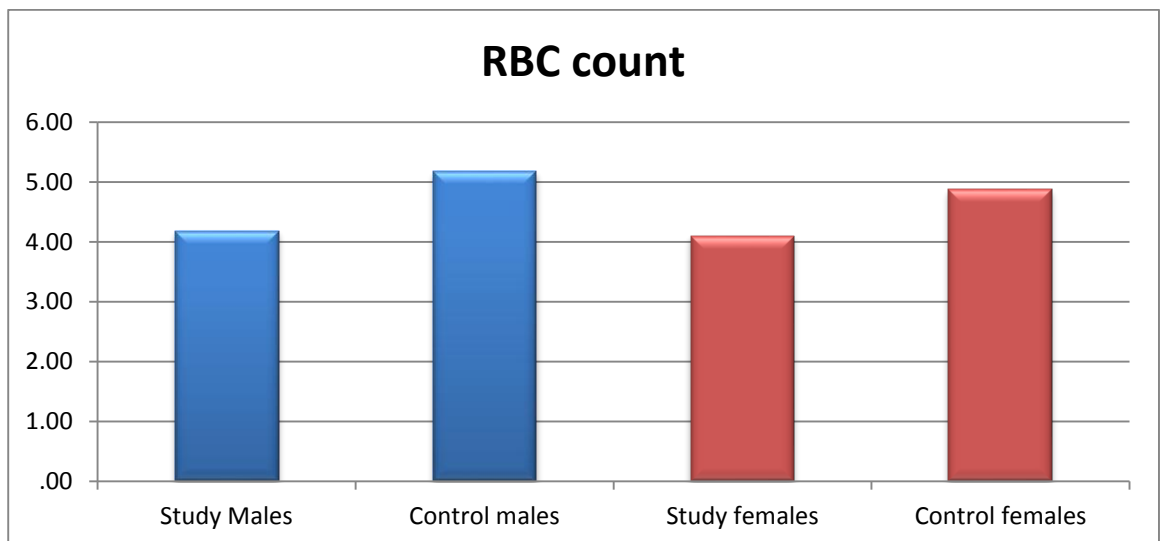
\*Student t test

\*\* p value < 0.05 is statistically significant

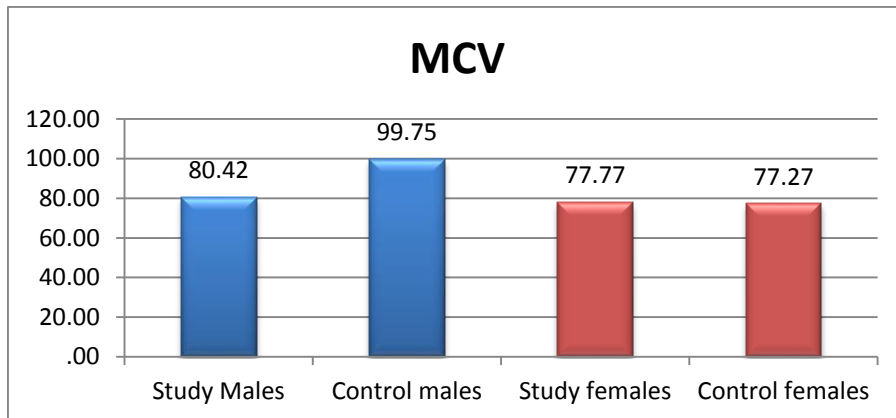
Graph 1: Showing mean hemoglobin levels in study and control groups of males and females



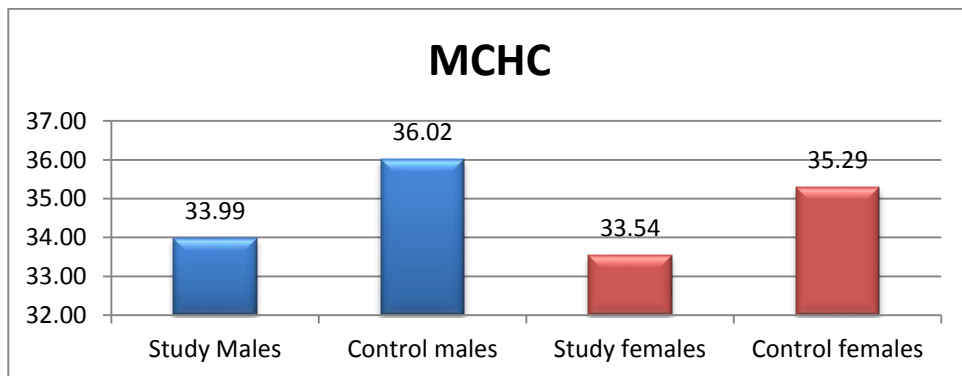
Graph 2: Showing mean erythrocyte counts in study and control groups of males and females



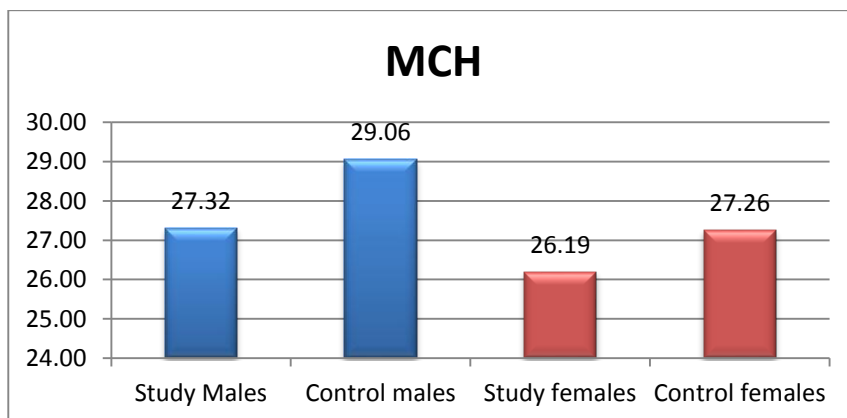
Graph 3: Showing mean MCV levels in study and control groups of males and females



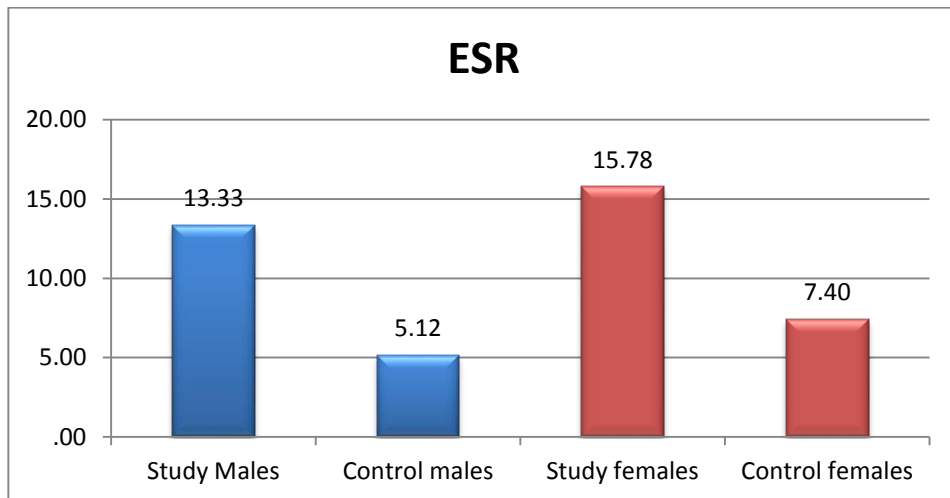
Graph 4: Showing mean MCHC levels in study and control groups of males and females



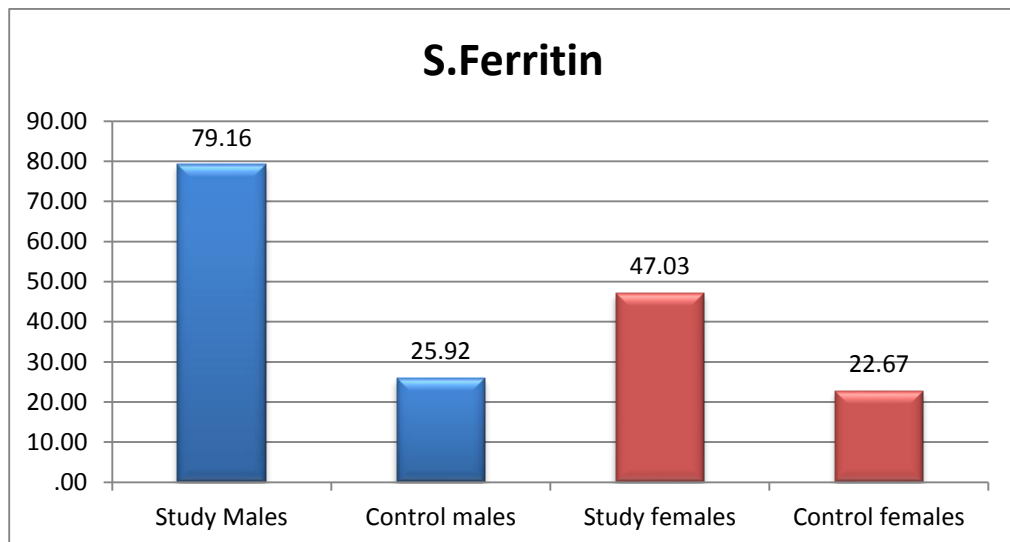
Graph 5: Showing mean MCH levels in study and control groups of males and females



Graph 6: Showing mean ESR levels in study and control groups of males and females



Graph 7: Showing mean ferritin levels in study and control groups of males and females



## Discussion

Periodontitis is a multi-factorial, chronic inflammatory disease of the supporting tissues of the teeth caused by host-microbial interaction in a susceptible environment.<sup>11</sup> The inflamed and ulcerated pocket epithelium forms an easy port of entry for dental plaque bacteria and their toxic products. This causes bacteremia and results in a sustained inflammatory response in the form of cytokines which offers an explanation to the various systemic effects of periodontal diseases.<sup>12</sup> For many years now, blood is regarded as the body fluid



that could indicate disease processes. During any disturbance in the normal physiological processes or during pathology, the changes are reflected in blood.<sup>12</sup> In the past decade a renewed interest developed to evaluate the relationship of periodontitis to cellular components namely red blood cells, white blood cells, platelets and molecular components namely C reactive proteins, fibrinogen and cytokines and in particular erythrocytes and haemoglobin levels which governed a medical condition called Anemia of chronic diseases.

Anemia is common condition and can be caused by various factors. It can also exist as a co-morbidity along with many chronic inflammatory infectious diseases, neoplasia and autoimmune disorders, where it is referred to as Anemia of chronic diseases (ACD). Anemia of chronic disease is known to be mediated by cytokines released in the blood stream due to underlying chronic inflammatory/infectious conditions<sup>13,14</sup> The association between anemia and periodontitis has been studied since a long time but with varying results. In the earlier studies, it was reported that anemia plays a direct role in the etiology of periodontal disease.<sup>7</sup> In contrary, Seigel et al<sup>15</sup> demonstrated that anemia occurred as a result of destructive periodontal disease. Few other authors have also supported this observation Hutter et al<sup>7</sup>, Agarwal et al<sup>16</sup>, Gokhale et al<sup>17</sup>, Naik V<sup>18</sup>, Yammomoto et al<sup>19</sup>, whereas other studies have not reported any such association<sup>20,21,22</sup>

Therefore in the present study, an attempt was made to find out the prevalence of Anemia of chronic diseases in patients with periodontitis. In present study the mean value of hemoglobin was lower in patients with chronic periodontitis (study males-11.18, study females-10.62) than their level in the control group (control males-14.95, control females-13.19). This result was in accordance with studies done by Hutter et al<sup>7</sup>, Prathap S et al<sup>23</sup>, Pradeep et al<sup>24</sup>, Gopinath et al,<sup>25</sup> Suzan ali<sup>26</sup>, Loos B.<sup>12</sup> Mean values of erythrocyte count was lower in study group (study males-4.18, study females-4.09) compared to control group (control male-5.17, control female-4.88) which was in accordance with studies by Yammomoto et al<sup>19</sup>, Harjit kaur<sup>27</sup>, Balwant rai et al<sup>28</sup>, Gokhale et al<sup>17</sup>.

On the contrary, studies done by wakai et al<sup>20</sup>, Aljohani<sup>22</sup>, and Anne Havemose-Poulsen et al<sup>21</sup> showed no changes in these parameters. Mean value of ferritin (control males-25.92, study males-79.16, control females-22.67, study female-47.03) and ESR (control males-5.13, study males-13.33, control females-7.40, study females-15.78) was elevated in our study which was in accordance with studies done by Ebru eldemir et al<sup>2</sup>, Shin yu lu et al<sup>30</sup> and N. Agarwal et al<sup>16</sup>, Kshitiz.Parashar et al<sup>31</sup>, Naik V et al<sup>18</sup>. respectively. This was opposite to the study done by Shobha prakash et al.<sup>32</sup>

Ferritin and ESR values are elevated in anemia of chronic disease. Parameters like hemoglobin and erythrocyte count are reduced in iron deficiency anemia and anemia of chronic disease but ferritin and ESR levels are elevated in anemia of chronic disease only. Thus, with these parameters we can rule out iron deficiency anemia from anemia of chronic disease. MCV and MCH were statically not significant in female groups which was in accordance with study done by Shobha prakash et al<sup>32</sup> and Harjit kaur et al<sup>27</sup>. MCV was statically insignificant for study males in our study which was in accordance with studies done by Shobha prakash et al<sup>32</sup>, and Ebru eldemir et al.<sup>2</sup>

MCHC was statistically significant in both males and females which was in accordance with studies by Hutter et al<sup>7</sup>, Harjit kaur et al.<sup>27</sup> Unlike a few previous studies, Siegel et al<sup>15</sup>, Agarwal et al<sup>16</sup>, Gokhale et al<sup>17</sup>, Naik V<sup>18</sup> female subjects were also included in our study but we considered separate reference levels for males and females. Since we assessed serum ferritin and ESR levels, we could therefore exclude patients with iron deficiency anemia. Serum ferritin is a reliable indicator of bone marrow stores of iron and is used to differentiate ACD from iron deficiency anemia.

A few early reports in the literature have investigated the bidirectional relationship between anemia and periodontitis. Goldstein et al<sup>33</sup>, Siegel et al<sup>15</sup>, Lainson et al.<sup>34</sup>, and Chawla et al.<sup>35</sup> 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. Hutter et al<sup>7</sup>. Thomas et al. Gokhale et al.<sup>17</sup>, Naik V et al.<sup>18</sup>, Moura C et al<sup>36</sup>., and Suzan ali et al<sup>26</sup> found that periodontitis patients have lower hematocrit, lower numbers of erythrocytes, lower hemoglobin levels and higher erythrocyte sedimentation rates when compared to healthy controls<sup>17,22</sup>.

All patients with periodontitis have anemia of chronic disease. The advantage of this study is that ferritin and ESR levels were measured and control group was taken. Only one study done by Shobha prakash et al<sup>32</sup> has included all the parameters which we have taken, but observed similar hematological and biochemical parameters among study and control group. Negative points of the study are that no treatment was done, as after treatment improvement in parameters was observed in studies done by Pradeep et al<sup>24</sup>, Hatipoglu et al<sup>1</sup>, Rai B et al<sup>28</sup> whereas no significant difference was observed in parameters after treatment in study done by Moura C<sup>36</sup> et al. Grading of periodontitis, no correlation between periodontal parameters and blood parameters and no correlation with age was done.

## **Conclusion**

These results show that Periodontitis could be a possible risk factor for ACD. The present study showed that periodontal inflammation results in a decrease in a number of red blood cells and levels of Hb and increased serum ferritin. Further long term studies with larger sample size with ferritin levels and treatment are warranted to support this finding. Good oral Hygiene and routine oral prophylaxis would be an improvement in health of the patient.

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