Association between High sensitivity C – Reactive Protein and Alveolar Bone Loss in Diabetic Periodontopathy

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Abstract: Objectives: This study was done to compare the severity of diabetic periodontopathy between type 2 diabetes (T2DM) patients who had good glycemic control and poor glycemic control and to explore whether high sensitivity c reactive protein (hs-CRP) could be used as a marker for diabetic periodontopathy.

Materials and Methods: Periodontal health of 30 T2DM patients (15 good glycemic control and 15 poor glycemic control diabetes) were recruited in the study based on their HbA1C levels. Periodontal status was assessed according to CDC/AAP periodontitis case definitions and Periodontal Inflamed Surface Area (PISA) Index and evaluation of hsCRP levels done. Panoramic radiographs were taken to assess alveolar boneloss and periodontontal.

Results: Analysis of the results showed that the mean hsCRP levels in poor glycemic control was 5.36mg/L while in the good glycemic control patients, the mean was 2.2mg/L. Patients with elevated hsCRP and poor glycemic control (HbA1c > 7.65%) had accelerated periodontal ligament destruction and alveolar bone loss compared to patients with good glycemic control.

Conclusion: Our study suggested that considerably elevated hsCRP levels with poor glycemic control showed increased alveolar boneloss in diabetic periodontopathy when compared to good glycemic control.

Keywords: Diabetic Periodontopathy, hs-CRP, HbA1C Glycosylated Hemoglobin, Alveolar bone destruction.

I . INTRODUCTION:

Diabetes mellitus (DM) is the most common endocrine disorder characterized by insufficient secretion and action of insulin on target tissues leading to hyper insulinemia [1]. India having approximately 68 million People living with diabetes mellitus [2]. Poorly controlled DM is associated with severe systemic inflammatory burden leading to Diabetic complications. One of such complications is periodontitis in the oral cavity.

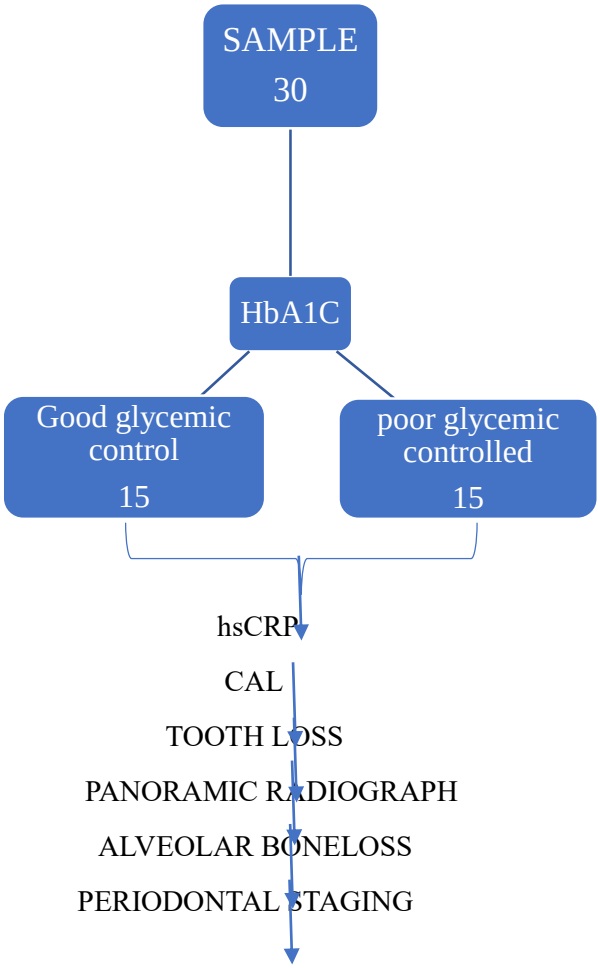
Periodontitis is characterized by gingival tissue attachment destruction, alveolar bone loss, and the formation of periodontal pockets [3]. The systemic inflammatory burden is characterized by elevated levels of pro inflammatory markers such as Interleukins, TNF - alpha, MCP-1, MIP-La, MTP-2, ICAM-1, and VCAM-1 [4, 3,5, 6]. One among these markers is high sensitivity C-reactive protein (hs-CRP) , it is mainly synthesised by hepatocytes in the liver in response to inflammation and tissue damage, it can also be produced locally by arterial tissue [14]. It is extremely sensitive and non-specific acute-phase marker for inflammation, produced in response to many forms of injury or found on the surfaces of pathogens[14]. CRP levels have an association with smoking, obesity, triglycerides, diabetes and periodontal disease. It is proposed that changes in cellular and molecular components of peripheral blood can be found in subjects with periodontitis because of inflammatory changes of the periodontal tissues [14,15]. Routine CRP which measures levels above 3mg/L in adults and High sensitivity (hs-CRP) measuring range up to 3mg/L especially in neonatal medicine, screening as a prognostic marker in adults. Here, in this study elevated hs-CRP levels are hypothesized as linked to insulin resistance and poor glycemic control leading to accelerated periodontal destruction in the presence of local factors. Role of hs-CRP presently remains controversial and need to be adequately assessed. Some studies have evaluated hs-CRP and found correlation between hs-CRP and insulin resistance, however results are still inconsistent.

II. AIMS& OBJECTIVES:

1. To find out whether hs-CRP contributes to systematic inflammatory burden in diabetic patients
2. To find out whether there ia an association between hs-CRP and alveolar bone loss in patients with diabetic periodontopathy
3. To find out whether hs-CRP levels vary among different stages of periodontitis in the diabetic patients.
4.

III. MATERIALS & METHODS:

1.Study design:



IV. SELECTION CRITERIA :

1.Inclusion criteria

All the participants with history of diabetes mellitus which was confirmed by measuring serum concentration of glycated haemoglobin (HbA1c).

7.Exclusion criteria

Participants with missing teeth, history of periodontal therapy in the last 6 months, trauma from occlusion, on any medication which suppresses the chronic inflammatory burden like systemic steroids, immunomodulatory drugs, and immunosuppressant drugs, any chronic medical conditions cardiac disease, renal disease, and liver disease, and not patients willing to participate were excluded from the study.

V. METHODOLOGY:

Thirty diabetic patients were recruited for this study and were divided in to two groups of good glycemic controlled and poor glycemic controlled diabetes based on their serum concentration of glycated hemoglobin (HbA1c). All the participant's detailed medical and dental history will be obtained. Periodontal clinical examination of all the teeth was done at six sites per tooth using Periodontal Williams probe.

Periodontal status was evaluated by assessment of gingival index (GL, Clinical attachment loss (CAL), Tooth loss (TL.) Clinical attachment loss was measured from Cemento-enamel junction to base of the sulcus and Tooth loss was assessed by counting the number of lost teeth. Inflammatory marker serum hs-CRP was assessed.

Blood sample collection, Methods, and Instruments used

3 ml of venous blood sample was withdrawn from each subject and transferred in serum collection tubes. All serum tubes was incubated for 12 min at room temperature for proper coagulation. Serum separation was done by centrifugation at 3000rpm for 15min at room temperature. Using the standard result, a test run was carried out in order to check the separation performance of the system, previous to analysis. HbA1C was estimated by HPCL method, Biorod Company and hs-CRP was estimated Immuno turbido metric method kit from Biorod Company.

Panoramic radiographs were taken to all the participants using Carestream C$8100 machine at 60-90KvP, 2-15Ma, and exposure time of 2-12.5 Sec using C$ imaging version 0.2.221.0.B software. The radiographic bone loss was measured interdentally from cemento- enamel Junction to the crest of the alveolar done. Based on the severity and complexity of the periodontal status, staging of the periodontitis was made by the above clinical and radiographic findings according to CDC/AAP periodontitis case definitions and Periodontal Inflamed Surface Area (PISA) Index. The levels of the mean hs-CRP and staging of periodontitis was compared between the good glycemic control and poorly glycemic control diabetes mellitus patients.

VI. STATISTICAL ANALYSIS :

The data was collected and entered in Microsoft excel 2013 and collected data was analyzed using SPSS version 21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0, IBM Corp., Armonk, NY, India). Intergroup comparison of high sensitivity C- reactive protein among the study groups (good glycemic control and poor glycemic control diabetes groups) was done using independent t test. The level of significance was kept as $P < 0.05$.

The data from patients who had completed the study were summarized using statistical descriptive indices of central tendency and dispersion (mean and standard deviation). The normality of distribution of the data was assessed using the Fisher's exact , Pearson correlation test. Data for periodontal stage, alveolar bone loss, tooth loss due to its periodontitis and CAL. Independent t test was used to compare means of hsCRP levels among study groups good glycemic control and poor glycemic control patients. Fischer's exact test was used to determine the levels of bone loss among study groups. Pearson correlation coefficient was calculated for hsCRP and bone loss.

VII. RESULTS :

Out of 30 patients included in the study, the distribution of male and female among the study population males were 9(60%) in poor glycemic control group and 6(40%) in good glycemic control group, females were 6(40%) in poor glycemic control group and 9 (60%) good glycemic control group with age 48.00+/-12.24 in poor glycemic control group and good glycemic control group 54.2+/-7.94. There was numerical significance between test and control groups seen **" table 1"**

Table 1: Demographic details

Gender	Poor glycemic control group	Good glycemic control group
Male	9(60)	6(40)
Female	6(40)	9(60)

Age	Mean±SD
Poor glycemic control group	48.00±12.24
Good glycemic control group	54.2±7.94

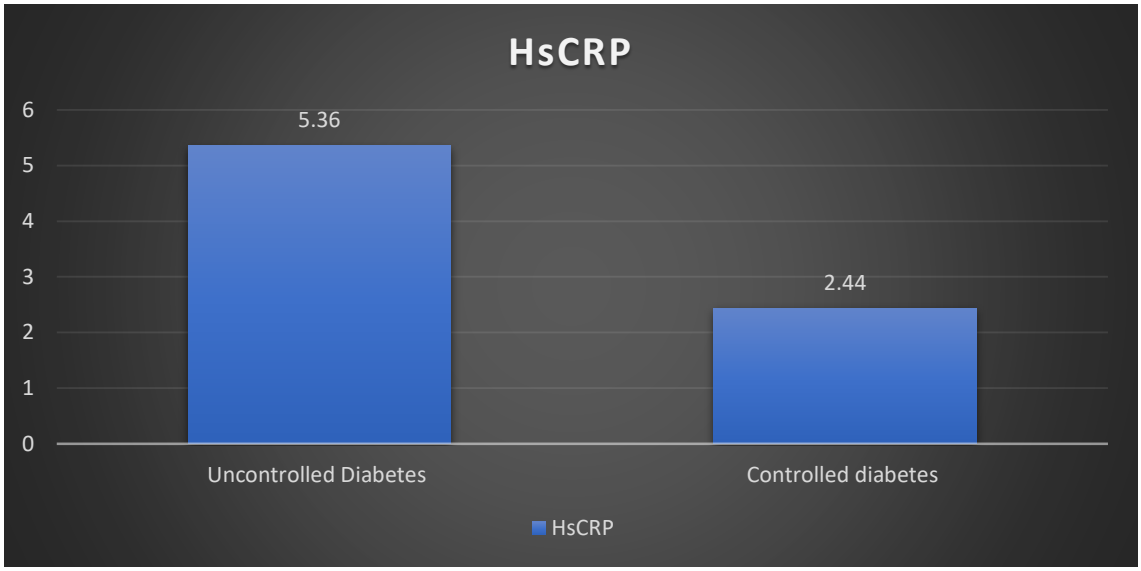
Inter group comparison of hsCRP among the study groups using independent t test showed increase hsCRP levels in Poor glycemic control group (5.36+/-5.98) compared to Good glycemic control group (2.44+/-2.90) **"table-2, Fig 1"**

Table 2: comparison of hsCRP levels among study groups

Groups	Mean ±SD	Tvalue	Pvalue
Poor glycemic control group	5.36±5.98	1.692	0.102(NS)
Good glycemic control group	2.44±2.97		

Independent t test p<0.05* significant

Figure 1:



Staging of the periodontitis using both clinical and radiographic findings shows 9(60%) in the test group and 11(73.3%) in control group in stage 1, 4(26.6%) in Test group and 4(26.7%) in control group are in stage 2, 1(6.7%)was in stage 3 and1(6.7%) in stage 4. No individuals in stage 3 and stage 4 were seen in control group. It is tabulated in **" table 3, Fig 2 "**

Table 3: levels of bone loss among study groups

Periodontitis stages	Test group	Control group
Stage 1	9(60)	11(73.3)
Stage 2	4(26.6)	4(26.7)
Stage 3	1(6.7)	0(0)
Stage 4	1(6.7)	0(0)
χ^2 value : 22.131 pvalue:0.532		

Fisher's exact test, p<0.05* significant

Figure 2

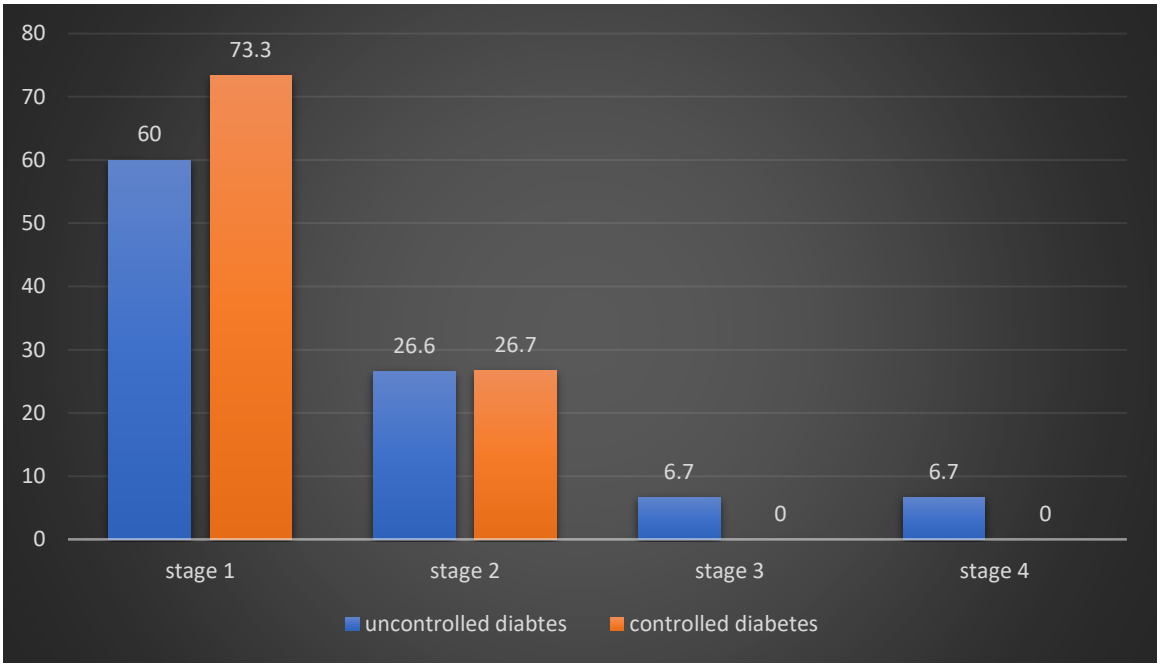


Table 4:Relation between hsCRP and Boneloss

	Boneloss
hsCRP	r =0.18
	p=0.52(NS)

Pearson correlation p<0.05* significant

VIII. DISCUSSION :

Several studies suggested the bidirectional relationship between Diabetes mellitus (DM) and Periodontal disease. Poorly controlled DM is associated with severe systemic inflammatory burden inhibiting osteoblastic differentiation and reduces bone remodelling capacity and act as a risk factor for bone resorption leading to many Diabetic complications. One of such complications is periodontitis in the oral cavity, considering the sixth classic diabetes complication. Periodontitis is characterized by gingival tissue attachment destruction, alveolar bone loss, and the formation of periodontal pockets [3].

The systemic inflammatory burden is characterized by elevated levels of pro inflammatory markers such as Interleukins, TNF - alpha, MCP-1, MIP-La, MTP-2, ICAM-1, and VCAM-1 [4, 3, 5]. One among these markers is high sensitivity C-reactive protein(hs-CRP) . CRP was first reported by Tillett and Francis in 1930 and was named so because it was discovered as a substance in the serum of patients with acute inflammation that reacted with the C-(capsular) polysaccharide of Pnuemococcus [14]. Clinically, CRP can be measured in serum in 2 ways i) routine CRP which measures level above 3mg/L in adults and ii) High sensitivity (hs-CRP) measuring range up to 3mg/L especially in neonatal medicine, screening as a prognostic marker in adults [14]. High-sensitivity assays that accurately measure levels of the inflammatory biomarker C-reactive protein [10,11,12] and elevated hs-CRP could lead to insulin resistance[10] and poor glycemic control leading to accelerated periodontal destruction in the presence of local factors.

The present study evaluated the correlation between the inflammatory burden and alveolar bone loss in diabetic patients. Individuals who were Diabetic were recruited in the study based on their serum glycated haemoglobin(HbA1C), followed by full mouth clinical examination for pocket depth, clinical attachment loss (CAL) and tooth loss using CDC/AAP periodontitis case definition and panoramic radiographs were taken for alveolar bone loss/assessment. Then evaluation of hs-CRP done. Staging of the periodontitis was made by the above clinical and radiographic findings and compared this with the levels of hs-CRP.

Demographic data of the present study shows 15 male and 15 female patients with mean age of 48 in study group and 54 in control group. These results are in accordance with these of E.B. sarmento et al.[4].

Inter group comparison of hsCRP among the study groups showed increase hsCRP levels in poor glycemic control group (5.36+/-5.98) compared to good glycemic control group (2.44+/-2.90) with numerical significance in accordance with Musunuru K, Kral BG, et al. [10]. This suggests that elevated hs-CRP levels correlated with developing insulin resistance and poor glycemic control. This study showed increase in the Alveolar bone loss in poor glycemic control group due to the rise in inflammatory burden, was in accordance with Sarmento EB, et al. [4] Saito et al. [16] observed that alveolar around posterior teeth was associated with elevated level of CRP and another study, Persson et al. [17] found the hs-CRP level to be above 10.0 mg/l in all the subjects in which evidence of significant alveolar bone loss was present indicating periodontitis. They concluded that control of periodontitis can be achieved with non-surgical periodontal therapy, significantly decreasing the serum mediators and markers of acute phase response. Once the cause for elevation of CRP is eliminated CRP levels fall drastically.

In contrast to the above study, Ide et al. [18] failed to observe a reduction in circulating CRP following non-surgical periodontal therapy. it may not be possible to eliminate all the microorganisms from deep inaccessible pockets. Removal of deposits and microorganisms from these locations may require surgical intervention and/or the use of antimicrobial agents

From the present evidence it can be concluded that the relation between hs-CRP and alveolar bone loss was in direct proportion and this was in accordance with the findings reported by Romano F, et al. [13]. This suggest as an unit rise in serum HbA1C and hs-CRP could increase severity of alveolar boneloss.

A limitation of this study was small sample size, which considerably reduced the statistical significance in hs-CRP and alveolar bone loss between groups.

Conclusion :

There is a strong association between hs-CRP and alveolar boneloss in diabetics. hsCRP contributes to the inflammatory burden in the T2DM leading to periodontal destruction there was high numerical level of hsCRP in poor glycemic control patients compared to good glycemic control group. This can be considered as a marker for Diabetic Periodontopathy, warranting an immediate therapeutic intervention **.**

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