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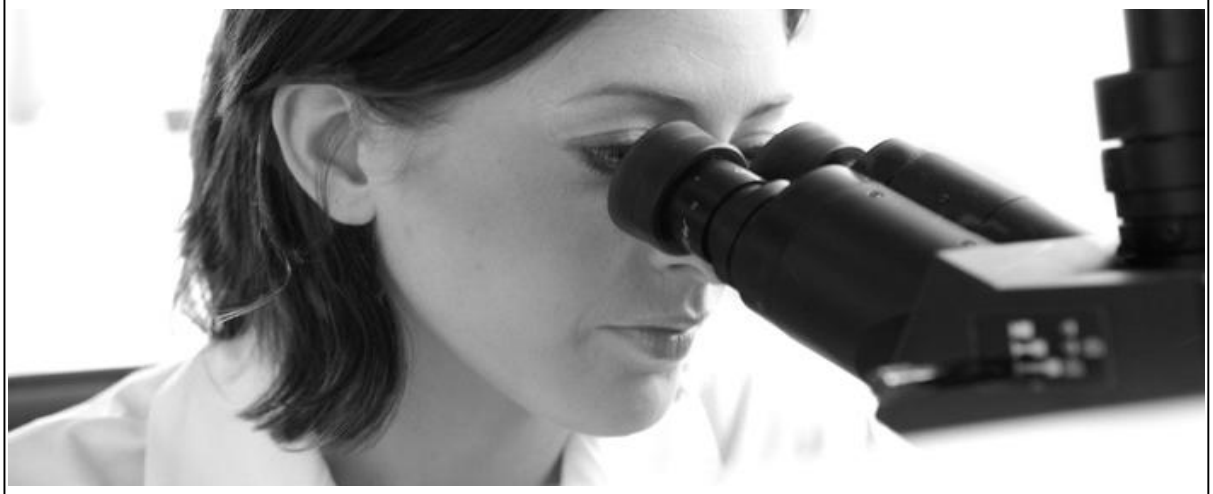

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RESEARCH ARTICLE

FRUCTOSAMINE A POSSIBLE MONITORING PARAMETER IN NON-INSULIN DEPENDENT DIABETES MELLITUS PATIENTS WITH PERIODONTAL DISEASE – A COMPARATIVE STUDY

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ABSTRACT

Aims: The aim of the study was to determine, the relationship between periodontitis, plasma fructosamine, and plasma glucose values in Type-II Diabetes Mellitus patients.
Materials And Methods: A total of 40, Type-II Diabetes Patients within the age group of 40 to 60 years, with Pocket depths having ≥5mm, who were diagnosed as chronic periodontitis were selected from department of Periodontics, Meenakshi Ammal Dental College and Hospital Chennai. The following parameters were evaluated before the assay, Plaque index, Gingival index, Probing pocket depth, Clinical attachment level, and Serum fructosamine was measured with nitroblue tetrazolium (NBT) calorimetric procedure using a commercial kit.
Results: Mean and standard deviations were estimated from the sample for each study group. Mean values were compared by student's paired 't'-test appropriately. The differences between the control (Group A) and test (Group B) groups were compared by using the **Student't' test**. The correlations were also recorded.
Conclusion: Diabetes Mellitus is one of the chronic health problems encountered by most of the population in the world. Since numerous oral changes and particularly, the influence of Diabetes Mellitus on periodontal tissues have been described, the onus is now on the peridontist to effectively treat those patients.

INTRODUCTION

Diabetes Mellitus encompasses a heterogeneous group of disorders with the common characteristics of altered glucose tolerance or impaired carbohydrate metabolism. Diabetes Mellitus affects approximately 4% of the population in the world, and is one of the major chronic health problems encountered by most of the population.

American Diabetes Association recently formed a classification system for Diabetes. It was based primarily on disease etiology, which includes type-I Diabetes Mellitus, type-II Diabetes Mellitus and diabetes due to secondary causes such as gestational Diabetes.

Numerous oral changes have been described in Diabetic patients, and the influence of Diabetes Mellitus on periodontal health has been discussed widely in the dental literature.

A variety of changeson the periodontium have been described in patients with Diabetes, which includes a tendency towards enlarged gingiva, sessile or pedunculated gingival polyps, multiple abscess formation, periodontitis and increased susceptibility to infection. It hasalso been proved that periodontal disease in Diabetes follows no consistent or distinct pattern.

A two-way relationship exists between Diabetes Mellitus and periodontal disease.

1. Periodontal disease often co-exists with Diabetes Mellitus.
2. Diabetes Mellitus is a risk factor for periodontal disease and also periodontal disease increases the severity of Diabetes Mellitus and complicates metabolic control.

This is especially true for patients with poor glycemic control and advanced periodontal destruction.

The American Diabetes Association has officially recognized periodontitis as a complication of Diabetes Mellitus, apart from other complications such as retinopathy, nephropathy, neuropathy, macrovascular diseases and altered wound healing.

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The increased prevalence and severity of periodontitis commonly seen in patients with Diabetes, especially those with poor metabolic control has led **Loe** to declare periodontitis as a "**sixth complication of Diabetes Mellitus**".

Hyperglycemia is the hallmark of Diabetes. Early diagnosis and control of plasma glucose is essential to prevent the various complications of Diabetes Mellitus.

The fasting glucose and random glucose test provide snap shots of the blood glucose concentration at the time blood is drawn. This parameter as an essential criterion for therapeutic decision can be misleading, because this may shift with the sudden change in diet and/or medication. Over the years several new tests have been developed to monitor long and short term control of plasma glucose concentration such as glycated heamoglobin (HbA1 and HbA1c) andfructosamine.

HbA1 assay reflects blood glucose concentration over the preceding 6 to 8 weeks (average half life of RBC 60 days),whereas fructosamine reflects the glycemic condition in the plasma over the preceding period of 1 to 3 weeks (half life of albumin is 14 to 20 days). In addition fructosamine assay has advantages such as low cost, simplicity for the clinical laboratory when compared to HbA1c assay.

Albumin is the major contributor to the total glycated serum or plasma proteins which makes up bulk of the serum proteins which is negligably affected by the other proteins. This study is yet another effort to evaluate the relationship between the periodontitis and plasma fructosamine values in Type-II Diabetes Mellitus patients.

Aims and Objectives

The aim of the study was to determine

- The relationship between periodontitis, plasma fructosamine, and plasma glucose values in Type-II Diabetes Mellitus patients.

MATERIALS AND METHODS

The patients for this study were selected from the patient pool of department of Periodontics, Meenakshi Ammal Dental College and Hospital Chennai during May 2004 to May 2005.

Inclusion Criteria

1. Patients within the age group of 40 to 60 years.
2. Patients who are suffering from Type-II Diabetes.
3. Patients having ≥5mm pockets, diagnosed as chronic periodontitis.

Exclusion Criteria

1. Patients with history of systemic diseases other than Type-II Diabetes
2. Patients who were on antibiotics one month prior to fructosamine assay

Study Design

A total of 40 patients were selected for this study. These were divided into two groups. Group A consisted of 20 patients (control group) and Group B consisted of 20 patients (test group). Ethical clearance and informed consent was obtained from the Hospital and patients prior to the treatment

Group A (Control Group): Patients diagnosed as having chronic periodontitis (≥ 5mm) probing pocket depth with no history of any systemic diseases including Diabetes.

Group B (Test Group): Patients who were suffering from Type-II Diabetes and receiving oral hypoglycemic drugs, diagnosed as having chronic periodontitis (pocket depth ≥ 5mm)

Informed consent was obtained from the patients prior to the treatment.

Clinical Parameters: The following parameters were evaluated before the assay

- Plaque index
- Gingival index
- Probing pocket depth
- Clinical attachment level

Blood Sample Collection

Blood was collected by veni puncture of anticubital vein. This sample was collected after 12 hours fasting.

Samples were collected on to the test tubes and analyzed on the same day.

Fructosamine Assay

Serum fructosamine was measured with nitroblue tetrazolium (NBT) calorimetric procedure using a commercial kit.

Glycated albumin reduces NBT molecule in alkaline medium at 37°C to formazine, which is expressed photometrically, read at 530nm and is expressed as deoximorpholion fructose (DMF) equivalent concentration. DMF being an analogue for the glycated bond, is used as a standard. Albumin and total protein levels were measured to assess the Diabetic status of the patient.

Blood Glucose Assay

Blood glucose was determined with a specific glucose oxidase method by using RA-50 analyzer. The **Liquizone Glucose (GOD-POD)** kit was used.

Principle;

$$\text{Glucose} + O_2 + H_2O \xrightarrow[\text{POD}]{\text{GOD}} \text{Gluconic acid} = H_2O$$

H_2O_2 + Phenol + 4 – Aminoantipyrine ⟶ Red quinoneimine complex + H_2O
GOD – Glucose oxidase
POD – Peroxidase.

Clinical Parameters

Plaque Index (Silness and Loe)

The selected teeth were evaluated using the criteria of plaque index. It examines the scoring units of the teeth; distofacial, facial, mesiofacial and lingual surfaces. A mouth mirror and a dental explorer were used after air drying of the teeth to assess plaque.

Criteria

1. No plaque in the gingival area.
2. A film of plaque adhering to the free gingival margin and adjacent area of the tooth. The plaque may be recognized by running the probe across the tooth surface.
3. Moderate accumulation of soft deposits within the gingival pocket and on the gingival margin and adjacent tooth. Surface that can be seen by naked eye.
4. Abundance of soft matter within the gingival pocket and/or on the gingival margin and adjacent tooth surface.

Plaque indexscores around each tooth are totaled and divided by four, the plaque index score per tooth is obtained. The plaque index score per person is obtained by adding the plaque index score per tooth and dividing by the number of teeth examined.

Gingival Index (Loe and Silness)

The selected teeth were evaluated using the criteria of gingival index. The tissues surrounding each tooth were divided into four gingival scoring units, the distofacial papilla, the facial margin, the mesiofacial papilla, and the entire lingual gingival margin. To minimize examiner variability in scoring, the lingual surface is not subdivided because it is most likely be viewed indirectly with a mouth mirror. A blunt instrument such as periodontal pocket probe is used to assess the bleeding potential of the tissues. Each of the four gingival units was assessed according to the following criteria.

1. Normal gingiva
2. Mild inflammation, slight change in color, slight edema, no bleeding on palpation
3. Moderate inflammation, redness, edema glazing and bleeding on probing
4. Severe inflammation, marked redness, edema, ulceration, and tendency to spontaneous bleeding.

Totaling the scores around each tooth yields the gingival index score for the area. If the scores around each tooth are totaled and divided by four, the gingival index score for the tooth is obtained. Totaling all of the scores per tooth and dividing by the number of teeth examined, provides the gingival index score per person.

The numerical scores of the gingival index are associated with varying degrees of clinical gingivitis as follows.

Gingival Scores	Degree of Gingivitis
0.1-1.0	MILD
1.1-2.0	MODERATE
2.1-3.0	SEVERE

Probing Pocket Depth

It is the distance between the base of the pocket and the gingival margin. The distance was calculated with a Williams graduated periodontal probe held parallel to the long axis of the tooth and walked circumferentially around each surface of the tooth. The pocket was measured at six sites; mesiobuccal, midbuccal, distobuccal, distolingual, midlingual, mesiolingual of each tooth and the deepest/highest penetration was recorded for each individual tooth.

Clinical Attachment Level

It is the distance between the base of the pocket and a fixed point on the crown, such as cemento-enamel junction.

Determining the Level of Attachment

When the gingival margin is located on the anatomic crown, the level of the attachment is determined by subtracting from the depth of the pocket, the distance from the gingival margin to the cemento-enamel junction. If both are same, the loss of attachment is "0". When gingival margin coincides with cemento-enamel junction, the loss of attachment equals the pocket depth. When the gingival margin is located apical to the cemento-enamel junction, the loss of attachment will be greater than the pocket depth, and therefore the distance between the cemento-enamel junction and the gingival margin should be added to the pocket depth.

RESULTS

Mean and standard deviations were estimated from the sample for each study group. Mean values were compared by student's paired 't'-test appropriately. The differences between the control (Group A) and test (Group B) groups were compared by using the **Student't' test**. The correlations were also recorded.

Table1 Mean And Standard Deviation Of Plaque Index, Gingival Index, Probing Pocket Depth, And Clinical Attachment Level In Group A [Non Diabetic] And Group B [Diabetic]

Clinical parameters	Group A	Group B	Significance
	Mean ± SD	Mean ± SD	**Student 't' test**
Plaque index	1.52 ± 0.30	1.81 ± 0.34	**p<0.01** [Significant]
Gingival index	1.75 ± 0.19	2 ± 0.34	**p<0.01** [Significant]
Probing Pocket depth	5.3 ± 1.2	5.69 ± 0.90	**p>0.05**[Not significant]
Clinical attachment level	2.88 ± 1.96	4.68 ± 1.81	**p<0.001**[Significant]

Inference

The mean plaque index score in Group A was 1.52±0.30 and in Group B it was 1.81±0.34. When both the groups were compared there was a statistically significant difference between the two groups. [p<0.01]. The mean gingival index in Group A was 1.75±0.19 and in Group B was 2±0.34. When compared there was statistically significant difference between the two groups. [p<0.01] The mean probing pocket depth in Group A was 5.3±1.2 and in Group B was 5.69±0.90. When both the groups were compared there was no statistically significant difference between them. [p>0.05]. The mean clinical attachment level in Group A was 2.88±1.96 and in Group B was 4.68±1.81, when both the groups were compared there was statistically significant difference between them. [p<0.001] [Table 1]

Table 2 Mean And Standard Deviation Of Blood Glucose, Fructosamine, Total Protein And Albumin In Group A [Non Diabetic] And Group B [Diabetic]

Laboratory parameters	Group A Mean ± SD	Group B Mean ± SD	Significance Student 't' test
Blood Glucose (mg/ dl)	102.8 ± 10.6	206.5 ± 59.4	**p<0.001** [Significant]
Fructosamine (m.mol/L)	1.88 ± 0.42	3.58 ± 0.59	**p.<0.001** [Significant]
Total Protein (mg/L)	7.17 ± 0.40	7.19 ± 0.41	**p>0.05** [Not significant]
Albumin (mg/L)	3.78 ± 0.52	3.74 ± 0.56	**p>0.05** [Not significant]

Inference

The mean blood glucose level in Group A was 102.8±10.6 and in Group B was 206.5±59.4. The mean fructosamine level in Group A was 1.88±0.42 and in Group B was 3.58±0.59. When both the groups were compared there was a statistically significant difference in these biochemical parameters. [p<0.001] [Table 2]

The mean total protein levels in Group A and Group B were 7.17±0.40 and 7.19±0.41 respectively. The mean albumin level in Group A was 3.78±0.52 and in Group B was 3.74 ±0.56. When both the groups were compared there was no statistical significance in these biochemical parameters. [p>0.05] [Table 2]

Table 3 The Relationship Between Gingival Index, Fructosamine And Blood Glucose Values Of Group A And Group B Patients

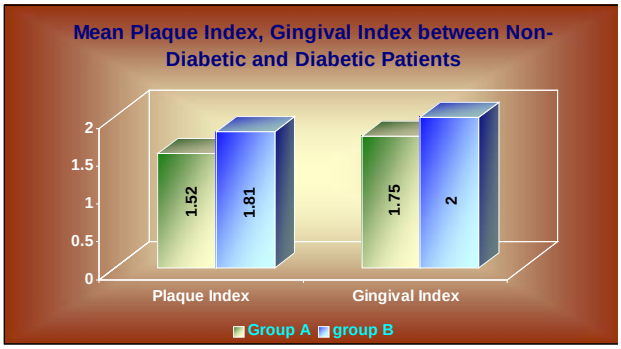
Gingival Index	Group A		Group B	
	Fructosamine m.mol/L Mean ± SD	Blood glucose mg/dl Mean ± SD	Fructosamine m.mol/L Mean ± SD	Blood glucose mg/dl Mean ± SD
1.0 – 1.9	1.88± 0.40	101±11.45	3.57±0.59	201.6±60.35
2.0 – 3.0	1.88± 0.46	104.6±9.97	3.65±0.78	250±31.11

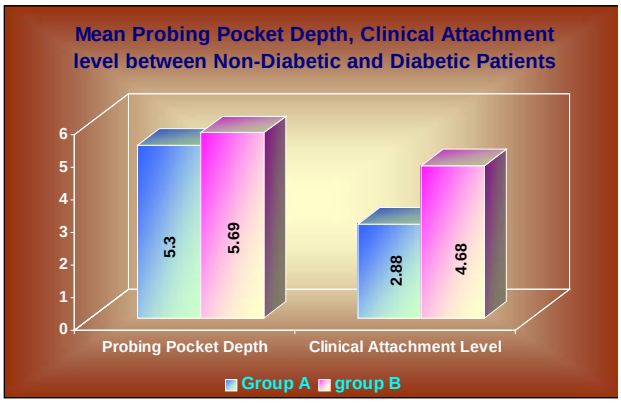
This table reveals the relationship between the gingival index, fructosamine and blood glucose values in Group A and Group B patients.

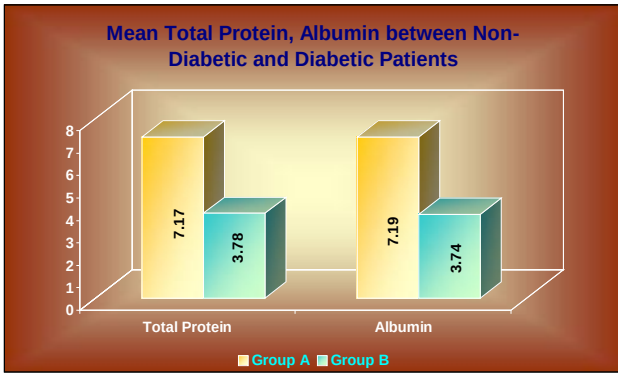
In Group A patients having mean gingival index score of 1.0 to 1.9, the mean fructosamine was found to be 1.88 ± 0.40 and the mean blood glucose level was 101±11.45. Patients having mean gingival index score of 2.0 to 3.0, the mean fructosamine level was found to be 1.88±0.46 and mean blood glucose level was 104.6±9.97.

In Group B patients having mean gingival index score of 1.0 to 1.9, the mean fructosamine was found to be 3.57±0.59 and the mean blood glucose level was 201.6±60.35. Patients having mean gingival index score of 2.0 to 3.0, the mean fructosamine level was found to be 3.65±0.78 and mean blood glucose level was 250±31.11. [table.3]

These findings reveal that while the gingival condition of the patients was deteriorating, the fructosamine levels were increasing along with the blood glucose levels in Group B than in Group A.







DISCUSSION

The influence of Diabetes Mellitus on the periodontal health has been discussed widely in the dental literature. Recent studies have strengthened the association of Diabetes Mellitus with periodontal breakdown but however the exact role of this disease is not completely understood. The severity of

periodontal disease increases in Diabetics when compared with Non-Diabetics. Metabolic imbalances in the tissues may lower the resistance of Diabetics to infections and thus influence the initiation, development and progression of periodontal disease.

Hyperglycemia is the hallmark of diabetes. Early diagnosis and control of plasma glucose concentrations are essential in order to prevent and ameliorate the various complications of Diabetes Mellitus. Although the plasma glucose levels would give a general overview of the Diabetic patients, two newer tests have been developed to monitor the long term and short term control of plasma or serum glucose, i.e., glycated hemoglobin and glycated fructosamine respectively.

While it is widely accepted that glycated hemoglobin is a measure of long term glycemia and glycated fructosamine reflects the glycemic conditions in the plasma during the preceding 1 to 3 weeks. In addition this assay has advantages such as low cost, technical ease and the simplicity for the clinical laboratory than the glycated Hb assays (Hindle EJ*1986*).

An attempt has been made in this study to investigate the relationship between the pathological status of the periodontal tissues and theplasma fructosamine values in diabetic patients.

Studies have shown that there is a relationship between periodontal status and the duration of Diabetes, and there is also more gingival bleeding in poorly controlled groups, which is important for the dentist to understand when treating Diabetic patients. It has also been shown that the collagenase activity in gingival tissues reaches a maximum in 15 to 22 days after the development of gingivitis in Diabetes. It should be noted that the time span of fructosamine turnover approximately coincides with the activation period of gingival collagenase. It may also be possible that vascular changes in Diabetes Mellitus result in increased gingival bleeding. The correlation between gingival inflammation and the loss of attachment in Diabetics due to loss of Diabetic control has been reviewed by many authors. (TahsinUnal 1993)

Fructosamine‘s capacity to screen over a considerable period of time makes it a possible and supportive criterion in determining the physiological status of a diabetic patient’s periodontal tissues. In addition, the fact that fructosamine assay is easily automated and does not require the patient to fast, makes it a more practical test than glucose determination.

The aim of the present study was to evaluate the relationship between periodontitis and plasma fructosamine in Diabetic and Non-Diabetic patients.

A total of 40 patients were selected for this study. And they were divided in to two groups,Group A consisted of 20 Non-Diabeticpatientsand Group B consisted of 20Diabetic patients

The clinical parameters evaluated were plaque index, gingival index, probing pocket depth and the clinical attachment level. These parameters were recorded before the fructosamineassay.

The biochemical parameters assessed were blood glucose level, serum fructosamine, total protein and the albumin levels.

The mean plaque index score in the Diabetic Group was 1.81and in the Non-Diabetic Group was1.52. There was a statistically significant difference between the two groups. [p<0.01] [Table1]. This is in contrast with the studies done by Unal *et al* [1993] values.

The mean gingival index in Diabetic Group was 2 and in the Non-Diabetic Group was 1.75 When compared there was statistically significant difference between the 2 groups. [p<0.01] [Table1]. This result correlated with the studies done by Sivas, Firalti *et al* [1993].

The mean pocket depth in Diabetic Group was 5.69 and in the Non-Diabetic Group was 5.3. When both the groups were compared there was no statistical difference between them. This result correlated with the studies done by Unal *et al* [1993]. [p>0.05] [Table 1]

The mean clinical attachment level in the Diabetic Group was 4.68 and in the Non-Diabetic Group it was 2.88. However, when both the groups were compared there was a statistically significant difference between them. [p<0.001] [Table 1]. This is in accordance with the studies done by Firalti *et al* [1997] and Unal *et al* [1993].

The blood glucose value ranged between 124 to 321mgs/dl in Diabetic patients and in Non-Diabetic patients it ranged between88t o 124mgs/dl. The wide range of variation in the Diabetic Group cannot be generalized, as there might be an influence of the oral medication regimen which might vary from one individual to another. The mean blood glucose level in Diabetic Group was 206.5mgs/dl and in the Non-Diabetic Group was 102.8mgs/dl.The fructosamine levels ranged between 2.9 to 4.71m.mol/L in Diabetic patients and in Non-Diabetic patients it rangedfrom 1.18 to 2.48m.mol/L. The mean fructosamine level in Diabetic Group was 3.58m.mol/L and in the Non-Diabetic Group it was 1.88m.mol/L. When both the groups were compared there was a statistically significant difference in both of these biochemical parameters. [p<0.001] [Table2]. This is in accordance with the studies done by Firalti *et al* [1993], Unal *et al*.

The mean total protein levels in Diabetic and Non-Diabetic groups were 7.19 and 7.17gms/L respectively. The mean albumin level in the Diabetic Group was 3.7478gms/L and in the Non-Diabetic Group it was 3.78gms/L. When both the groups were compared there was no statistical significant difference in both of these biochemical parameters. [p>0.05] [Table2]. This is in contrast with the studies done by Firalti *et al* [1993], Unal *et al*.

The relationship between the gingival index, fructosamine and the blood glucose levels in both the groups revealed that while the gingival condition of the patient was deteriorating, there was an increase in fructosamine and blood glucose levels. [Table 3].This was due to the mean glycemic status of the patient which was high throughout the previous week. On the other hand the periods of elevated blood glucose values may be

too short to introduce tissue changes, the levels of fructosamine may reflect the inflammatory changes in the gingiva appropriately. In this study, there was an increase in the levels of the fructosamine and the blood glucose levels as the gingival index increased in Group B. This data shows that while the gingival condition of the patients was deteriorating, fructosamine levels were increasing.

Only two patients in the Diabetic Group had gingival index more than 2, where as in Non-Diabetic Group there were ten patients who had a score of more than 2. Since the gingival index assesses the amount of inflammation in the gingival tissues, the destruction in the Diabetic patients were mainly due to increase in the blood glucose levels. Hence control of blood glucose should be our prime aim in the treatment of these patients. For monitoring the levels of the blood glucose in Diabetics, we need extensive laboratory measurements. Here in this study, we have also evaluated the levels of fructosamine in both the groups, which has shown an increase as that of blood glucose in the Diabetic Group. This study tried to emphasize the advantages of monitoring Diabetes control by fructosamine which correlates with the severity of gingival inflammation, as well as explain the validity of its use by the periodontist. It has been shown that the measurement of fructosamine correlates well with the glycated hemoglobin values [Armbruster DA *et al* 1987]. Fructosamine yielded similar information as HbA1c about glycemic control, the only clinically significant difference was found to be longer half-life of hemoglobin when compared to serum proteins (Guillausseauetal 1990). Hence it is very prudent to check the levels of fructosamine rather than blood glucose level. Since the procedure is cost effective and less invasive, this procedure can be used for the monitoring the glycemic control.

SUMMARY AND CONCLUSION

Diabetes Mellitus is one of the chronic health problems encountered by most of the population in the world. Since numerous oral changes and particularly, the influence of Diabetes Mellitus on periodontal tissues have been described, the onus is now on the peridontist to effectively treat those patients.

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