

Original Research Article

Comparative Evaluation of Fructosamine and HbA1c as a Marker of Glycemic Control in Type 2 Diabetes: A Hospital Based Study

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ABSTRACT

Introduction: Management of type 2 diabetes revolves around achievement of target glycemic control with the help of antidiabetic drugs or insulin. There are various markers for measurement of glycaemic control like HbA1c, Mean Blood Glucose and fructosamine levels. Though HbA1c is a well validated standard method for assessment of glycemic control but it has also got certain limitations. Fructosamine, a less explored method may be used as an alternative marker for an assessment of glycemic control in cases where HbA1c is unreliable or unavailable. The objective of this study is to compare the fructosamine levels with HbA1c in assessment of glycemic control in type 2 diabetics so as to assess the utility of fructosamine as an alternative marker for evaluation of glucose control.

Materials and Methods: This is a cross-sectional study of retrospective data collected from 48 type 2 diabetic patients who attended the medical outdoor of Nayati Medicity, Mathura, Uttar Pradesh. Data was collected from January 2018 to June 2018. Data was collected in terms of age, sex, BMI, duration of diabetes, fructosamine, HbA1c and FBS levels. Level of glycemic control was assessed with HbA1c and Fructosamine and fasting blood glucose levels.

Results: Analysis of glycemic control of 48 type 2 diabetic patients showed that fructosamine and HbA1c level have statistically significant correlation with each other (p value < 0.001).

Conclusion: The level of fructosamine and HbA1c are significantly correlated with each other; and hence Fructosamine can be used as an alternative biomarker for assessment of glycaemic control in type 2 diabetics especially when hba1c values are unreliable or not available.

Keywords: FBS (Fasting Blood Sugar), HbA1c (Glycosylated Hemoglobin), Fructosamine, BMI (Body Mass Index), Type 2 Diabetes

INTRODUCTION

Diabetes Mellitus particularly Type II is increasing in its incidence all around the world, and particularly in India it is

becoming a significant health problem. It is a major contributory factor in increasing the morbidity, disability and pre-mature mortality. Recent estimates from

International Diabetes Federation (IDF) mentions that, approximately 425 million adults (20-79 years) are living with diabetes and by 2045 this figure is expected to rise to 629 million. ^[1] India is a sole contributor for over 72.9 million cases of diabetes. ^[2] It is postulated in many studies that diabetes related microvascular complications are directly related to the glycemic control and hence the achievement of target glycemic control with help of antidiabetic drugs or insulin forms the mainstay of treatment of diabetes. There are various methods available for assessment of glycemic control. Mean blood glucose concentration is considered to be the most accurate method for assessing the glycemic control. ^[3] Mean blood glucose value is obtained by calculating the mean of pre and post 90 minutes sugars before each meal and before sleep every day. The measurement of SMBG is cumbersome and it is very difficult for patient to do multiple blood sugar checks in a day. This problem of frequent checking for blood sugars had been overcome by introduction of concept of measurement of glycated proteins. The ability of glucose to bind hemoglobin or albumin has been utilized in assessment of glycemic control over period of 3 months or 2-3 weeks respectively.

Glycosylated Hemoglobin (HbA1C) is one of the most commonly used method in clinical practice and it reflects the mean blood glucose level over a period of 120 days (lifespan of RBC). It was introduced in clinical practice in 1980s and presently it is used not only for assessment of glycemic control but also for diagnosis of diabetes and prediabetes. ^[4] HbA1C correlates very well with the mean blood glucose concentration derived from seven measurements of glucose level in a day. The national glycohemoglobin standardization program has standardized the HbA1C level, and hence making it a highly reliable assay. Its use avoids the need of very frequent monitoring of blood sugars as well as helps in better titration of antidiabetic regimens. However it has certain disadvantages like

cost, lack of availability and lack of standardization in certain remote areas. HbA1c is also affected by various hematological and genetic factors like increased or decreased erythropoiesis, hemoglobinopathies, presence of jaundice, chronic renal failure, chronic liver disease etc. and hence become unreliable in certain medical conditions described above.

Fructosamine assay, similar to HbA1c is also a marker of assessment of glycemic control. This test measures the fraction of serum proteins mainly, the albumin that becomes glycosylated. As half life of albumin is 20 days, serum fructosamine determines the glycemic control over a period of last 2-3 weeks. ^[5] Fructosamine is a quick and technically simple test. However it is very sparingly used in clinical practice and the reason for this are not very clearly discussed. There may be variety of reasons of its unpopularity for ex.: It reflects the change of glycemic control over a shorter period which is an insufficient time to assess the effect of treatment of antidiabetic drugs as these medications take time to reach to a steady state level. Secondly its higher variability, lack of standardization and paucity of studies on this makes it less commonly used test in clinical practice. Fructosamine has got certain other limitations also, as its value varies with the change in serum albumin level and therefore it can be falsely low in conditions with rapid albumin turn over and low albumin states.

Though HbA1C is a well validated method to assess glycemic control, however has certain limitations in clinical practice and can give spuriously high or low readings. Some of the conditions that would give false values of HbA1C are anemia with either high or low red cell turn over, hemoglobinopathies (fetal hemoglobin, sickle cell anemia, thalassemia), chronic kidney disease (with or without hemodialysis), patients receiving erythropoietin and blood transfusions. Fructosamine being an alternative marker for assessment of glycemic control, can be utilized to substitute HbA1C in special

clinical situations mentioned above, wherein HbA1C would be unreliable. Fructosamine gives us the glycemic control in a much shorter period (2-3 weeks) in comparison to HbA1C levels (2-3 months), hence it could be used as a more appropriate test for monitoring the early response of treatment specially in cases of pregnancy with diabetes where antidiabetic regimen needs to be titrated more rapidly. [6]

In this study we have done the comparative evaluation of fructosamine versus HbA1C assay for monitoring the level of glycemic control with the intent of improving the appropriate usage of fructosamine in clinical practice.

Aim:

The present study aims at comparative evaluation of fructosamine versus HbA1C assay as the indicators of glycemic control.

Objective:

1. Estimation of fasting blood glucose, Fructosamine and HbA1c levels in the same blood sample.
2. Determine the correlations amongst the above test parameters to evaluate the comparative importance of fructosamine with HbA1c and fasting blood glucose in the assessment of glycemic control.

MATERIALS AND METHODS

The present study is a cross-sectional study of retrospective data collected from the diabetic patients who attended the medical outdoor of Nayati Medicity, Mathura, Uttar Pradesh. Data was collected from January 2018 to June 2018. Data from 48 diabetic patients was collected retrospectively. Data was collected in terms of age, gender, BMI, duration of diabetes, fructosamine, HbA1c and FBS levels. Diabetic and Non-Diabetic patients were diagnosed according to criteria given by American Diabetes Association. [7] After obtaining informed consent, the fasting blood glucose, HbA1c, Fructosamine levels were measured. Fructosamine test was offered free of cost to all the participants for this study purpose. This research was performed after taking the approval from the

Ethics committee of Nayati Multi Superspeciality hospital. Fructosamine was measured by Roche Cobas C311 and HbA1c was measured with Bio-Rad D-10 machine and evaluated with the principle based on HPLC. At the end of the study, the data obtained was analysed using Pearson's test to evaluate the correlations among the different parameters. A *P*-value of less than 0.05 was considered significant.

Inclusion criteria:

1. All patients with type 2 diabetes mellitus attending medicine OPD and requiring assessment of glycemic control
2. Age > 20 years

Exclusion criteria:

1. Type 1 Diabetics
2. Prediabetics
3. Critically ill patients
4. Anemia of any cause, Chronic renal disease, Hemoglobinopathy, Jaundice, Patient receiving erythropoietin or blood transfusion

Statistical Analysis:

The data was analysed using SPSS software (version 21.0). Categorical data, such as age group, gender, BMI, fasting blood glucose, HbA1c, Fructosamine were presented as number and percentage. Mean and Standard deviation of fasting blood glucose, HbA1c and Fructosamine were also calculated. The Pearson's test was used to evaluate the correlations among the different parameters with statistical significance set at *P* value <0.01 where appropriate.

Ethical consideration:

This is a cross-sectional study of retrospective data and no variables allowed identification of individuals. No extra cost and time was incurred to the patients for the study purpose. Fructosamine test was offered free of cost to all study participants. The data was retrieved from hospital information system and OPD prescriptions.

RESULTS

We have included 48 known type 2 diabetic subjects in our study. Distribution

of all the subjects age wise and gender wise is give in figure 1 and figure 2 respectively. 52% of our patients were females and 48% were males and our gender distribution was almost balanced. Maximum percentage of patients (35.4%) were in the age group of 51-60years. 30% patients were of more than 60 years of age. Among all subjects included in our study 45.8% were coming in over-weight and approx. 23% were in obese category. Overall approximately 70% of our patients were not coming in ideal body weight category.

We examined fasting blood sugar, fructosamine and HbA1c levels in all 48 patients included in the study. Clinical characteristics of all the subjects are presented in Tables. Table 1 is showing that 56% patients were having fructosamine more than 285umol/lit and 44% were having values in the ranges of 205-285umol/lit. Approx. 94% patients had glyclated heamoglobin (HbA1c) value of >6.5% and only 6% patients were having its value in the range of 5.7-6.4%. Similarly approx. 90% patient had FBS values >126 mg/dl and only 10% of patients had its value below 126mg/dl. Table 2 is showing mean and S.D of Fbs, Hba1C and Fructosamine. Mean values for FBS, HbA1c and Fructosamine were 237.6 (SD87.3), 10(SD2.53) and 323.2 (SD92.2) respectively. Table 3 is showing Pearson correlation between Fbs, Hba1C and Fructosamine. HbA1c value strongly and positively correlated with the fructosamine value with the P value of < 0.001. We found good agreement between HbA1c and fructosamine with correlation of 0.51. In addition to that fructosamine and FBS values were also significantly correlated with the P value of 0.002. Across all glucose level this association was found significant.

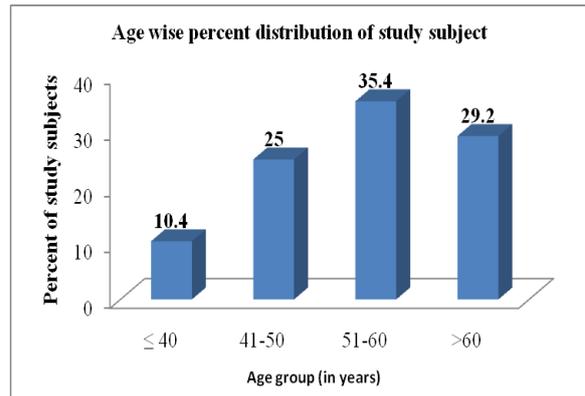


Figure 1: Distribution of study subjects age wise

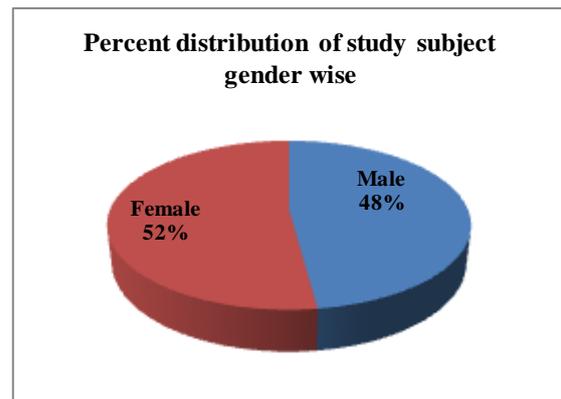


Figure 2: Distribution of study subjects' gender wise

Table 1: Distribution of study subject according to different factors

BMI(kg/m ²)	Number of patients	Percentage
<25	15	31.3
25-29.9	22	45.8
≥30	11	22.9
DM (in years)		
<5	13	27.1
5-10	24	50.0
>10	11	22.9
Fructosamine(umol/lit)		
205-285	21	43.8
>285	27	56.3
HbA1C (%)		
5.7-6.4	3	6.3
≥6.5	45	93.8
FBS		
<126	5	10.4
≥126	43	89.6

Table 2: Mean and S.D of FBS, Hba1C and Fructosamine:

Characteristics	Number of patients	Mean	S.D
FBS	48	237.6	87.3
HbA1C	48	10.0	2.53
Fructosamine	48	323.2	92.2

Table 3: Pearson correlation between FBS, Hba1C and Fructosamine:

Characteristics	Number of patients	Correlation	P-value
FBSVs Hba1C	48	0.46	0.003*
HbA1Cvs Fructosamine	48	0.51	<0.001*
FBS Vs Fructosamine	48	0.44	0.002*

* Correlation is significant at the 0.01 level

DISCUSSION

The result of our study is derived from studying the 48 patients who came to Internal Medicine OPD of Nayati Multi Super Speciality Hospital, Mathura of western Uttar Pradesh region. In our study we found significant correlation between FBS v/s Fructosamine and HbA1C v/s Fructosamine. P value of hba1c and fructosamine was <0.001 and fasting blood sugar with fructosamine was 0.002, both of which are statistically significant. Similar result and strong correlation has also been defined in various other studies. In a similar study conducted by JR Baker et.al, significant correlation of Fructosamine with HbA1c and Fasting Blood Sugar was seen. They concluded that fructosamine is a simple and rapid test to perform and can be used as an alternative marker to HbA1c in assessment of glycemic control. [8] Similarly in a study done by P Koskinen et al also found good correlation of Fructosamine with HbA1c, FBS and mean blood glucose values. This study also recommended that fructosamine is a simple and inexpensive test and can be used to assess glycemic control. However lack of uniformity of assay, protocol, calibration and standardization can sometimes lead to interlaboratory variations and can give erroneous readings and hence while assessing the glycemic control with help of Fructosamine assay, these factors should be taken into consideration before making any final conclusions. [9] In a study done by TO Limetal it was found that in comparison to fructosamine, the fasting blood sugar has got limited value in predicting the level of glycemic control especially in patients having good diabetic control. [10] It has been postulated in one study that fructosamine can be used as an alternative to HbA1c or FBS in conditions where HbA1c and FBS readings are unreliable. [11] In our study the correlation between all the 3 parameters were studied with overt type 2 diabetics. We have not included prediabetics in our study. In one study it was found that the association between HbA1c, FBS and

fructosamine was not as significant in prediabetics as it is present in Diabetics, indicating a curvilinear relationship between all these parameters. [12] In the AMORIS study it was found that fructosamine can be utilized in a similar way as HbA1c for assessment of glycemic control. In this study they measured the fructosamine and HbA1c levels simultaneously for 6 and 12 months and found the parallel changes between these two parameters with both high and low sugar levels and thus help in assessing the effects of changes in diabetes management. [13]

In some studies the relationship between various parameters of glycemic control such as Fructosamine, HbA1c and FBS remains unchanged when controlling with BMI, Lipid profile, age and gender. [14] In our study we have not evaluated the relationship of BMI and duration of diabetes with glycemic control and its parameters. Though we think that fructosamine can also be used for diagnosis of diabetes along with monitoring of glyceamic control We have not assessed the utility of fructosamine in diagnosis of diabetes as already diagnosed cases of type 2 diabetes are included in the study. We have included all type 2 diabetics who were classified and diagnosed with help of standard ADA criteria for diagnosis of type 2 diabetes. All biochemical parameters available for assessment of glycemic control (HbA1c, FBS, fructosamine) can have certain limitations in clinical practice and can give us unacceptable and misleading results. Hence the clinical acumen and knowledge of certain deviations while interpretation of value of these parameters is required and hence every parameter has its unique place in monitoring, diagnosis as well as in prediction of long term complications of diabetes.

CONCLUSION

Fructosamine can be used as an alternative or adjunct to HbA1c in assessment of blood glucose control as its correlation with HbA1c is found to be

statistically significant. Though the use of fructosamine in clinical practice is not very common but it has the potential of becoming a very useful marker not only for assessment of glycemic control. Future studies are required to examine this marker in circumstances in which HbA1c measurements is unreliable or inaccurate.

Conflict Of Interest:

The author(s) declared no conflicts of interests with respect to the research and publication of this article.

Declaration of Funding:

The present study did not receive any specific grant from any funding agencies. No funding agency has participated in writing as well as in submission of the manuscript.

ACKNOWLEDGEMENTS

We would like to show our gratitude to Ms. Niira Radia for her continuous support, guidance and providing all infrastructural support for this research project. We are also thankful to Ms. Purnimabajpai for helping us in data collection and compilation.

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How to cite this article: Goyal J, Das N, Kumar N et. al. Comparative evaluation of fructosamine and hba1c as a marker of glycemic control in type 2 diabetes: a hospital based study. *Int J Health Sci Res.* 2019; 9(9):269-274.
