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Association of fructosamine, glycated albumin and hba1c in prediabetes, diabetic and associated complications

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Abstract---Background: The efficient diagnosis and accurate monitoring of diabetic patients are cornerstones for reducing the risk of diabetic complications. Aims: Aim of the study is to assess level of Glycated hemoglobin, serum fructosamine, Glycated albumin in Prediabetes, type-2 Diabetic patients with and with out microvascular complications and to find out their correlation with diabetes complications. Materials and methods: This is a Case-control study in 200 subjects will be involved in this study and they will be divided into 4 groups. The controls and subjects (cases) were age and gender matched. Samples collected from patients after obtaining Informed written Consent. Results: . Differences between these groups for serum fructosamine, glycated albumin were statistically significant. Glycated albumin showed excellent correlation with fructosamine across groups ($p \leq 0.0003$ in all groups) and correlation coefficient r was >0.9 in groups 2 and 3. Serum fructosamine and glycated albumin correlated well with FBS, PP2BS, HbA1C in groups 2, 3 and 4. Irrespective of the groups, serum glycated albumin showed excellent correlation with serum fructosamine. In group 3, as compared to group 1, there was 49% more glycated albumin. Conclusions: GA can complement or even replace conventional

measures of glycemic control such as HbA1c, GA may help the clinical management of patients with diabetes in whom HbA1c values might be unreliable.

Keywords---Glycated albumin (GA) ,Glycated Hemoglobin (HbA1C), Fructosamine (FA).

Introduction

Diabetes is one of the most severe and frequent human disorder. The current diagnostic and prognostic strategies in diabetes are strongly based on plasma glucose and Glycated Hemoglobin (HbA1C). Fructosamine (FA) is an alternate glycemic marker for diabetes screening and may be potentially useful for diagnosing prediabetes. It is a ketoamine created by glycosylation of total serum proteins. FA increases in states of high glucose concentrations. Since it reflects average blood glucose concentrations over the previous 1–4 weeks, it can be a useful clinical marker of short term glycaemic fluctuation and glucose control. Glycated albumin (GA) does not require fasting for its measurement and reflects short-term glycemia due to the half-lifetime of the albumin, which is approximately 3weeks. HbA1c provides a long-term record of glycemic control (2-3months). The measurement of Fructosamine or GA provides information on glucose control over 2 -4 weeks. The rate of non-enzymatic glycation of albumin, which is approximately 9 to10 fold higher than that of human hemoglobin.^{1,2,3}

Several studies assessed possible correlations between HbA1c values and average glucose blood concentrations. Recognizing also other advantages related to the absence of preparation (no need to subject the individual to fasting or the time needed to perform an OGTT), soon HbA1c was introduced and easily adapted in clinical practice as an indicator of the metabolic control of people with diabetes and most of the guidelines on diabetes propose HbA1c goals as a surrogate for glycaemic control. The negative points were mainly correlated to the associated costs, the absence of a widely accepted process of standardisation and the possible interferences with its reliability, namely haemoglobinopathies, genetic defects and concomitant presence of other illnesses . The discussion of diagnostic value of HbA1c for diabetes only recently achieved consensus .⁴ Earlier studies had demonstrated a good correlation between HbA1c and fasting glycaemia and OGTT values, even if not with microvascular complications.⁵ Based on larger population studies, it was possible to find not only a good correlation with the other diagnostic tests but also with microvascular complications. Based on that, an International Expert Committee proposed the adoption of HbA1c not only as a diagnostic criterion for diabetes (HbA1c: < 6.5%) but also for prediabetes and people at high-risk of developing diabetes (HbA1c: 5.7%-6.4%).⁶

There is an important disparity between a marker of exposure (the period of exposure and glucose variability) and a marker of risk (predictor of what will occur). The latter can also be related to the prediction of progression to diabetes or risk for associated diseases. More recently, fructosamine has been validated in some studies as a marker of exposure that may also serve as a marker of disease risk , however, more data is needed to allow comparison of the different markers.⁷

Measurement of Fructosamine and GA also useful for identifying impaired control of blood glucose before any noticeable changes in HbA1c may occur as well as for monitoring diabetics with fluctuating and/or poor controlled diabetes

Material and Methods:

This is a Case-control study conducted at ESIC Medical college and Hospital, Sanathnagar. Total 200 subjects will be involved in this study and they will be divided into 4 groups. The controls and subjects (cases) were age and gender matched. Samples collected from patients after obtaining Informed written Consent.

Inclusion Criteria: Age group: 25-70yrs

Group-1 (n=50) consisted of Apparently healthy adult volunteers. (controls)

Group -2 (n=50), Prediabetes patients. HbA1C value between 5.7-6.4%,

FBS-110-126mg/dl and PLBS-140-199mg/dl.

Group -3 (n=50), Type-2 Diabetes mellitus patients without any microvascular Complications. Duration of diabetes 3 years or more, on lifestyle modifications and oral anti-diabetic drugs and free from clinical or laboratory evidence of any microvascular complication of diabetes mellitus

Group -4 (n=50), Type-2 Diabetes mellitus patients with any microvascular complications. Having one or more microvascular complication of diabetes mellitus, either diabetic retinopathy or diabetic neuropathy or diabetic nephropathy.

Exclusion Criteria:

Patients with type-1 diabetes mellitus, Pregnant females, Patients with hepatic diseases, Hematological malignancy, Chronic infections and inflammations like tuberculosis, sarcoidosis, infectious mononucleosis, AIDS, Auto Immune disorders and Patients on steroid treatment.

Parameters:

FBS and PLBS- Hexokinase method, Fructosamine and Glycated albumin- ELISA method. HbA1C- HPLC method. In all subjects FBS, PLBS, HbA1C, Fructosamine and Glycated albumin Values were Estimated and Compared in all 4 Groups.

Statistics: Data collected were recorded and analysed statistically to determine the significance of different parameters by MedCalc version 12.4. Statistical analysis was done by using unpaired t-test to find out significance of difference between two groups and correlation coefficient to find out statistical correlation between two variables and its significance. p value less than 0.05 was considered significant.

Results

Patients having one or more microvascular complications were having poor glycemic control. Differences between these groups for serum fructosamine, glycated albumin were statistically significant. Glycated albumin showed excellent correlation with fructosamine across groups ($p \leq 0.0003$ in all groups) and correlation coefficient r was >0.9 in groups 2 and 3. Serum fructosamine and glycated albumin correlated well with FBS, PP2BS, HbA1C in groups 2, 3 and 4.

Irrespective of the groups, serum glycated albumin showed excellent correlation with serum fructosamine. In group 3, as compared to group 1, there was 49% more glycated albumin.

Table-1
Comparison of the demographic details in present study groups

	Group 1	Group 2	Group 3	Group 4
Number of Participants	50	50	50	50
Sex(M/F)	42/46	45/44	48/52	50/53
Average age (years)	44	46	51	52
Average duration of Diabetes mellitus (years)	-	-	3 Years or more	3 Years or more

Age and gender matched subjects are selected for study.

Table-2
Categories in Persons with and without Diagnosed Diabetes Mellitus

	Group 1	Group 2	Group 3	Group 4
Average FBS (mg/dl)	80.21	95.11	192.78	242.43
Average PPBS(mg/dl)	100.34	125.62	295.45	323.1
Average HbA1C	5.4	5.8	8.5	11.1

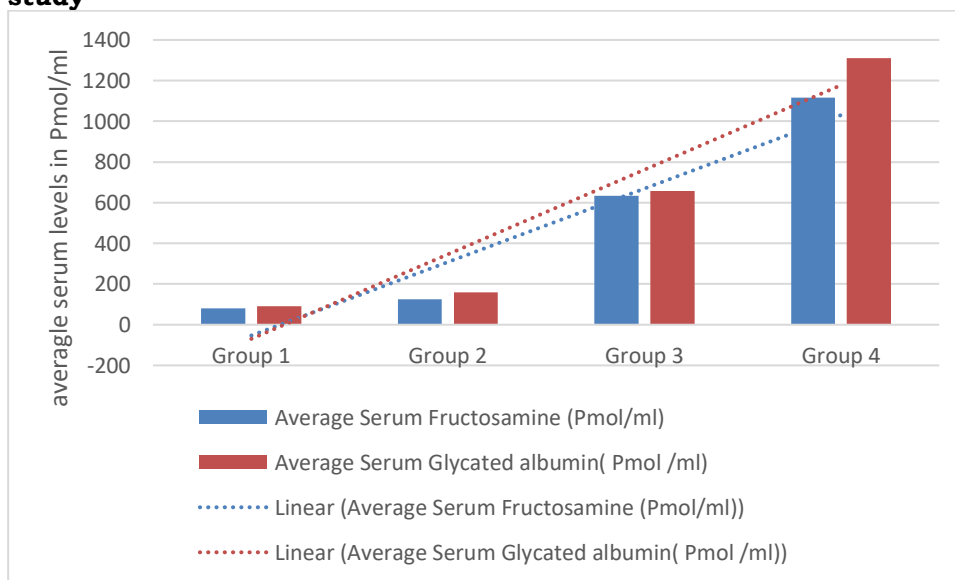
Average FBS, PLBS and HbA1C are significant when compare in all 3 groups ie group,2,3,4 when compared to controls ie group-1

Table-3
General parameters in patients in present study

	Group 1	Group 2	Group 3	Group 4
Average Blood urea(mg/ dl)	20.22	21.74	25.61	29.33
Average Serum Creatinine(mg/ dl)	1.0	1.0	0.8	0.9
Average Serum Total protein (g/ dl)	6.0	6.2	6.3	7.6
Average Serum albumin (g/ dl)	3.5	3.4	3.6	3.6
Average Serum Total Cholesterol(mg/ dl)	139.12	141.22	183.67	172.91
Average Serum LDL Cholesterol(mg/ dl)	75.45	76.56	102.27	100.18
Average Serum Triglycerides(mg/ dl)	95.19	96.23	149.23	159.15
Average Urinary protein/Creatinine (mg/ dl)	0.1	0.1	0.5	1.1

Average blood urea, total protein, total cholesterol, LDL, triglycerides are significant when compared to controls and group-2,3,4.

Figure-1: Average serum fructosamine and glycated albumin in present study



Discussion

The level of GA is strongly dependent on recent changes of blood glucose, but also reflects very rapid variations that cannot be accurately identified measuring blood glucose. The concentration of GA also decreases more rapidly than that of HbA1c during intensive insulin therapy, so that it can be of value for monitoring glycemic control during treatment with hypoglycemic agents and insulin. Moreover, continuous glucose measurements were more tightly correlated to GA compared to HbA1c. Since fructosamine reflects the average levels of blood glucose during the former 1 to 3 weeks, fructosamine would also expectedly mirror a poorly controlled glucose metabolism better than HbA1c. Subsequent studies demonstrated the utility of fructosamine and GA in diabetic patients who required tighter control, or in patients with conditions that rendered HbA1c testing unreliable.

By this study we can identify prediabetes early and we can prevent progression to Diabetes and prevent complications in Diabetes. Both Fructosamine and Glycated albumin levels are used for assessing glucose control over a short to intermediate time frame. By using this novel marker we can improve clinical outcome both in Diabetics and Prediabetics.

Comparative studies of these biomarkers will help to ascertain their clinical utility. Both Fructosamine and Glycated albumin are more sensitive and precise biomarkers capable of predicting progression to dysglycemic states at the earliest time point when β -cell function is still relatively more optimal and may be more responsive to lifestyle modification. ⁸Combining biomarkers in a clinical setting may provide better sensitivity and specificity in predicting prediabetes and diabetes. Additionally, there has been an increased interest to study these markers during recent past as they are now very well established as markers of intermediate term glycemia. The efficient diagnosis and accurate monitoring of diabetic patients are cornerstones for reducing the risk of diabetic complications. The current diagnostic and prognostic strategies in diabetes are mainly based on two tests, plasma (or capillary) glucose and glycated hemoglobin (HbA1c). Nevertheless, these measures are not fool proof, and their clinical usefulness is biased by a number of clinical and analytical factors. ⁹

The introduction of other indices of glucose homeostasis in clinical practice such as fructosamine and glycated albumin (GA) may be regarded as an attractive alternative, especially in patients in whom the measurement of HbA1c may be biased or even unreliable. These include patients with rapid changes of glucose homeostasis and larger glycemic excursions, and patients with red blood cell disorders and renal disease. According to available evidence, the overall diagnostic efficiency of GA seems superior to that of fructosamine throughout a broad range of clinical settings. The current method for measuring GA is also better standardized and less vulnerable to preanalytical variables than those used for assessing fructosamine. Additional advantages of GA over HbA1c are represented by lower reagent cost and being able to automate the GA analysis on many conventional laboratory instruments. Although further studies are needed to definitely establish that GA can complement or even replace conventional measures of glycemic control such as HbA1c, GA may help the clinical

management of patients with diabetes in whom HbA1c values might be unreliable.¹⁰

Conclusion

GA can complement or even replace conventional measures of glycemic control such as HbA1c, GA may help the clinical management of patients with diabetes in whom HbA1c values might be unreliable.

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