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Utility of Glycated Albumin over Glycated Hemoglobin as a Marker to Monitor Glycaemic Status in Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: Diabetes mellitus is a metabolic syndrome characterized by hyperglycemia due to alteration in carbohydrate homeostatic mechanisms due to absolute or relative insulin deficiency. Monitoring of glycemic status plays an important role in diabetes management. The study aimed to compare the sensitivity and specificity of glycated hemoglobin and glycated albumin(GA) as markers of glycemic control in type 2 diabetes mellitus patients as well as to find the correlation between fasting plasma glucose and glycated albumin as well as glycated hemoglobin in DM patients.

Methodology: Forty diabetics and age and gender-matched forty no-diabetic controls were recruited. Fasting plasma glucose, Glycated hemoglobin, and glycated albumin were assayed in cases and controls. Statistical analysis was carried out using appropriate tests with SPSS 23.

Results: Glycated albumin was also significantly high (p=0.0186) in diabetics as compared to non-diabetics. A positive correlation was observed between FBS and HbA1c (Pearson's correlation coefficient, r=0.452, P<0.01) as well as FBS and glycated albumin (r=0.402 P<0.01) .A strong positive correlation between glycated albumin and hemoglobin was also noted (r=0.52 P<0.001).ROC for glycated albumin as a marker of DM, area under the curve (AUC)=0.639, sensitivity=55.2%, specificity=75%.ROC for HbA1C as a marker for diabetes, AUC=0.755, sensitivity=76.7% specificity=78.6%.

Conclusion: Glycated albumin can be used as an additional marker to glycated hemoglobin in the monitoring of glycaemic status in type 2 diabetes.

Key words: HbA1c, Glycated albumin, Glycemic status monitoring

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INTRODUCTION

Diabetes mellitus is a chronic metabolic syndrome characterized by hyperglycemia due to alteration in-car homeostatic mechanisms either due to an absolute or relative deficiency of insulin in addition to deranged lipid and protein metabolism [1]. Onset and progression of various complications in diabetes mellitus are due to hyperglycemia [2]. The wide fluctuation seen in plasma glucose may independently contribute to diabetes-related complications. The increased cardiovascular events in DM are attributed to the postprandial spikes in blood glucose and hypoglycemic events [3].

The management of diabetes revolves around the monitoring of Glycemic status and titrate the dose of anti-diabetic drugs accordingly. Monitoring blood sugar provides the person an idea about how well they are doing (both for avoiding hypoglycemia and blood glucose control).It is also useful for health care providers to evaluate and make changes in the treatment regimen of the patient. Hence we need a robust, accurate, reliable, sensitive, and specific laboratory test that can measure current glycaemic status as well recent past the search for such an ideal blood glucose monitoring system continues [4].

The degree of hyperglycemia in diabetics can be monitored by using Glycated proteins as biomarkers. HbA1c is the "gold standard" for the assessment of glycaemic control during diabetes management. American Diabetes Association (ADA) and World Health Organization (WHO) have given HbA1c>6.5% (48 mmol/

mol) as the diagnostic cut-off value for the diagnosis of diabetes mellitus [5].

This HbA1c reflects the average blood glucose control of an individual over 120 days preceding the test. Certain genetic factors, hematological factors, and the presence of co-morbidities like hemoglobinopathies, anemia's, and disorders associated with shorter erythrocyte lifespan affect the linear correlation between HbA1c levels and average blood glucose concentration. Hence there is a need for a new biomarker that is devoid of the above-mentioned limitation to measure for glycaemic control when HbA1c can't be used.

One such candidate biomarker in such cases is Glycated albumin (GA). Albumin contributes to f 60% of plasma proteins and its blood concentration is 30-50 g/L. The presence of arginine and lysine residues in albumin near the terminals makes it highly susceptible to glycation. Glycated albumin persists for 2-3 weeks in the circulation after release, it may be a potential biomarker for short and mid-term monitoring of Glycemic status.

Serum albumin levels do not affect glycated albumin level because the ratio of Glycated albumin to total albumin is considered. Glycation product of albumin is specifically measured [6]. Serum glycemic index has been suggested to be a sensitive and reliable marker compared to HbA1c in diabetic nephropathy patients [7-10]. Glycated albumin may reflect glycaemic status faster than HbA1c. It may be of great benefit to patients with varying degree of blood glucose levels.

There are not many studies that have compared glycated albumin and glycated hemoglobin as markers to monitor glycaemic status in diabetic patients.

Objectives

- ✓ To compare the sensitivity and specificity of glycated hemoglobin and glycated albumin as markers of glycemic control in type 2 diabetes mellitus patients.
- ✓ To find the correlation between fasting plasma glucose and glycated albumin as well as glycated hemoglobin in DM patients.

METHODOLOGY

Study design

The observational cross-sectional study was carried out in the Department of Clinical Biochemistry, KS Hegde Medical Academy, and Mangalore.

Study population

Subjects with the following criteria were included in the study.

Study duration

Jan 2020 to Jan 2021.

Cases

Forty type 2 Diabetes Mellitus patients in the age group of 18-65 years, with/without complications visiting clinical laboratory for biochemical investigations, diagnosed as per American Diabetic Association 2019 guidelines [11]. Sample size of forty was taken as it is a pilot study.

Controls

Forty age and gender-matched healthy subjects who attend the hospital for routine checkups.

Exclusion criteria

Subjects with liver, renal diseases, trauma and injuries, pregnancy, drugs affecting liver functioning.

Ethics

Institutional Ethics Committee approval was sought before starting the study.

Sample collection

2 ml of blood sample was collected in fluoride, EDTA, and plain tubes for fasting plasma glucose, glycated hemoglobin, and glycated albumin respectively. Blood samples were centrifuged at 3000rpm for 10 min to separate plasma or serum. Fasting plasma glucose and glycated hemoglobin were estimated using a fully automated chemistry analyzer, CobasC311, and glycated albumin was assayed using ELISA.

Statistical analysis

Software SPSS 16 was used to analyze the data. The data will be checked for errors during coding and data entry. An unpaired t-test was used to compare the means of biochemical parameters. ROC curve analysis was carried out to compare the sensitivity and specificity of the two parameters (Glycated hemoglobin versus albumin) using fasting plasma glucose as diagnostic criteria. The correlation between glycated hemoglobin, albumin, and fasting plasma glucose levels was calculated by Pearson's correlation coefficient. Albumin and fasting plasma glucose levels.

RESULTS

FBS and HbA1c were highly significantly higher ($p<0.0001$) in cases (Table 1). Glycated albumin was also significantly high ($p=0.0186$) in diabetics as compared to non-diabetics. A positive correlation was observed between FBS and HbA1c (Pearson's correlation coefficient, $r=0.452$, $P<0.01$) as well as FBS and glycated albumin ($r=0.402$ $P<0.01$). A strong positive correlation between glycated albumin and hemoglobin was also noted ($r=0.52$ $P<0.001$).

On constructing ROC for glycated albumin as a marker of DM, area under the curve (AUC)=0.639, sensitivity=55.2%, specificity=75%.ROC for HbA1C as a marker for diabetes, AUC=0.755, sensitivity=76.7% specificity=78.6%.Positive and negative predictive values were 65% and 63% respectively for glycated albumin (Figure 1).

Table1: Comparison of biochemical parameters in diabetics compared to non-diabetics.

Biochemical parameters	T2DM cases(n=40)	Healthy controls(n=40)	P value
FBS(mg/dl)	134.78	92.76	<0.0001
Glycated hemoglobin (gm%)	9.04	5.77	<0.0001
Glycated albumin (ng/ml)	42.71	25.08	0.0186

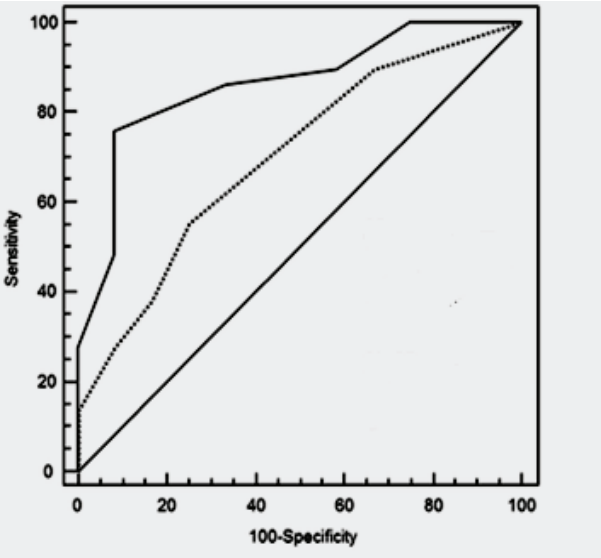

Figure 1: ROC for glycated hemoglobin versus glycated albumin as a marker of diabetes.

DISCUSSION

Significantly elevated Glycated albumin and Glycated hemoglobin were noted in type 2 diabetics of our study group the extent of elevation were similar for the parameters, Glycated albumin being 1.68 times and Glycated hemoglobin 1.57 times. This fact is suggestive that the extent of glycosylation of these two proteins may be the same. A strong positive correlation between Glycated albumin and Glycated hemoglobin suggests that Glycated albumin may be an alternative marker for blood glucose monitoring in diabetics.

However, lower AUC, sensitivity, specificity for Glycated albumin as a marker for diabetes monitoring suggests that it may not be used as an independent marker. But it can be used as an additional marker along with Glycated hemoglobin.

Several studies have documented the reliability of glycosylated albumin as a biomarker in the monitoring of diabetes mellitus [7-11]. A few studies are available which highlighted comparison between the clinical utility of Glycated albumin with that of the traditional glycemic markers for the diagnosis of diabetes. The reports suggested that GA could be of great use for clinicians if there is a discrepancy between traditional biomarkers [12-17].

A large epidemiological cohort study from a large Japanese population evidenced that GA could diagnose diabetes accurately [7]. However, the study has highlighted the role of GA as a screening test for diabetes. Ikezaki et al reported that GA was able to diagnose diabetes, with accuracy, equivalent tohack [9]. In a retrospective study conducted by Hwang et al. optimal cut-off of glycosylated albumin was calculated using linear regression models based on FPG and 2hPG values [8], When the diagnostic performance of GA was compared with that off HbA1c, GA showed higher sensitivity, but lower specificity. In an epidemiological study, GA was found to be a good marker for diabetes [10]. The study concluded that the GA along with FOG would reduce the need for OGTT , without compromising the accuracy of diagnosis. Similar observations were also documented in the literature by the Chinese study group [12]. Hsu et al. conducted a case control study found that GA was an accurate marker [13]. He et al. studied the importance of GA in diagnosing diabetes in patients with ambiguous clinical and biochemical findings. The GA may add to the diagnosis of DM along with other biomarkers [17].

Bellia et al. studied the clinical utility of GA in the diagnosis of diabetes and found it to be sensitive and specific [11]. GA was highly specific for newly diagnosed diabetes. However the study reported that GA was less sensitive than HbA1c but significantly more specific. In Afro-Americans, Sumner et al. evaluated the ability of GA and other Glycemic measures to detect prediabetes. The combination of GA and HbA1c would identify a significant percentage of people with diabetes not detected by HbA1c alone [14,18].

Studies have shown that GA may be a reliable marker for the purpose of screening and diagnosis. However it is the fact that different diagnostic criteria need to be evaluated against the utility of GA [19,20]. Various biomarkers reflect different aspects of the pathophysiology of diabetes. They provide information on the actual glucose homeostasis. According to the current guidelines, fasting blood sugar, postprandial blood glucose and HbA1c may be used for the diagnosis of diabetes [6]. Diagnosis may be based on the combination of two or more biomarkers [20]. The utility of glycated albumin as an effective marker for screening for diabetes mellitus has been documented in DM by several researchers [21-23]. Ma et al reported that GA was a sensitive and specific marker for diabetes screening [23].

Serum GA can be a short-term marker (2–3 weeks) of glycemic status. This may also be useful in monitoring drug dose adjustment [35]. Reports that suggest that GA may be a marker of the vascular complications of DM. Several reports are available that suggest the value of GA in the screening of DM. It has also been suggested that GA can be an additional investigation in assessing the glycemic status [24-37].

CONCLUSION

- ✓ Glycated albumin can be used as an additional marker for short and intermediate-term regulation of Glycemic status along with Glycated hemoglobin in type 2 diabetes.

✓ It may be a better marker in conditions where hemoglobin levels are affected.

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