

**Research Article**

**Glycated albumin and glycated hemoglobin- A comparison**

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**Abstract**

**Introduction:** The progressive complications of unmanaged diabetes include heart disease, blindness, kidney failure, amputation of extremities due to circulation problems, and nerve disorders, as well as other chronic conditions. Decades of research have established that prolonged exposure to excess glucose is the cause of diabetes complications, and that long-term control of blood glucose levels is required to avoid or lessen the damage caused by excess glucose. The process of protein glycation is now understood to be both a marker for the progress of diabetes complications and an underlying cause of many of the most serious complications.

Diabetes monitoring for protein glycation, an essential element for the long-term control of the complications of diabetes mellitus, is currently managed by a combination of daily self-monitoring of blood glucose (SMBG) measurements and physician-assessed hemoglobin A1c (A1C) levels every 3–6 months. Short term methods like self monitoring of blood glucose and long term methods like measurement of HbA1c have limitations. Various researchers have identified glycated albumin (GA) as the ideal marker for an intermediate index to measure glycation.

**Methods:** 50 patients with DM history more than 5 years were divided into 2 groups, 25 with micral positive and 25 with micral negative in spot urine sample. Hba1c and GA were estimated in the patients and findings were noted

**Results:** Microalbuminuric patients had significantly higher GA levels ( $p < 0.05$ ) than normoalbuminuric patients. Correlation between HbA1c and GA was very good ( $r = 0.87$ )

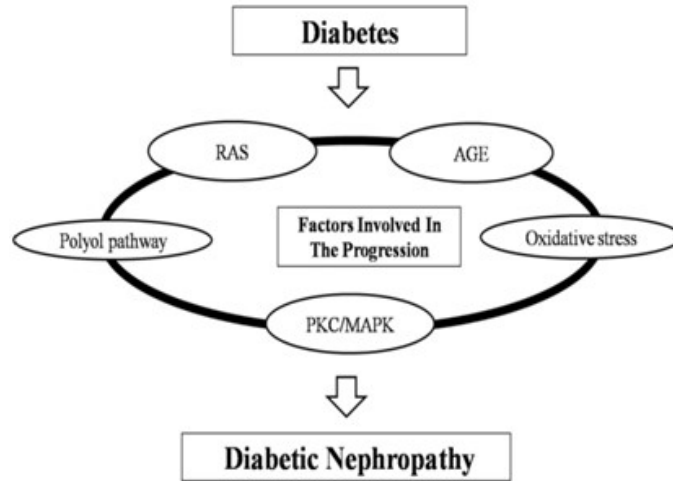
Key words:

**Keywords:** HbA1c, glycated albumin (GA), SMBG

**1. Introduction**

The progressive complications of unmanaged diabetes include heart disease, blindness, kidney failure, amputation of extremities due to circulation problems, and nerve disorders, as well as other chronic conditions.<sup>1,2,3</sup> The process of protein glycation is now understood to be both a marker for the progress of diabetes complications and an underlying cause of many of the most serious complications. Diabetes monitoring for protein glycation, an essential element for the long-term control of the complications of diabetes mellitus, is currently managed by a combination of daily self-monitoring of blood glucose (SMBG) measurements and physician-assessed hemoglobin A1c (A1C) levels every 3–6 months.<sup>4,5,6,7,8</sup>

**Figure I- Factors involved in pathogenesis of Diabetic Nephropathy**



**1.1 Glycated Haemoglobin**

A form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. It is formed in a non-enzymatic glycation pathway by hemoglobin's exposure to plasma glucose. Normal levels of glucose produce a normal amount of glycated hemoglobin. As the average amount of plasma glucose increases, the fraction of glycated hemoglobin increases in a predictable way.<sup>9,10,11</sup>

In the normal ~120-day lifespan of the red blood cell, glucose molecules react with hemoglobin, forming glycated hemoglobin. Once a hemoglobin molecule is glycated, it remains that way. The HbA<sub>1c</sub> level is proportional to average blood glucose concentration over the previous four weeks to three month.<sup>12,13</sup>

**1.2 Glycated Albumin**

Human serum albumin is the most abundant protein in human blood plasma. It is produced in the liver. Albumin constitutes about half of the blood serum protein. It is soluble and monomeric. The reference range for albumin concentrations in blood is 3.4 to 5.4 g/dL. It has a serum half-life of approximately 20 days. It has a molecular mass of 67 kDa. Approximately 10% of the albumin in normal human serum is modified by nonenzymatic glycosylation, primarily at the epsilon-amino group of lysine residue 525. The amount of glycosylated albumin in serum is markedly elevated in diabetes and thus its determination may help in the monitoring of the disease.<sup>14,15</sup>

**Figure II- Oxidative stress and AGE's**

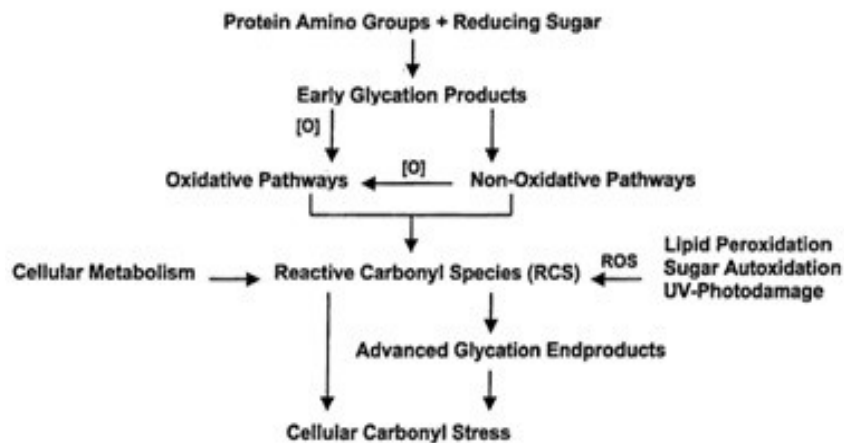
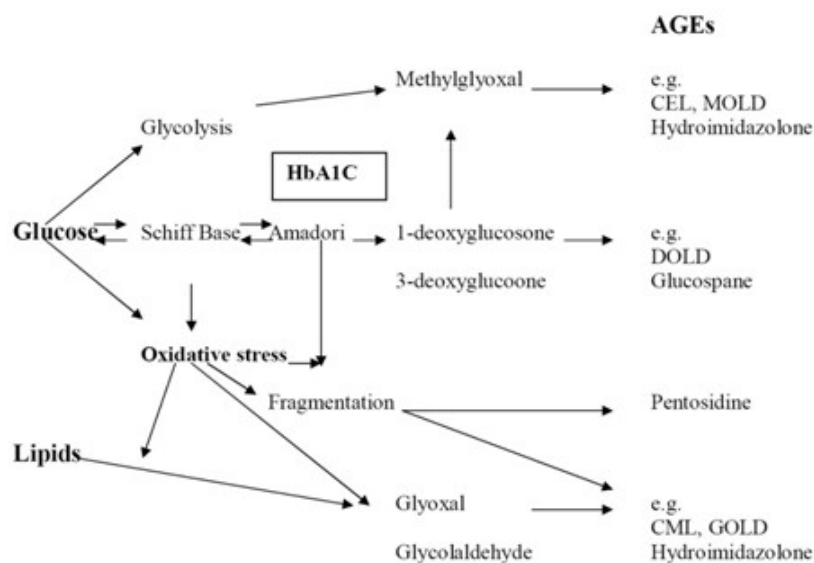


Figure III- Formation of HbA1c and AGE's



## 2. Materials

Hospital's Ethical Committee clearance was obtained to carry out the study.

The patients for the study were selected from Medicine OPD, KIMS and were divided into three groups:

- 25 healthy patients (non diabetic) were included as controls.
- 25 patients were included with diabetic history of more than five years and urine micral levels less than 20 $\mu$ g/ml.
- 25 patients were included with diabetic history of more than five years and urine microalbumin levels between 20-200 $\mu$ g/ml.

Inclusion criteria for the project was patient with DM >5 years and presence of hypercholesteremia (>250 mg/dl).

Exclusion criteria were patient with ESRD and participation in another clinical trial. HbA1c levels and Glycated Albumin levels were measured in all the three groups along with Fasting Glucose levels.

## 3. Methods

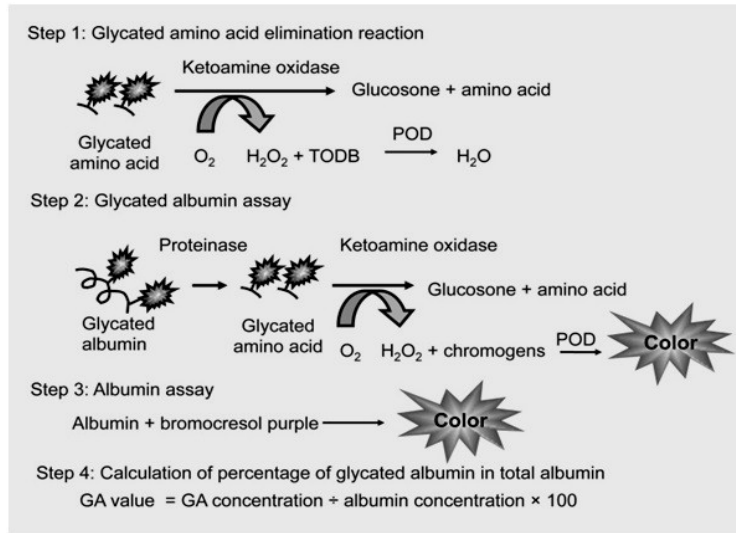
Fasting blood glucose levels were measured by Glucose Oxidase Peroxidase Method.

Urine Micral levels were measured by Immunoturbidimetric Method using latex coated anti albumin antibodies.

HbA1c levels were measured by High Performance Liquid Chromatography using D10 HbA1c Analyzer.

Glycated Albumin was measured by enzymatic method (Lucica GA-L glycated albumin assay kit) using albumin specific protease, ketoamine oxidase and albumin assay reagent. GA was hydrolyzed to amino acids by albumin specific proteinase and then oxidized by ketoamine oxidase to produce hydrogen peroxide, which was measured quantitatively. The GA value was calculated as the percentage of GA relative to total albumin, which was measured with bromocresol purple method.

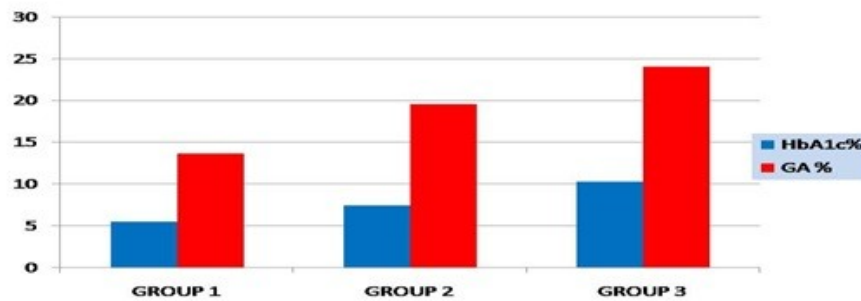
**Figure IV- Principle of glycated albumin assay**



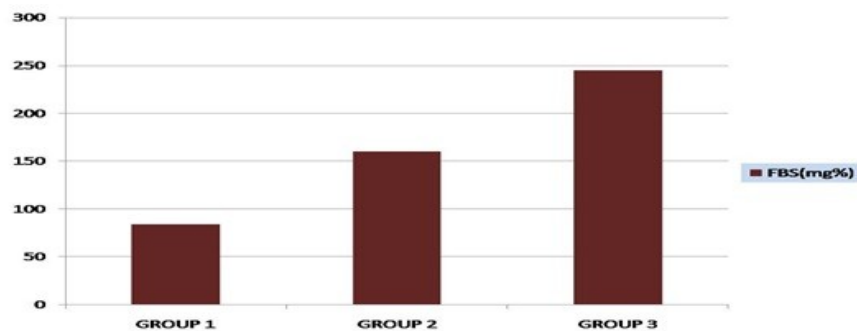
**Table 1. Correlation of HbA1c and GA in different Groups**

Variables	Group 1 (n=25)	Group 2 (n=25)	Group 3 (n=25)
FBS (mg%)	84.2 ± 8.75	160.5 ± 20	245.0 ± 70.6
HbA1c (%)	5.5 ± 0.3	7.5 ± 0.81	10.3 ± 2.30
Glycated Albumin (%)	13.7 ± 0.9	19.6 ± 2.1	24.1 ± 5.3
Urine Micral (µg/ ml)	Negative	Negative	91.4 ± 41.5

**Figure V- Correlation of HbA1c and GA in different Groups**

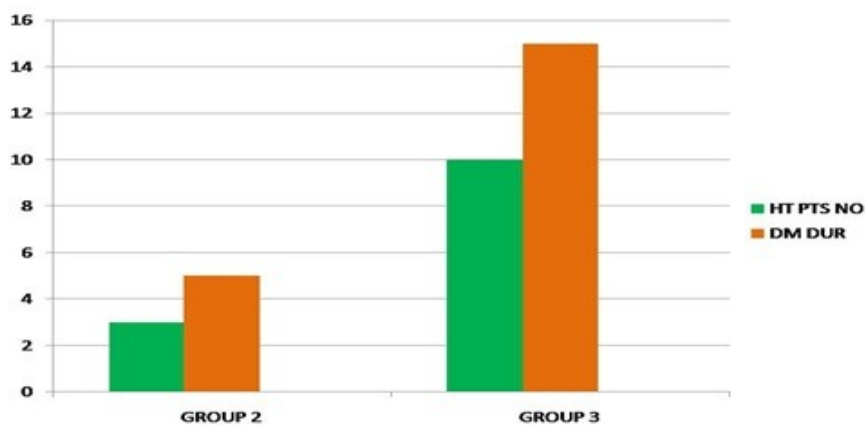


**Figure VI- Increasing FBS Levels with duration of DM in patient**



**Table 2. Correlation of Duration of DM and Hypertension**

Variable	Group 1 (n=25)	Group 2 (n=25)	Group 3 (n=25)
DM in years	NA	5- 7	6- 15
Hypertension (No. of patients)	NA	3	10

**Figure VII- Correlation of Duration of DM and Hypertension**

#### 4. Discussion

The normal cut of value for GA was calculated using the control group and was found to be around 14%. GA was significantly higher in diabetic patients indicating its role in assessing glycemic control. Microalbuminuric patients had significantly higher GA levels (Normal Range- 11 to 16%) than normoalbuminuric patients ( $p < 0.05$ ) indicating poor glycemic control patients are more likely to have diabetic complications. The increase in GA levels correlated with the increase in HbA1c levels ( $r = 0.87$ ), which proves GA can be used as an alternative glycemic indicator. Patients with microalbuminuria had higher % of hypertension compared with diabetic patients in whom microalbumin in urine was negative, signifying hypertension can be a factor for diabetic complications.

Microalbumin in urine was present in patient with longer diabetic history (around 10 years). This results correlated well with documented evidence that diabetic nephropathy usually occur after 10-15 years after diagnosis of diabetes.

#### 5. Conclusion

Glycated Albumin can be used as marker for glycemic control. As half life of albumin is significantly lower compared to life span of RBC, GA can be used as an intermediate glycemic indicator (every three to four weeks). Monthly assessment of GA in patients of Diabetes more than 5 years can prevent complications.

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