# Association of Glycosylated Albumin Level with Gestational Diabetes Mellitus

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## Abstract

**Background:** Gestational Diabetes Mellitus (GDM) is a common medical disorder detected during pregnancy with adverse consequences on the health of the mother and the fetus. Glycosylated hemoglobin ($HbA_1c$) is an important parameter of glycemic control in patients with diabetes mellitus. However, it only reflects the long-term glycemic status, but can't reflect short term glycemic control. It has also been demonstrated that $HbA_1c$ does not reflect glycemic control accurately during pregnancy because of iron deficiency. But Glycosylated Albumin (GA) reflects average blood glucose within 2-3 weeks and is not influenced by iron deficiency. Therefore, glycosylated albumin may be used to measure recent changes in blood glucose level in GDM patients. The aim of the study is to evaluate the association of glycosylated albumin and glycemic status in GDM.

**Materials and methods:** This case control study was carried out in the Department of Obstetrics & Gynecology, Bangabandhu Sheikh Mujib Medical University, BSMMU, Dhaka between August 2017 and December 2018. Atotal of 140 pregnant women between 18-35 years of age attending outdoor antenatal clinic in their second and third trimester of pregnancy were enrolled in this study. Among them 70 diagnosed case of GDM were considered as group I and rest 70 non-diabetic pregnant women were considered as control and group II. Plasma glycosylated albumin was measured in all of these patients. Statistical analysis of the results was obtained by using Windows based computer software devised with Statistical Packages for Social Sciences (SPSS-22).

**Results:** The mean glycosylated albumin was 17.12±2.00 (%) in group I and 12.90±1.03 (%) in group II. The difference was statistically significant ($p<0.05$) between two groups. There was a positive significant moderate correlation ($r=0.643$, $p=0.001$) between glycosylated albumin (%) and 2 hours after 75 gm glucose in GDM patients. There was also a positive significant weak correlation ($r=0.258$, $p=0.031$) between GA and FBS in GDM patients.

**Conclusion:** A significant positive association was found between glycemic status in GDM and maternal glycosylated albumin levels. Therefore,glycosylated albumin may be applied to reflect the average blood glucose status in pregnant women with GDM.

**Key words :** Gestational diabetes mellitus; Glycosylated Albumin; $HbA_1c$.

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## Introduction

Hyperglycemia first detected at any time during pregnancy is classified as either Diabetes Mellitus in pregnancy or Gestational Diabetes Mellitus (GDM). GDM is diagnosed when FBS is 5.1-6.9mmol/L or plasma glucose is >8.5-11.0 mmol/L 2 hours aftera 75g oral glucose load.[1] GDM diagnosis is made when any of the following plasma glucose values are met or exceeded: Fasting: 92 mg/dL (5.1 mmol/L): 1 h: 180 mg/dL (10.0 mmol/L) and 2 h: 153 mg/dL (8.5 mmol/L).[2] Worldwide GDM affects 7% of all pregnancies and the incidenceof GDM ranges from 1 to 14% depending on the population sample and diagnostic criteria used.[3] In Bangladesh, the prevalence of GDM is 9.7%.[4] Certain groups of women are at increased risk of developing GDM. The risk factors include age >35 years, BMI >30kg/$m^2$, prior history of GDM, previous macrocosomic baby (Weight >4.5kg), prior history of unexplained still birth, family history of diabetes (In 1$^{st}$ degree) and polycystic ovarian syndrome.[3]

During pregnancy, it gives rise to miscarriage, increased incidence of preeclampsia, polyhydramnios, urinary tract infection, vulvovaginitis, diabetic retinopathy, diabetic nephropathy. During labor, there is increased incidence of prolong labor, shoulder dystocia due to macrosomia, birth trauma and increased operative interference. Fetal and neonatal complications include fetal macrosomia, congenital malformations, birth injuries, IUD, neonatal hypoglycemia, respiratory distress syndrome, hyperbilirubinemia, polycythemia and hypocalcemia.[5] Fifty percent of women diagnosed with GDM will ultimately develop type 2 DM later in life.[3]

Different guidelines and associations have suggested different screening regimes for GDM. However, in this study GDM is diagnosed according to standard WHO guideline using 75gm glucose load.[1] The treatment of GDM is mainly focused on the monitoring, evaluation and control of blood sugar. Usually, two types of indicators are monitored: one is sclf monitored blood glucose level (Such as fasting blood sugar and 2 hours after meal) and other is long term blood glucose monitoring indicator glycosylated hemoglobin ($HbA_1c$). Fasting blood sugar is greatly influenced by previous diet, duration of fasting, mental state and other factors such as stress, which exhibits great fluctuations. Since the lifespan of erythrocytes is about 120 days, $HbA_1c$ only reflects the blood glucose level during the previous 3 months and has a relatively shorter observation period for GDM, thus it is less sensitive.

Glycosylated albuminis a ketoamine formed from nonenzymatic reaction and binding between four lysine residues of albumin and glucose. It is another index of glycemic control, which correlates with the plasma glucose levels during the recent past few weeks as the turnover of albumin is about 20 days.[6] Thus, glycosylated albumin is an useful index for measurement of the recent changes in blood glucose level and thus have been proposed to be useful in following diabetic pregnant patients in whom glycemic control must be maintained all the time.[7] Normal level of glycosylated albumin is 11.5 to 15.7%.[8]

GDM is a common pregnancy complication and is associated with increased maternal and neonatal morbidity. Good glycemic control is the key to reduce maternal, fetal and neonatal complications and to improve the obstetric outcome. Therefore, markers that can more accurately reflect the alteration of blood glucose levels and mean glycemic statusover short-term period in GDM women are genuinely required. Glycosylated albumin may be applied to reflect the recent blood glucose status in pregnant women with GDM. It would offer an opportunity for earlier interventions to obtain a better glycemic control during pregnancy and help toachieve better obstetric outcome and to reduce maternal and neonatal morbidity and mortality.

**Materials and methods**

This antegrade case control study was conducted in the Department of Obstetrics and Gynecology, BSMMU, Dhaka between 1st August 2017 and 31st December 2018.Ethical clearance was taken from the institutional review board of BSMMU. A total of 140 pregnant women, who attended the outdoor antenatal clinic at their 2nd and 3rd trimester (13-40 weeks) of pregnancy were enrolled for the study by purposive sampling. Recruited pregnant women were divided into case and control groups. Case group (Group A) consisted of 70 pregnant women who were diagnosed as GDM. Control group (Group B) comprised of 70 apparently healthy non-diabetic pregnant women. Age range of all study subjects werewithin 18-35 years. Pregnant women with renal diseases, acute or chronic liver diseases, chronic kidney disease,thyroid disorders and preeclampsia were excluded from this study.

Detailed socio-demographic history, obstetric history, gestational age, family history and medical history were recorded. Antenatal records and early ultrasound scans were reviewed to confirm the duration of gestation. Medical records of diagnosis of GDM were reviewed. Pregnant mothers who had undergone GDM screening, and diagnosed as GDM as per the WHO, with FBS 5.1 to 6.9mmol/L and 2 hours after 75g glucose of >8.5 to 11.0 mmol/L were recruited for the study as case group. Routinephysical examination, anthropometric measurements (Height, weight) were taken and obstetric examination were conducted and recorded. After selecting cases and controls, with all aseptic precaution 3ml antecubital venous blood sample was collected from each subject. Blood sample was allowed to clot and plasma was separated by centrifugation at

room temperature. Glycosylated albumin was measured by using human Glycosylated Albumin (GA) ELISA kit and based on the Enzyme Linked Immuno-Sorbent Assay (ELISA). Glycosylated Albumin (Human) ELISA is a direct non-radiolabel enzyme-linked immunoassay in which glycosylated albumin in human plasma binds to an immobilized monoclonal antibody that specifically recognizes the glycosylated moieties on human albumin. After incubation for a fixed time, an enzyme-conjugated polyclonal antibody directed against human albumin is added. A chromogenic substrate is then added. After the reaction is stopped, the intensity of the color is read in an ELISA reader at 450 nm. The concentration of glycosylated albumin in the specimen sample is read from a calibration curve. The amount of glycosylated albumin can be expressed as absolute concentration (mg/ml) or as a relative %, determined by dividing the glycosylated albumin in the sample by the total albumin in the sample.

Statistical analyses of the results were performed using Windows based computer software devised with Statistical Packages for Social Sciences (SPSS-22). In comparison of the baseline characteristics and outcomes between the two groups, student's t-test was used for continuous variables and chi-square tests for categorical variables, Odds Ratio (OR) with 95% confidence interval and Pearson's correlation test was utilized between plasma glycosylated albumin with fasting plasma glucose (mmol/L) and postprandial plasma glucose (mmol/L) and p value < 0.05 was considered significant.

## Results

**Table I** Distribution of the study patients by age and gestational age (n=140)

| Age (In years) | Group A (n=70) | | Group B (n=70) | | p value |
|---|---|---|---|---|---|
| | n | % | n | % | |
| 18-25 | 11 | 15.7 | 28 | 40.0 | |
| 26-30 | 31 | 44.3 | 30 | 42.9 | |
| >30 | 28 | 40.0 | 12 | 17.1 | |
| Mean±SD | 29.65 | ±3.83 | 28.53 | ±4.39 | 0.110$^{ns}$ |
| Duration of gestation (Week) | Group A (n=70) | | Group B (n=70) | | p value |
| | n | % | n | % | |
| 13-28 | 45 | 64.3 | 40 | 57.1 | |
| 29-40 | 25 | 35.7 | 30 | 42.9 | |
| Mean±SD | 28.15 | ± 4.06 | 27.8 | ± 3.67 | 0.593$^{ns}$ |

Group A= Pregnant women with GDM, Group B= Pregnant women without GDM.

Table I shows age distribution of the study patients. The age distribution of the patients was similar and the difference was statistically not significant (p>0.05) between two groups. This table also shows gestational age of the study subjects. There wasn't any significant difference in terms of gestational age as well.

**Table II** Distribution of the study patients by gravida (n=140)

| Parity | Group A (n=70) | | Group B (n=70) | | p value |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Primi | 28 | 40.0 | 36 | 51.4 | 0.174$^{ns}$ |
| Multi | 42 | 60.0 | 34 | 48.6 | |

Table II shows the distribution of the study patients according to gravida.It was observed that 60.0% patients were multigravida in Group A and 48.6% in Group B. The difference was statistically not significant (p>0.05) between two groups.

**Table III** Glycosylated Albumin concentration in study patients (n=140)

| | Group A (n=70) Mean±SD | Group B (n=70) Mean±SD | p value |
|---|---|---|---|
| Glycosylated Albumin ( %) | 17.12 ± 2.00 | 12.90± 1.03 | 0.001$^{s}$ |

Table III shows Glycosylated Albumin concentration of the study patients and the difference was statistically significant (p<0.05) between the two groups.

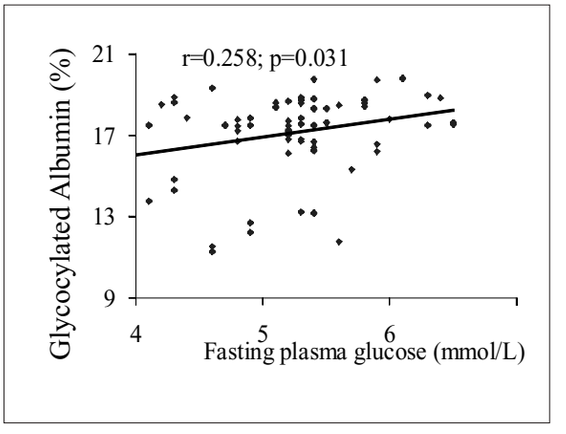


**Fig 1** Scatter diagram showing positive significant Pearson's correlation (r=0.258, p=0.031) between glycosylated albumin (%) and fasting plasma glucose (mmol/L)

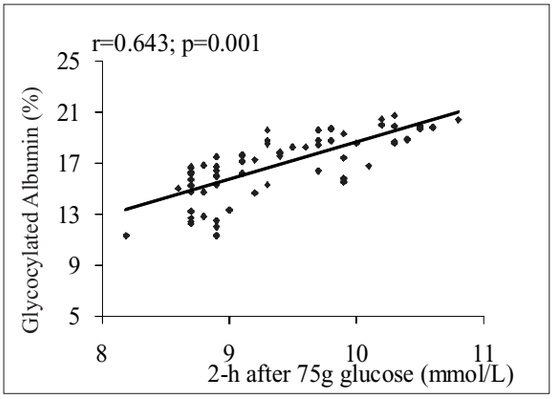


**Fig 2** Scatter diagram showing positive significant Pearson's correlation (r=0.643, p=0.001) between glycosylated albumin (%) and 2-h after 75g glucose (mmol/L)

**Discussion**

This case control study was carried out with an aim to evaluate the association of glycated albumin in gestational diabetes mellitus. In this current study it was observed that 44.3% patients belonged to age 26-30 years in group I and 42.9% in group II. The mean age was 29.65±3.83 years in group I and 28.53±4.39 years in group II. Kondaveeti and colleagues found the mean age was 29.63±4.62 years in pregnant women with GDM and 24.0±3.00 years in pregnant women without GDM, which is comparable with the present study.[7] Seshiah and colleagues found that the mean age was 27.10±4.05 years and 23.80±3.61 years in case and control group respectively, which is also comparable with the present study.[9] On the other hand, Sugawara and colleagues conducted a study which found the mean age was 35.1±4.6 years in patients with gestational diabetes mellitus and 34.9±3.5 years in control group, which is higher than the present study.[10] The higher mean age obtained by the above authors maybe due to striking variations in ethnicity, geographical variations, racial, and genetic causes may have significant influence on gestational diabetes mellitus in their study subjects. Regarding the gravida, it was observed in this present study that 60.0% patients were multipara in group I and 48.6% in group II. The difference was statistically not significant (p>0.05) between two groups. Similar findings also observed by study conducted by Ostlund and colleagues.[11] In the current study, it was observed that 64.3% patients belonged to 13-28 weeks gestation in group I and 57.1% belonged to 29-40 weeks gestation in group II. The mean duration of gestation was 28.15±4.06 weeks in group I and 27.8±3.67 weeks in group II. The difference was statistically not significant (p>0.05) between two groups. Kwik and colleagues conducted a study which showed the mean gestational age was 32.1 weeks.[12] Similarly, Yogev, Visser and Metzger conducted two similar types of studies, whichfound gestational age varied from 29 to 36 weeks.[13-15] Sugawara and colleagues conducted a study which found the mean gestational weeks was 38.2±1.4 weeks in case and 38.1±1.0 weeks in control group, which is higher than the current study.[10] In the present study, it was observed that the mean glycosylated albumin was 17.12±2.00 (%) in group I and 12.90±1.03 (%) in group II. The difference was statistically significant (p<0.05) between two groups.The study conducted by Kondaveeti and colleagues showed the mean Glycocylated Albumin was 16.75±1.85%, in pregnant women with GDM and 14.25±1.65% in pregnant women without GDM, which is consistent with the present study.[7] Hiramatsuand his colleagues conducted a study which revealed that glycosylated albumin levels in healthy pregnant Japanese women ranged from 11.5% to 15.7%.[16,17] Another study conducted by Huang and colleagues reported that glycosylated albumin level in the pregnant women with GDM at different gestational weeks were relatively higher compared to the pregnant women in the normal control group.[6]

In this study it was observed that there is a positive significant Pearson's correlation (r=0.258, p=0.031) between Glycosylated albumin (%) with fasting plasma glucose (mmol/L) in GDM patients. There is also a positive significant Pearson's correlation (r=0.643, p=0.001) between Glycosylated albumin (%) with 2-h after 75g glucose (mmol/L) in GDM patients. Ma and colleagues conducted a study, which showed that GA levels were strongly correlated with FPG (r=0.640, p<0.001), with 2-h PG (r = 0.661, p<0.001) which is closely resembled with the present study.[18] Seshiahand colleagues conducted a study which reported that GA levels correlated with FPG and PPG, similar to the study observation of Yang and colleagues.[8,19] The study conducted by Kondaveeti and colleagues reported

that there was a reasonable sensitivity of GA over HbA1c when compared with 2 hours plasma glucose concentration.[7] Hashimoto and colleagues conducted a study which documented that HbA1c but not GA was elevated because of iron deficiency anemia inwomen with late pregnancy.[20] Another observation by the study conducted by Seshiah and colleagues was GA indicates maternal glycemic control of the past few weeks whereas $HbA_1c$ level indicates of the past few weeks to months, but the important clinical advantage of GA is that, it reveals glycemic excursions earlier.[9]

**Limitations**

The present study was conducted within a short period of time. The study population was selected from one selected hospital, so that the results of the study may not be reflect the exact picture of the country.It is not compared with $HbA_1c$ in GDM, so doesn't reflect its superiority over $HbA_1c$. Small sample size with purposive sampling was also a limitation of the present study. Therefore, in future further studies may be under taken with large sample size.

**Conclusion**

This study showed that glycosylated albumin level was markedly higher in women with Gestational Diabetes mellitus than in non-diabetic pregnant women. Therefore, glycosylated albumin may be applied to reflect the recent blood glucose status in pregnant women with GDM.

**Recommendation**

This study suggests, glycosylated albumin have positive association with GDM. Further study with large samole size in multiple centers may strengthen the outcome of the study.

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**Contribution of authors**

FI-Conception, acquisitation of data, drafting & final approval.
RKK-Data analysis, critical revision & final approval.
NH-Design, critical revision & final approval.
NH-Interpritation of data, critical revision & final approval.
BR-Acquisitation of data, drafting & final approval.
KD-Acqusitation of data, drafting & final approval.
RA-Data analysis, drafting & final approval.
MB-Acquisitation of data, data analysis, drafting & final approval.
FA-Design, critical revision & final approval.

**Disclosure**

All the authors declared no competing interest.

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