

PROSPECTIVE ASSESSMENT OF GLYCATED ALBUMIN AS AN EARLY MARKER FOR GLYCEMIC CONTROL IN GESTATIONAL DIABETES MELLITUS

Kiran Malik¹, Devesh Kumar², Jay Ballabh³

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Corresponding Author:

Dr. Kiran Malik

Email: devkiran.2016@gmail.com

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¹Associate Professor, Department of Biochemistry, Autonomous State Medical College, Shahjahanpur, Uttar Pradesh, India.

²Professor, Department of Physiology, Autonomous State Medical College, Shahjahanpur, Uttar Pradesh, India.

³Professor, Department of Physiology, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, Uttar Pradesh, India.

ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a common metabolic disorder in pregnancy, associated with adverse maternal and fetal outcomes. Conventional glycemic markers such as HbA1c and glucose levels have limitations in reflecting short-term glycemic fluctuations, particularly during the dynamic metabolic changes of pregnancy. Glycated albumin (GA) has emerged as a promising short-term marker of glycemic control, with potential advantages over traditional measures. The aim is to evaluate glycated albumin as an early and reliable marker for monitoring glycemic control in pregnant women diagnosed with gestational diabetes mellitus. **Materials and Methods:** This prospective observational study was conducted in the Department of Biochemistry at a tertiary care teaching hospital. A total of 110 pregnant women diagnosed with GDM between 24 and 28 weeks of gestation, based on IADPSG criteria, were enrolled. GA, fasting blood glucose (FBG), postprandial blood glucose (PPBG), and HbA1c were assessed at baseline, 4 weeks, and 8 weeks. Statistical analysis included repeated measures ANOVA and Pearson's correlation coefficient, with a p-value <0.05 considered statistically significant. **Result:** The mean baseline GA was $13.41 \pm 1.12\%$, which significantly reduced to $11.36 \pm 0.94\%$ at 8 weeks ($p < 0.001$). Mean FBG decreased from 108.24 ± 8.67 mg/dL to 93.88 ± 6.87 mg/dL, and PPBG from 154.61 ± 12.84 mg/dL to 126.21 ± 10.28 mg/dL over the same period ($p < 0.001$ for both). GA showed strong correlation with FBG ($r = 0.642$), PPBG ($r = 0.587$), and HbA1c ($r = 0.712$) at baseline ($p < 0.001$). A $\geq 2\%$ reduction in GA was observed in 79.09% of participants by 8 weeks. Most patients (66.36%) were managed with lifestyle modifications alone, and 94.55% achieved fasting glucose control. **Conclusion:** Glycated albumin correlated strongly with standard glycemic markers and responded sensitively to short-term glycemic changes in GDM. Its dynamic response to treatment and ability to reflect glycemic control over weeks rather than months make it a valuable adjunct to HbA1c for monitoring GDM.

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most common metabolic disorders complicating pregnancy, defined as glucose intolerance with onset or first recognition during pregnancy. It poses significant health risks to both mother and fetus, including preeclampsia, macrosomia, birth trauma, neonatal hypoglycemia, and a heightened risk of developing type 2 diabetes mellitus (T2DM) later in life. In recent decades, the global incidence of GDM has been rising, largely due to increasing rates of maternal obesity, sedentary lifestyle, and advanced maternal age at conception.^[1] Early diagnosis and

effective glycemic control are central to reducing perinatal morbidity and long-term complications for both mother and child.^[2]

Traditionally, the diagnosis of GDM is made during the second trimester, typically between 24 and 28 weeks of gestation, using the oral glucose tolerance test (OGTT). This timing, however, may delay intervention and management, particularly in high-risk groups such as older or obese women.^[3] By the time hyperglycemia is detected using conventional methods, deleterious metabolic and vascular changes may have already been initiated, reducing the window for preventive strategies to be effective. Moreover, conventional biomarkers such as fasting

plasma glucose and HbA1c have inherent limitations in reflecting acute glycemic fluctuations, especially during the dynamic physiological changes of pregnancy.^[4]

Hemoglobin A1c (HbA1c), although widely used in diabetes diagnosis and management, reflects average glycemia over approximately 2 to 3 months and is influenced by factors such as erythrocyte lifespan, hemoglobinopathies, and iron deficiency anemia. These factors are particularly relevant during pregnancy, when altered hematological profiles may compromise the reliability of HbA1c readings.^[5] This creates a need for alternative glycemic markers that can accurately reflect shorter-term glucose control and are less affected by physiological confounders.

One such emerging marker is glycated albumin (GA), a product of non-enzymatic glycation of serum albumin that reflects glycemic status over a period of 2 to 3 weeks. Unlike HbA1c, GA is unaffected by erythrocyte turnover, making it a promising biomarker in pregnancy and other clinical scenarios where HbA1c may be unreliable.^[6] Glycated albumin has shown particular value in identifying short-term glycemic fluctuations, assessing glycemic variability, and evaluating the efficacy of recent therapeutic interventions. In the context of GDM, where glycemic dynamics can change rapidly within weeks, GA could potentially serve as an early and responsive indicator of treatment effectiveness and disease progression.

The clinical utility of GA has been demonstrated in both epidemiological and interventional studies. Research has shown that GA correlates well with average glucose levels and can predict the development of diabetes-related complications, including retinopathy and nephropathy.^[7] In large cohort analyses, GA and other short-term markers such as fructosamine have been associated with incident diabetes and microvascular outcomes, independently of HbA1c levels.^[8] These findings underscore the potential of GA not only as a diagnostic aid but also as a valuable tool for stratifying risk and guiding management.

Moreover, the ability of GA to respond more quickly to therapeutic changes presents a distinct advantage in managing GDM, where timely interventions can significantly alter maternal and neonatal outcomes. For example, the initiation of dietary modifications or insulin therapy may not immediately impact HbA1c but can lead to measurable improvements in GA within one or two weeks. This responsiveness allows clinicians to assess treatment adequacy in a timely fashion and make necessary adjustments before glycemic control deteriorates.^[9] In addition, GA testing is relatively simple, cost-effective, and reproducible, making it suitable for widespread clinical use.

Despite these advantages, the use of GA in routine pregnancy care has not been widely adopted, partly due to the lack of standardized cut-off values and limited awareness among clinicians. There is also a need for further prospective studies to validate the

clinical performance of GA across diverse populations and pregnancy conditions. However, early investigations suggest that GA may outperform traditional markers in certain contexts, particularly in early pregnancy or in women with conditions affecting hemoglobin levels. As such, the integration of GA into diagnostic and monitoring protocols for GDM could enhance early detection, enable better monitoring of glycemic trends, and ultimately improve maternal-fetal outcomes.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Biochemistry at a tertiary care teaching hospital. Ethical clearance was obtained from the Institutional Ethics Committee prior to the commencement of the study. Written informed consent was obtained from all participants prior to enrollment in the study. A total of 110 pregnant women diagnosed with Gestational Diabetes Mellitus (GDM) were enrolled consecutively based on predefined inclusion and exclusion criteria. The diagnosis of GDM was established between 24 to 28 weeks of gestation using the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria, following a 75-gram oral glucose tolerance test (OGTT).

Inclusion Criteria

Eligible participants included women with a singleton pregnancy, gestational age between 24 to 28 weeks at the time of diagnosis, and newly diagnosed cases of GDM. Participants were included only if they expressed willingness to comply with the study protocol and attend regular follow-up visits.

Exclusion Criteria

Women with known pregestational diabetes mellitus (Type 1 or Type 2), multiple gestations, or chronic conditions such as liver disease, nephrotic syndrome, or thyroid dysfunction that could influence albumin metabolism were excluded. Additionally, patients with hemoglobinopathies or anemia (Hb < 10 g/dL), or those receiving corticosteroids or immunosuppressive therapy, were not considered for the study.

Procedure: Upon diagnosis of GDM, each participant underwent a comprehensive clinical assessment, including a detailed medical history and physical examination. Baseline laboratory investigations were carried out, including fasting blood glucose (FBG), postprandial blood glucose (PPBG), glycated hemoglobin (HbA1c), and glycated albumin (GA). GA levels were measured using a validated enzymatic method with a commercial kit (Lucica® GA-L; Asahi Kasei Pharma, Japan), and results were expressed as a percentage of total albumin.

Follow-up evaluations were conducted at 4 weeks and 8 weeks post-diagnosis. At each visit, FBG, PPBG, HbA1c, and GA were repeated to monitor glycemic control. All patients received standard

dietary counseling and lifestyle modification guidance. Management was in accordance with institutional protocols, including medical nutrition therapy and insulin administration as needed. Patient compliance and clinical response were monitored throughout the follow-up period.

Statistical Analysis: All collected data were entered and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD), and categorical data were presented as frequencies and percentages. The relationship between glycated albumin and other glycemic indicators was evaluated using Pearson's or Spearman's correlation coefficient, depending on the data distribution. Changes in glycemic parameters over time were assessed using repeated measures ANOVA. A p-value less than 0.05 was considered statistically significant.

RESULTS

Baseline Demographic and Clinical Characteristics [Table 1]

The mean age of the study participants was 29.42 ± 4.76 years, indicating that most of the women were in their late twenties or early thirties. The average gestational age at the time of diagnosis of GDM was 25.67 ± 1.22 weeks, aligning with the typical screening window of 24–28 weeks. The mean Body Mass Index (BMI) was 26.48 ± 2.31 kg/m², placing the majority of participants in the overweight category, a known risk factor for GDM. A positive family history of diabetes was reported in 46 women (41.82%), reflecting a significant hereditary component. Additionally, 18 women (16.36%) had a history of GDM in a prior pregnancy. The vast majority of pregnancies were spontaneous (92.73%), while only 7.27% were conceived via assisted reproductive techniques, indicating that GDM was prevalent across both naturally conceived and assisted pregnancies.

Baseline Biochemical Parameters [Table 2]

At the time of diagnosis, the mean fasting blood glucose (FBG) was 108.24 ± 8.67 mg/dL, exceeding the normal pregnancy threshold of <92 mg/dL. The mean postprandial blood glucose (PPBG) was 154.61 ± 12.84 mg/dL, also above the recommended <153 mg/dL, confirming the diagnosis of GDM per IADPSG criteria. The mean HbA1c value was $5.92 \pm$

0.45%, close to the pregnancy target of $<6.0\%$, indicating mild to moderate hyperglycemia. The glycated albumin (GA) level was $13.41 \pm 1.12\%$, which fell within the reference range of 11–16% but was at the higher end, suggesting poor short-term glycemic control at baseline.

Glycemic Trends Over 8 Weeks [Table 3]

Significant improvements in glycemic parameters were observed over the 8-week follow-up period. The mean FBG reduced from 108.24 mg/dL at baseline to 93.88 mg/dL at 8 weeks, and PPBG dropped from 154.61 mg/dL to 126.21 mg/dL, both showing statistically significant improvement ($p < 0.001$). Similarly, HbA1c decreased from 5.92% to 5.56%, and GA levels fell from 13.41% to 11.36% by the end of the 8-week period. The reduction in GA was especially notable, confirming its sensitivity in reflecting short-term glycemic fluctuations. All changes in glycemic markers were statistically significant as shown by repeated measures ANOVA ($p < 0.001$ for all).

Correlation of Glycated Albumin with Glycemic Markers [Table 4]

Glycated albumin exhibited a strong and statistically significant positive correlation with fasting blood glucose ($r = 0.642$, $p < 0.001$) and postprandial blood glucose ($r = 0.587$, $p < 0.001$). The highest correlation was observed between GA and HbA1c ($r = 0.712$, $p < 0.001$), supporting the validity of GA as a reliable early marker of glycemic control. These findings demonstrate that GA can serve as an effective adjunct or alternative to HbA1c, especially in pregnancy where rapid changes in glycemic status may not be fully captured by HbA1c alone.

Management and Glycemic Control Outcomes [Table 5]

Out of the 110 participants, 73 women (66.36%) were managed successfully with diet and lifestyle modifications alone, while the remaining 37 women (33.64%) required additional insulin therapy. At the end of 8 weeks, 104 women (94.55%) achieved optimal fasting glucose control (<95 mg/dL), and 100 women (90.91%) met the postprandial glucose target (<140 mg/dL). Importantly, 87 women (79.09%) demonstrated a $\geq 2\%$ reduction in glycated albumin from baseline, indicating substantial improvement in short-term glycemic control. These outcomes reflect the overall effectiveness of standard GDM management strategies and highlight the clinical utility of GA in monitoring response to therapy.

Table 1: Baseline Demographic and Clinical Characteristics (n = 110)

Parameter	Value
Mean Age (years)	29.42 ± 4.76
Mean Gestational Age (weeks)	25.67 ± 1.22
BMI (kg/m ²)	26.48 ± 2.31
Family History of Diabetes	46 (41.82%)
History of GDM in Previous Pregnancy	18 (16.36%)
Mode of Conception (Spontaneous)	102 (92.73%)
Mode of Conception (Assisted)	8 (7.27%)

Table 2: Baseline Biochemical Parameters at Time of Diagnosis (n = 110)

Parameter	Mean $\pm$ SD	Reference Range
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Fasting Blood Glucose (mg/dL)	108.24 ± 8.67	<92 (normal)
Postprandial Blood Glucose (mg/dL)	154.61 ± 12.84	<153 (normal)
HbA1c (%)	5.92 ± 0.45	<6.0% (pregnancy goal)
Glycated Albumin (%)	13.41 ± 1.12	11–16% (reference)

Table 3: Glycemic Parameters over Time (Baseline, 4 Weeks, 8 Weeks)

Parameter	Baseline (Mean ± SD)	4 Weeks (Mean ± SD)	8 Weeks (Mean ± SD)	p-value (Repeated Measures ANOVA)
FBG (mg/dL)	108.24 ± 8.67	98.13 ± 7.42	93.88 ± 6.87	<0.001
PPBG (mg/dL)	154.61 ± 12.84	132.94 ± 11.33	126.21 ± 10.28	<0.001
HbA1c (%)	5.92 ± 0.45	5.70 ± 0.39	5.56 ± 0.36	<0.001
Glycated Albumin (%)	13.41 ± 1.12	12.12 ± 1.03	11.36 ± 0.94	<0.001

Table 4: Correlation of Glycated Albumin with Glycemic Parameters at Baseline

Parameter	Correlation Coefficient (r)	p-value
Fasting Blood Glucose	0.642	<0.001
Postprandial Blood Glucose	0.587	<0.001
HbA1c	0.712	<0.001

Table 5: Mode of Management and Glycemic Control Outcome at 8 Weeks

Management Type	Number of Patients	Percentage (%)
Diet and Lifestyle Only	73	66.36%
Diet + Insulin Therapy	37	33.64%
Achieved FBG < 95 mg/dL	104	94.55%
Achieved PPBG < 140 mg/dL	100	90.91%
GA Reduction ≥ 2% from Baseline	87	79.09%

DISCUSSION

The demographic profile of the study participants aligns with established risk factors for Gestational Diabetes Mellitus (GDM). The average maternal age of 29.42 years corresponds with the age group where insulin resistance tends to increase due to physiological and lifestyle factors, supporting findings by Xiong et al (2024),^[10] who noted that advancing maternal age is independently associated with higher GA and glucose levels in pregnancy. The mean BMI of 26.48 kg/m² in our cohort also confirms the association between overweight status and GDM development, a relationship well established in the literature. A significant proportion of women (41.82%) had a family history of diabetes, reinforcing the genetic predisposition reported in the work of Freitas et al (2017),^[11] who emphasized the relevance of hereditary insulin resistance in GDM pathogenesis. Furthermore, the 16.36% prevalence of past GDM in our study population highlights recurrence trends previously noted by Yazdanpanah et al (2017) in their review on glycemic markers.^[12] Biochemically, our baseline data showed elevated mean FBG and PPBG levels, confirming hyperglycemia consistent with IADPSG thresholds. Although the mean HbA1c of 5.92% was near the pregnancy target of <6.0%, it does not fully reflect postprandial excursions and short-term glucose fluctuations, especially in newly diagnosed cases. In contrast, GA at baseline (13.41%) provided a better representation of early dysglycemia. According to Selvin et al (2018),^[13] GA levels offer enhanced sensitivity in identifying glycemic changes over a 2–3 week period, which is particularly useful in pregnancy where glucose dynamics evolve rapidly.

This emphasizes the value of GA as a complement to HbA1c in GDM monitoring.

Over the 8-week follow-up, all glycemic parameters showed statistically significant improvement, but the decline in GA levels was particularly noteworthy, dropping from 13.41% to 11.36%. This supports the conclusions of Desouza et al (2015),^[14] who demonstrated that GA reflects glycemic control within weeks of therapy initiation, unlike HbA1c which requires 2–3 months to show comparable change. In a pregnancy context, such responsiveness is critical, as rapid adjustment of glycemic therapy is often required to mitigate fetal risks. Our data reinforce the utility of GA in short-term monitoring, corroborating the findings of Ueda and Matsumoto (2015),^[15] who highlighted GA's superior temporal sensitivity in response to intervention.

A strong positive correlation was found between GA and both fasting ($r = 0.642$) and postprandial glucose ($r = 0.587$), with the highest correlation seen between GA and HbA1c ($r = 0.712$). This mirrors the observations of Xiong et al (2021),^[16] who in their meta-analysis confirmed robust associations between GA and standard glycemic indices. These correlations validate GA as a reliable biomarker not just for baseline assessment but for tracking glycemic patterns throughout pregnancy. Moreover, Armbruster (1987),^[17] had earlier described GA as a stable alternative to fructosamine, less influenced by albumin turnover variability, adding further weight to its clinical application.

Regarding management outcomes, 66.36% of women were successfully managed with lifestyle modifications alone, while 33.64% required insulin—a ratio similar to that reported in studies by Al-Lahham et al (2024),^[18] in gestational cohorts stratified by GA cut-off values. Importantly, 94.55% of participants achieved fasting glycemic targets by 8

weeks, and 79.09% showed a $\geq 2\%$ reduction in GA, supporting its role in early response monitoring. These outcomes affirm the findings of Yazdanpanah et al (2017),^[12] who proposed GA as a dynamic and practical tool for evaluating the effectiveness of therapy in diabetic populations, including GDM.

CONCLUSION

Glycated albumin (GA) demonstrated strong correlation with conventional glycemic markers and effectively reflected short-term glycemic changes in pregnant women with GDM. Its levels significantly decreased over 8 weeks, indicating responsiveness to treatment. GA proved valuable in both initial assessment and follow-up, particularly where rapid glucose control is essential. These findings support GA as a reliable adjunct to HbA1c in monitoring glycemic control during pregnancy.

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