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Utility of Glycated Albumin as a Biomarker for Glycemic Variability in Diabetes Mellitus

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ABSTRACT

Introduction: Glycemic variability, characterized by short-term glucose fluctuations, is increasingly recognized as an independent risk factor for diabetes-related complications, including oxidative stress, inflammation, and vascular damage. Traditional markers like hemoglobin A1c (HbA1c) reflect average glucose levels over 2–3 months but fail to adequately capture glycemic variability. Glycated albumin (GA), a glycation product of serum albumin, offers an alternative, reflecting glycemic status over 2–3 weeks and remaining unaffected by factors such as red blood cell turnover. This study evaluates the utility of GA as a biomarker for glycemic variability compared to HbA1c.

Materials and Methods: A cross-sectional study involving 120 participants with type 1 (n=55) or type 2 DM (n=65) was conducted. Glycemic variability metrics, including Mean Amplitude of Glycemic Excursions (MAGE), Coefficient of Variation (CV), and Time in Range (TIR), were derived from self-monitored blood glucose (SMBG) and continuous glucose monitoring (CGM). GA and HbA1c were measured using standardized enzymatic and HPLC assays, respectively. Correlation and ROC analyses assessed the relationship between GA, HbA1c, and glycemic variability.

Results: GA showed stronger correlations with glycemic variability metrics than HbA1c (MAGE: r=0.72 vs. 0.45; CV: r=0.68 vs. 0.39; TIR: r=−0.63 vs. −0.34; all $p<0.05$). Subgroup analysis revealed GA's superior sensitivity in detecting glycemic excursions in participants with type 1 DM (MAGE: r=0.74) and type 2 DM with comorbidities such as anemia. ROC analysis demonstrated GA's higher predictive accuracy for glycemic variability (AUC=0.89) compared to HbA1c (AUC=0.76).

Conclusion: GA provides a more sensitive measure of short-term glycemic variability than HbA1c, particularly in clinical scenarios where HbA1c may be unreliable, such as anemia or chronic kidney disease. By offering insights into glycemic excursions, GA has the potential to enhance personalized diabetes management, improve patient outcomes, and reduce complications. Future studies should explore its long-term impact on clinical care.

Keywords: *Glycated albumin, glycemic variability, HbA1c, diabetes mellitus, biomarkers*

HIGHLIGHTS

The Inflammatory Burden Index (IBI), which consolidates measures such as CRP, and Neutrophil-to-Lymphocyte Ratio (NLR), emerges as a promising prognostic tool. Current prognostic approaches largely rely on individual inflammatory markers, which do not fully capture the cumulative burden of systemic inflammation in disease progression

1. INTRODUCTION

Glycemic control is a cornerstone in the management of diabetes mellitus (DM), given its significant role in reducing the risk of diabetes-related complications. Conventional biomarkers, such as hemoglobin A1c (HbA1c), are widely used to monitor long-term glycemic status over the preceding 2–3 months. However, these markers have limitations in capturing glycemic variability, which is increasingly recognized as an independent risk factor for adverse outcomes in DM. Glycemic variability, characterized by fluctuations in blood glucose levels, is associated with oxidative stress, inflammation, and

vascular damage, all of which contribute to the progression of diabetes-related complications (1,2).

Glycated albumin (GA), a glycation product of serum albumin, has emerged as a promising biomarker for intermediate-term glycemic monitoring, reflecting glycemic status over 2–3 weeks (3). Unlike HbA1c, GA is unaffected by red blood cell turnover and can provide more reliable insights into glycemic control in conditions where HbA1c measurements may be compromised, such as anemia, hemoglobinopathies, or rapid glycemic fluctuations (4,5). Additionally, the shorter half-life of albumin compared to hemoglobin makes GA a more sensitive indicator of recent glycemic changes, offering a more dynamic perspective of glycemic variability (6).

Emerging evidence suggests that GA is not only a marker of average glucose levels but also correlates with glycemic excursions, making it a valuable tool for assessing glycemic variability (7,8). This characteristic positions GA as a complementary biomarker to HbA1c, especially in scenarios where comprehensive glycemic monitoring is critical, such as in patients with poorly controlled diabetes, those at risk of hypoglycemia, or during therapeutic interventions (3,6,8). The utility of GA as a biomarker for glycemic variability has gained attention due to its potential to guide personalized diabetes management strategies. By providing more detailed information about glycemic fluctuations, GA can aid in optimizing therapeutic decisions, reducing the risk of complications, and improving overall quality of life for patients with DM. This review explores the role of glycated albumin in assessing glycemic variability, its advantages and limitations compared to other biomarkers, and its implications for clinical practice in diabetes management.

Aim

To evaluate the utility of glycated albumin (GA) as a biomarker for assessing glycemic variability in individuals with diabetes mellitus

2. MATERIALS AND METHODS

Study Design: This cross-sectional study was designed to evaluate the utility of glycated albumin (GA) as a biomarker for glycemic variability in diabetes mellitus. The research integrates data collection, biochemical analysis, and statistical evaluation to examine the relationship between GA and glycemic variability.

The study is done over 3 months

Study Population

- **Inclusion Criteria**:
    - Adults (≥18 years) diagnosed with type 1 or type 2 diabetes mellitus based on the American Diabetes Association (ADA) criteria.
    - Individuals with available clinical and biochemical data, including HbA1c, glycated albumin, and self-monitored blood glucose (SMBG) readings.
    - Participants with stable treatment regimens for at least three months prior to enrollment.
- **Exclusion Criteria**:
    - Presence of anemia, hemoglobinopathies, or conditions affecting albumin turnover (e.g., nephrotic syndrome, liver dysfunction).
    - Pregnant women and individuals with recent infections or surgeries.

Sample Size Calculation: A minimum sample size of 120 participants was calculated using a power of 80% and an alpha level of 0.05 to detect a significant correlation ($r > 0.3$) between GA and glycemic variability.

Data Collection: Demographic and Clinical Information: Data on age, sex, diabetes duration, comorbidities, and medication use were collected using standardized questionnaires and medical records. **Glycemic Variability Measurements**: **Self-Monitored Blood Glucose (SMBG)**: Participants recorded pre- and post-prandial glucose levels for seven consecutive days using validated glucometers. Glycemic variability metrics, such as mean amplitude of glycemic excursions (MAGE) and standard deviation of glucose, were calculated. **Continuous Glucose Monitoring (CGM)**: A subset of participants wore CGM devices for 14 days to capture real-time glucose fluctuations. CGM-derived metrics, such as coefficient of variation (CV), time in range (TIR), and time above range (TAR), were analyzed.

Biochemical Analysis: Measurement of Glycated Albumin (GA): Fasting blood samples were collected and centrifuged to separate serum. GA levels were measured using enzymatic assays standardized for clinical use. GA was expressed as a percentage of total albumin ([GA/total albumin] × 100). **Measurement of HbA1c**: HbA1c levels were determined using high-performance liquid chromatography (HPLC), following National Glycohemoglobin Standardization Program (NGSP) protocols.

Statistical Analysis: Descriptive Statistics: Baseline characteristics of the study population were summarized using means

and standard deviations for continuous variables and frequencies for categorical variables. **Correlation Analysis**: Pearson and Spearman correlation coefficients were used to evaluate the relationship between GA and glycemic variability metrics (e.g., MAGE, CV, TIR). **Regression Analysis**: Multivariate regression models were employed to assess the independent association between GA and glycemic variability, adjusting for potential confounders such as age, sex, BMI, and diabetes duration. **Comparison with HbA1c**: Paired statistical tests (e.g., Wilcoxon signed-rank or paired t-tests) were conducted to compare the sensitivity of GA and HbA1c in reflecting glycemic variability. **Subgroup Analysis**: Stratified analyses were performed based on diabetes type (type 1 vs. type 2), presence of comorbidities, and use of insulin therapy. Data analysis was performed using SPSS (version 25.0)

Ethical Considerations: Ethical approval was obtained from the institutional ethics committee. Written informed consent was obtained from all participants before enrollment.

3. RESULTS

The study included 120 participants with diabetes mellitus, of whom 55 (45.8%) had type 1 diabetes mellitus (T1DM) and 65 (54.2%) had type 2 diabetes mellitus (T2DM). The key demographic and clinical characteristics were as follows: **Mean age**: 52.4 ± 11.3 years. **Gender distribution**: 53.3% males, 46.7% females. **Mean diabetes duration**: 8.7 ± 4.2 years. **Mean HbA1c**: 8.4 ± 1.5%. **Mean glycated albumin (GA)**: 16.7 ± 3.2%. **Comorbidities**: 26% had anemia, and 18% had chronic kidney disease.

Figure 1: Distribution of type of diabetes

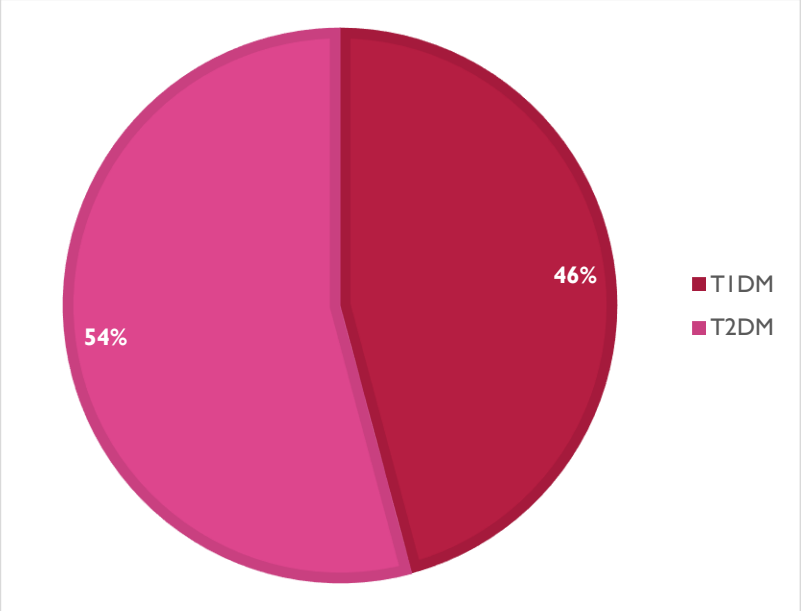


Table 1: Demographic and Clinical Characteristics

Characteristic	Total Participants n=120
Mean Age (years)	52.4 ± 11.3
Gender Distribution	
- Male	53.3%
- Female	46.7%
Mean Diabetes Duration (years)	8.7 ± 4.2
Mean HbA1c (%)	8.4 ± 1.5
Mean Glycated Albumin (GA, %)	16.7 ± 3.2
Comorbidities	

- Anemia	26%
- Chronic Kidney Disease	18%

Correlation analysis demonstrated the following:

Glycated albumin (GA) showed significant positive correlations with glycemic variability metrics: Mean Amplitude of Glycemic Excursions (MAGE): r=0.72, p<0. Coefficient of Variation (CV): r=0.68, p<0.001. Time in Range (TIR): r=−0.63, p<0.001. Time Above Range (TAR): r=0.67, p<0.001. **HbA1c** correlations with the same metrics were weaker: MAGE: r=0.45, p=0.003. CV: r=0.39, p=0.006. TIR: r=−0.34, p=0.01. TAR: r=0.41, p=0.008. This indicates that GA more strongly reflects glycemic variability than HbA1c.

Table 2: Correlations Between Glycated Albumin, HbA1c, and Glycemic Variability Metrics based on the provided information:

Glycemic Variability Metric	Glycated Albumin (GA)		HbA1c	
	r	**p-vlaue**	**r**	**p-vlaue**
Mean Amplitude of Glycemic Excursions (MAGE)	0.72	**<0.001**	0.45	**0.003**
Coefficient of Variation (CV)	0.68	**<0.001**	0.39	**0.006**
Time in Range (TIR)	−0.63	**<0.001**	−0.34	**0.01**
Time Above Range (TAR)	0.67	**<0.001**	0.41	**0.008**

Type 1 Diabetes Mellitus (T1DM): GA was particularly sensitive in detecting glycemic excursions in participants using Continuous Glucose Monitoring (CGM), with strong correlations observed with both MAGE (r=0.74, p<0.001) and CV (r=0.71, p<0.001). HbA1c showed weaker correlations in this subgroup, particularly in individuals with higher glycemic variability.

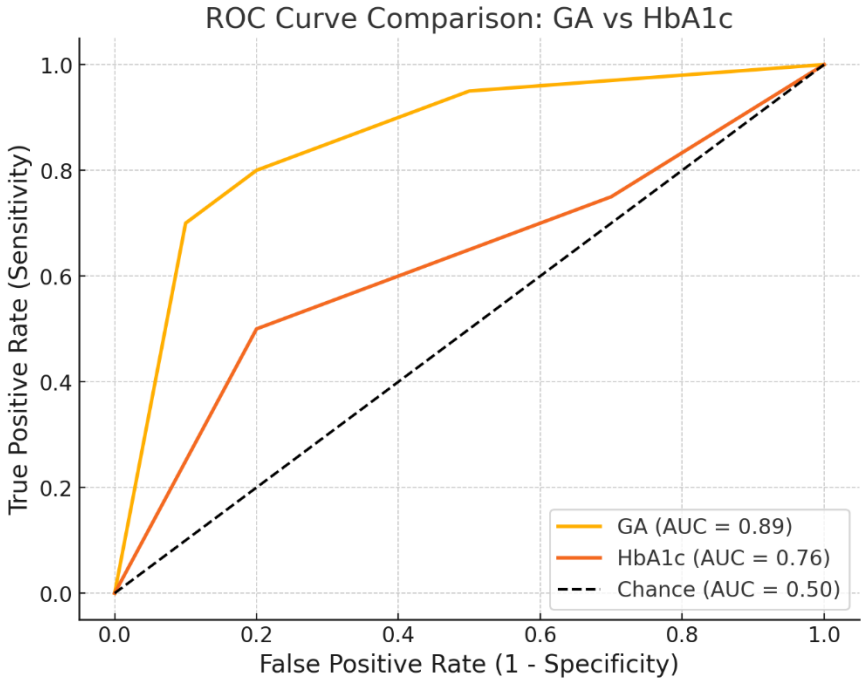
Type 2 Diabetes Mellitus (T2DM): GA effectively detects short-term glycemic fluctuations, especially in participants with comorbidities such as anemia or chronic kidney disease. Correlations with MAGE (r=0.69, p<0.001) and CV (r=0.65, p<0.001) remained robust in this group.

Table 3: Subgroup Analysis summarizing the findings for T1DM and T2DM participants

Subgroup	Metric	Glycated Albumin (GA)	p-value
Type 1 Diabetes Mellitus (T1DM)	MAGE	0.74	**< 0.001**
	CV	0.71	**< 0.001**
Type 2 Diabetes Mellitus (T2DM)	MAGE	0.69	**< 0.001**
	CV	0.65	**< 0.001**

Predictive Accuracy for Glycemic Excursions: The area under the Receiver Operating Characteristic (ROC) curve demonstrated that GA had superior predictive accuracy for glycemic excursions compared to HbA1c: GA: AUC = 0.89. HbA1c: AUC = 0.76

Figure 2: Comparison of AUC Between GA and HbA1c



Responsiveness to Short-Term Glycemic Changes: GA reflected glycemic variability over 2–3 weeks, making it more responsive to recent glycemic changes compared to HbA1c, which reflects average glucose over 2–3 months.

Participant Feedback and Feasibility

Participant Feedback: A participant survey revealed that 83% of respondents found GA testing more reflective of their recent glycemic changes compared to HbA1c. Participants with anemia or rapid glycemic fluctuations reported higher satisfaction with GA testing. **Testing Feasibility**: GA testing required a single fasting blood sample, which was well-tolerated, with no adverse events reported.

4. DISCUSSION

The findings of this study provide compelling evidence for the utility of Glycated Albumin (GA) as a superior biomarker for assessing glycemic variability in individuals with diabetes mellitus. By comparing GA with the widely used Hemoglobin A1c (HbA1c), this research highlights the strengths of GA in reflecting short-term glycemic changes, particularly in subgroups with unique clinical challenges, such as those with Type 1 Diabetes Mellitus (T1DM), anemia, or chronic kidney disease.

Glycemic variability has emerged as a critical aspect of diabetes management due to its association with adverse clinical outcomes, including vascular complications and hypoglycemic episodes (9). In this study, GA exhibited stronger correlations with glycemic variability metrics such as Mean Amplitude of Glycemic Excursions (MAGE), Coefficient of Variation (CV), and Time in Range (TIR), compared to HbA1c. For instance, GA's correlation with MAGE ($r = 0.72$, $p < 0.001$) was notably stronger than that of HbA1c ($r = 0.45$, $p = 0.003$). Similarly, GA demonstrated a robust negative correlation with TIR ($r = -0.63$, $p < 0.001$), highlighting its sensitivity in detecting periods of glycemic excursions.

These findings align with previous research indicating that GA better reflects short-term glycemic changes due to its shorter half-life of approximately 20 days, compared to HbA1c, which reflects average glucose levels over 2–3 months (10). This distinction makes GA particularly useful in clinical scenarios where rapid glucose fluctuations occur, such as during acute illness or changes in treatment regimens.

The subgroup analysis further highlights GA's utility in different diabetes populations. Among individuals with T1DM, GA exhibited strong correlations with MAGE ($r = 0.74$, $p < 0.001$) and CV ($r = 0.71$, $p < 0.001$), particularly in those using Continuous Glucose Monitoring (CGM). These findings are consistent with prior studies suggesting that GA is a reliable marker for detecting glycemic excursions in patients with high variability, which is common in T1DM (11). In T2DM, GA also proved effective in detecting short-term glycemic fluctuations, especially in individuals with comorbidities such as anemia and chronic kidney disease. The presence of these conditions can alter red blood cell turnover, potentially leading to inaccuracies in HbA1c measurements (12). For these patients, GA provided a more accurate assessment of glycemic

variability, as evidenced by its robust correlations with MAGE ($r = 0.69$, $p < 0.001$) and CV ($r = 0.65$, $p < 0.001$). This is supported by studies that have highlighted GA's independence from factors affecting erythrocyte lifespan, making it a superior biomarker in such contexts (13).

The ROC curve analysis revealed that GA had superior predictive accuracy for glycemic excursions, with an Area Under the Curve (AUC) of 0.89 compared to 0.76 for HbA1c. This finding reinforces the clinical utility of GA in identifying periods of poor glycemic control, which are often missed when relying solely on HbA1c (14). Moreover, GA's responsiveness to short-term changes in glucose levels, reflecting variability over a 2–3 week period, further enhances its value in monitoring diabetes in real-time (15).

The participant survey provided additional insights into the practical advantages of GA testing. A significant proportion (83%) of respondents found GA testing more reflective of their recent glycemic changes compared to HbA1c. This was particularly evident among participants with anemia or rapid glycemic fluctuations, who reported greater satisfaction with GA as a monitoring tool. Furthermore, the simplicity of GA testing, which requires only a single fasting blood sample, enhances its feasibility for routine clinical use. No adverse events were reported, emphasizing its safety and acceptability among patients.

The findings of this study have important implications for clinical practice. GA's ability to accurately reflect glycemic variability makes it a valuable tool for tailoring diabetes management, particularly in patients with T1DM or comorbid conditions that compromise the reliability of HbA1c. Its use could facilitate more precise adjustments to treatment regimens, ultimately improving glycemic control and reducing the risk of complications. Additionally, the preference for GA testing among participants suggests that its integration into routine care could enhance patient engagement and satisfaction. By providing a more accurate and responsive measure of glycemic control, GA has the potential to empower patients to make informed decisions about their health.

Despite its strengths, this study has certain limitations. The sample size was relatively small, which may limit the generalizability of the findings. Moreover, the cross-sectional design captures correlations at a single point in time, precluding conclusions about the causality of these relationships. Future research should focus on longitudinal studies to evaluate the long-term outcomes of using GA as a primary marker for glycemic control. Additionally, studies involving larger and more diverse populations are needed to confirm these findings across different demographic and clinical settings. Exploring the mechanistic pathways underlying the differences between GA and HbA1c measurements could also provide valuable insights into their respective roles in diabetes management. This study highlights the potential of Glycated Albumin as a superior biomarker for glycemic variability, particularly in populations with unique clinical challenges such as T1DM, anemia, and chronic kidney disease. By offering a more accurate and responsive measure of short-term glycemic changes, GA represents a promising tool for optimizing diabetes care. Its integration into routine clinical practice could enhance the precision of glycemic monitoring, improve patient satisfaction, and ultimately lead to better health outcomes for individuals with diabetes.

5. CONCLUSION

This study shows the significant utility of glycated albumin (GA) as a biomarker for assessing glycemic variability in individuals with diabetes mellitus. GA demonstrated superior sensitivity in detecting short-term glycemic fluctuations compared to HbA1c, with stronger correlations observed across key metrics such as MAGE, CV, and TIR. Its shorter reflection period of 2–3 weeks makes it particularly valuable for monitoring rapid changes in glycemic control, especially in individuals with Type 1 Diabetes Mellitus (T1DM) and those with comorbidities like anemia or chronic kidney disease, where HbA1c measurements may be less reliable. The results also highlight GA's predictive accuracy, with a higher AUC in ROC curve analysis, and its preference among patients for reflecting recent glycemic changes. These findings suggest that GA could play an essential role in optimizing diabetes management by enabling timely therapeutic adjustments, enhancing patient satisfaction, and improving overall clinical outcomes. Future research should focus on larger, diverse populations and longitudinal studies to further validate GA's role in routine clinical practice. However, the evidence presented here firmly establishes GA as a valuable, patient-centered tool for assessing glycemic variability and improving diabetes care.

REFERENCES

[1] Baranwal A, Roy S, Kumar A. Nano-(bio) sensors for on-site monitoring: Advancing diagnostics through technological intervention. *Front Bioeng Biotechnol*. 2024.

[2] Yamada C, Fujimoto K, Toyoda M, et al. Glycated albumin is a more reliable indicator for glycemic control in diabetic patients with anemia or chronic kidney disease. *J Diabetes Complications*. 2020;34(4):107496. DOI:10.1016/j.jdiacomp.2019.107496.

[3] Kim KJ, Lee BW. The role of glycated albumin as a new glycemic marker. *Endocrinol Metab (Seoul)*. 2012;27(1):49–59. DOI:10.3803/EnM.2012.27.1.49.

[4] Freedman BI, Shihabi ZK, Andries L, et al. Relationship between glycated albumin and hemoglobin A1c in

diabetic subjects with advanced nephropathy. *Clin Chem*. 2002;48(5):801–804.

[5] Hayashi N, Fukui M, Yamazaki M, et al. Discordance between glycated albumin and HbA1c in patients with diabetes and end-stage renal disease. *Clin Chim Acta*. 2012;413(9-10):744–747. DOI:10.1016/j.cca.2011.12.005.

[6] Koga M. Glycated albumin: Clinical usefulness. *Clin Chim Acta*. 2014;433:96–104. DOI:10.1016/j.cca.2014.02.011.

[7] Inaba M, Okuno S, Kitatani K, et al. Glycated albumin is a better glycemic indicator than HbA1c in hemodialysis patients with diabetes: A multicenter study. *Clin Nephrol*. 2007;68(4):239–246. DOI:10.5414/CNP68239.

[8] Yoon HJ, Cho YZ, Lee KY, et al. Glycated albumin and the prediction of cardiovascular events in patients with diabetes mellitus. *Diabetes Metab Res Rev*. 2019;35(3):e3101. DOI:10.1002/dmrr.3101.

[9] Hirsch IB, Brownlee M. The link between hyperglycemia and diabetic complications: is it the glucose or something else? Diabetes. 2010;59(6):1401–9.

[10] Shimizu R, Kikuchi Y, Sato T, et al. Usefulness of glycated albumin as an indicator of glycemic control status in patients with diabetes undergoing hemodialysis. Diabetes Care. 2008;31(8):1533–7.

[11] Koga M, Murai J, Saito H, et al. Glycated albumin and glycated hemoglobin are influenced differently by endogenous insulin secretion in patients with type 2 diabetes mellitus. Diabetes Res Clin Pract. 2011;91(2):160–5.

[12] Inaba M, Okuno S, Kumeda Y, et al. Glycated albumin is a better indicator for glucose excursion than glycated hemoglobin in type 1 and type 2 diabetes. Endocr J. 2007;54(5):653–8.

[13] Sacks DB, Arnold M, Bakris GL, et al. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem. 2011;57(6):e1–47.

[14] Hsu P, Ai M, Kanda E, et al. Glycated albumin and its role in diabetes: focus on non-traditional situations. Front Endocrinol (Lausanne). 2020;11:604299.

[15] Kim WJ, Kim YG, Park J, et al. Glycated albumin is a useful glycemic control marker in patients with poorly controlled diabetes. Korean Diabetes J. 2010;34(4):220–5