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EVALUATION OF GLYCATED ALBUMIN AS AN ADDITIONAL DIAGNOSTIC BIOMARKER OF GLYCEMIC STATUS IN PREDIABETES

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ABSTRACT
Prediabetes is an intermediate metabolic state characterized by impaired glucose homeostasis and increased risk of progression to overt diabetes mellitus and cardiovascular disease. Glycated hemoglobin (HbA1c) is widely used for long-term assessment of glycemic control; however, it may be affected by conditions altering red blood cell turnover, thereby limiting diagnostic accuracy in certain clinical settings. Glycated albumin (GA), reflecting glycemic exposure over approximately 2–3 weeks, may represent a useful supplementary biomarker for early dysglycemia.To evaluate the role of glycated albumin as an additional biomarker of glycemic status in individuals with prediabetes. The study included 200 participants divided into two groups: prediabetes (n=100) and healthy controls (n=100). Serum glycated albumin, fasting blood glucose (FBS), post-lunch blood sugar (PLBS), and HbA1c were analyzed using standardized biochemical methods. Statistical analysis was performed using SPSS version 24.0. A p-value <0.05 was considered statistically significant.Mean glycated albumin levels were significantly elevated in the prediabetes group (18.1 ± 2.7%) compared with healthy controls (13.1 ± 1.9%, p<0.001). HbA1c levels were also significantly increased among individuals with prediabetes (6.11 ± 0.31%) relative to controls (5.12 ± 0.34%, p<0.001). Receiver operating characteristic analysis revealed strong diagnostic discrimination for glycated albumin (AUC=0.944) and HbA1c (AUC=0.981).Glycated albumin is significantly increased in prediabetic individuals and may serve as an additional biomarker for early glycemic abnormalities. It may be particularly useful in situations where HbA1c values are unreliable.

KEYWORDS: Glycated albumin, prediabetes, HbA1c, glycemic status,dysglycemia

INTRODUCTION

Prediabetes is an intermediate metabolic condition between normal glucose regulation and overt diabetes mellitus and is characterized by impaired fasting glucose, impaired glucose tolerance, or mildly elevated glycated hemoglobin levels. Individuals with prediabetes are at an increased risk of developing type 2 diabetes mellitus and cardiovascular complications if early intervention is not undertaken [1,2]. The prevalence of prediabetes has increased considerably worldwide because of sedentary lifestyle, obesity, dietary changes, and urbanization, thereby creating a major public health challenge [3].

Early diagnosis of prediabetes is important because timely lifestyle modifications and therapeutic interventions can delay or prevent disease progression and reduce long-term complications [4]. Conventionally, fasting blood glucose (FBS), postprandial blood glucose, oral glucose tolerance testing, and glycated hemoglobin (HbA1c) are used for assessing glycemic status and diagnosing abnormalities in glucose metabolism [5].

HbA1c is one of the most commonly used biomarkers for long-term glycemic assessment because it reflects average plasma glucose concentrations over approximately 8–12 weeks. Despite its clinical usefulness, HbA1c measurements may be affected by conditions influencing erythrocyte turnover such as anemia, hemoglobinopathies, chronic kidney disease, and recent blood transfusion, thereby reducing its reliability in selected clinical situations [6].

Glycated albumin (GA) has emerged as an alternative marker for glycemic assessment because it reflects average blood glucose levels over a shorter duration of approximately 2–3 weeks due to the shorter half-life of albumin. Since GA formation is independent of hemoglobin metabolism, it may provide a more accurate estimate of glycemic status in patients where HbA1c interpretation becomes unreliable [7].

Several investigators have reported a significant relationship between glycated albumin and glucose metabolism in diabetic and pre-diabetic populations, indicating its usefulness as an additional biomarker for early dysglycemia and glycemic variability [8]. Therefore, the present study was undertaken to evaluate glycated albumin as an additional diagnostic biomarker of glycemic status in individuals with prediabetes and to compare its diagnostic performance with HbA1c.

MATERIALS AND METHODS

Study Design and Setting

A cross-sectional observational study was carried out in the Department of Biochemistry, Chaitanya Deemed to be University, Hyderabad, Telangana, India, between 2023 and 2025 after obtaining institutional ethical committee approval.

Study Population

A total of 200 participants were enrolled and categorized into two groups:

- **Group 1:** Individuals with prediabetes (n=100), aged 32–61 years
- **Group 2:** Apparently healthy controls (n=100), aged 20–57 years

Inclusion Criteria: Individuals diagnosed with prediabetes based on standard glycemic criteria, Individuals not previously diagnosed with overt diabetes mellitus.

Exclusion Criteria: Patients with type 1 diabetes mellitus, renal disorders, acute or chronic renal failure, altered albumin metabolism, chronic liver disease, thyroid dysfunction, nephritic syndrome, severe systemic disease, psychiatric illness, and individuals receiving medications affecting glucose metabolism were excluded.

Sample Collection

Venous blood samples were collected under aseptic precautions following 8–12 hours of fasting. Approximately 5 ml of fasting blood was obtained for fasting blood sugar (FBS), glycated hemoglobin (HbA1c), and glycated albumin analysis. Post-lunch blood sugar (PLBS) estimation was carried out using blood samples collected two hours after lunch. After collection, blood samples were centrifuged for serum separation and analyzed immediately according to standardized laboratory protocols.

Laboratory Methods

- **Fasting blood glucose and post-lunch blood sugar:** GOD-POD method using Mind ray BS-430 auto analyzer
- **HbA1c estimation:** High-performance liquid chromatography (HPLC) using Bio-Rad D10 system
- **Glycated albumin estimation:** Peroxidase enzymatic method using Mind ray BS-430 analyzer

Reference Values

- Fasting blood sugar: 70–100 mg/dL
- Post-lunch blood sugar: 70–140 mg/dL
- HbA1c: <5.7%
- Glycated albumin: 10.8–17.1%

RESULTS

The present study evaluated glycated albumin as an additional diagnostic biomarker of glycemic status in individuals with prediabetes and compared its diagnostic utility with glycated hemoglobin (HbA1c) in healthy controls and prediabetes subjects. A total of 200 participants were included and categorized into two groups: healthy controls (n=100) and prediabetes (n=100). The results demonstrated significant alterations in glycemic biomarkers among prediabetes individuals, indicating impaired glucose regulation and early metabolic abnormalities. Comparative analysis showed elevated levels of glycated albumin and HbA1c in the prediabetes group compared to healthy controls, supporting the potential role of glycated albumin as a supplementary biomarker for early detection and assessment of glycemic status in prediabetes.

Statistical Analysis: Data were analyzed using SPSS version 24.0. Results were expressed as mean ± standard deviation (SD). Student's t-test was employed to compare quantitative variables between groups.Receiver operating characteristic (ROC) analysis was performed to evaluate diagnostic performance. A p-value <0.05 was considered statistically significant.

Table-1: Comparison of Glycemic Parameters Between Controls and Prediabetes

Biomarker	Prediabetes (Group 1)	Controls(Group 2)
FBS (mg/dL)	112.1 ± 8.4	88.4 ± 6.8
PLBS (mg/dL)	155.8 ± 13.3	113.7 ± 14.3
HbA1c (%)	6.11 ± 0.31	5.12 ± 0.34
GA (%)	18.1 ± 2.7	13.1 ± 1.9

Table-1: Shows that all glycemic parameters were significantly higher in the prediabetes group compared to healthy controls. Mean FBS increased from 88.4 ± 6.8 mg/dl in controls to 112.1 ± 8.4 mg/dl in prediabetes ($p<0.001$). Similarly, PLBS was 113.7 ± 14.3 mg/dL vs 155.8 ± 13.3 mg/dL ($p<0.001$). HbA1c showed a significant rise from 5.12 ± 0.34% to 6.11 ± 0.31% ($p<0.001$). Glycated albumin levels were also highly significantly elevated in prediabetes (18.1 ± 2.7%) compared to controls (13.1 ± 1.9%), with $p<0.001$.

Table-2: Mean HbA1c (%) Levels in Healthy Controls and Prediabetes

Group	Mean	SD	p vs Controls
Healthy controls	5.12	0.34	p<0.001***
Prediabetes	6.11	0.31	p<0.001***

Table-2: Describes that the mean Glycated Hemoglobin level was significantly higher in the prediabetes group (6.11 ± 0.31%) compared to healthy controls (5.12 ± 0.34%), indicating altered glucose metabolism. Healthy controls demonstrated normal glycemic status with lower HbA1c values, reflecting stable long-term blood glucose regulation.

The elevated HbA1c observed in prediabetes individuals suggests impaired glucose homeostasis and increased risk of progression to diabetes mellitus. The statistically significant difference ($p<0.001$) indicates that this increase is highly unlikely to be due to chance. These findings support the role of HbA1c as an important marker for identifying early glycemic abnormalities in prediabetes.

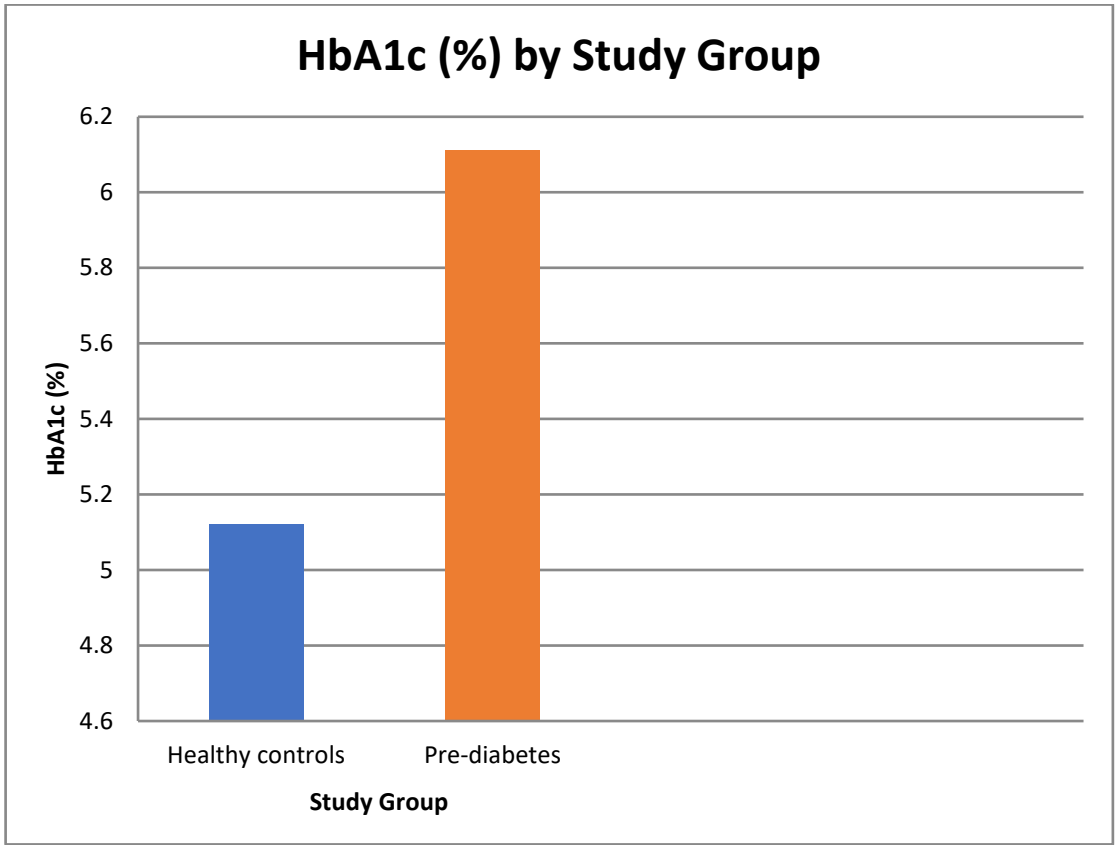

Figure-1: Comparative Analysis of HbA1c (%) in Healthy Controls and Prediabetes

Figure-1: Explains that the mean HbA1c level was higher in the prediabetes group (6.11%) compared to healthy controls (5.12%). This increase indicates impaired glucose regulation and early hyperglycemia in prediabetes individuals. Since HbA1c reflects average blood glucose levels over the past 8–12 weeks, elevated HbA1c suggests an increased risk of progression to Type 2 Diabetes Mellitus (T2DM).

Table-3: Glycated Albumin Levels in Healthy Controls and Prediabetes

Group	Mean	SD	p vs Controls
Healthy controls	13.1	1.88	p<0.001***
Prediabetes	18.14	2.68	p<0.001***

Table-3: The mean biomarker level was significantly higher in the prediabetes group (18.14 ± 2.68) compared to healthy controls (13.1 ± 1.88), with a statistically highly significant difference ($p < 0.001$). These findings indicate an elevation of the biomarker in prediabetes individuals and support its potential role in early glycemic assessment.

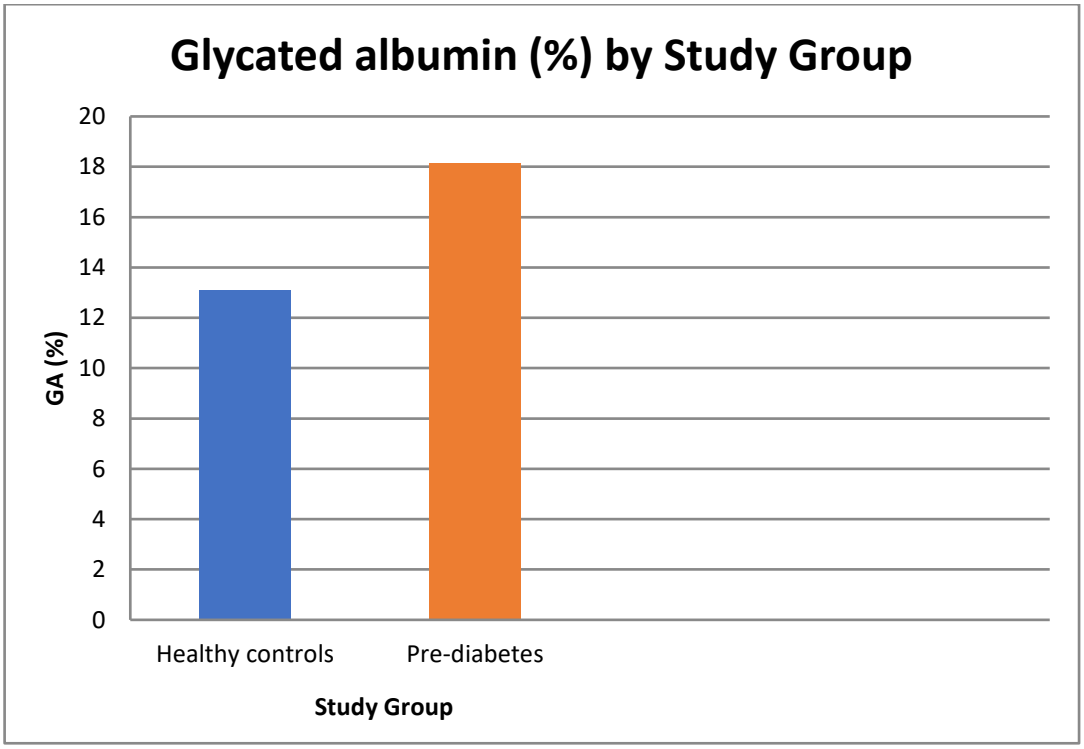

Figure-2: Comparative Analysis of Glycated Albumin (%) Between Healthy Controls and Prediabetes

Figure-2: Explains the comparison of mean glycated albumin (GA) levels between healthy controls and prediabetes individuals. Healthy controls showed a lower mean GA value (13.1%), indicating normal short-term glycemic status, whereas the prediabetes group demonstrated a markedly higher mean GA level (18.14%). This increase suggests impaired glucose metabolism and early glycemic abnormalities in prediabetes individuals.

The higher glycated albumin levels observed in the prediabetes group indicate worsening short-term glycemic control compared to healthy subjects. The findings suggest that glycated albumin may serve as a useful biomarker for identifying early disturbances in glucose regulation and assessing the risk of progression toward diabetes mellitus.

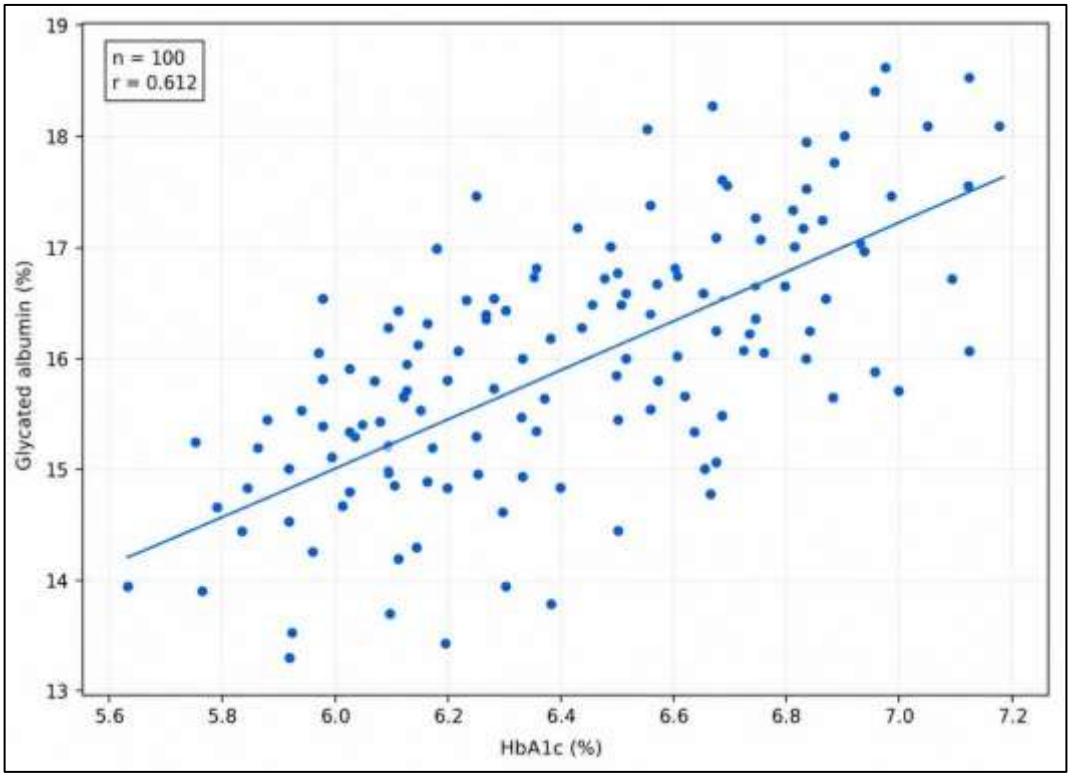

Figure-3: Correlation between HbA1c and Glycated Albumin in Prediabetes

Figure-3: Shows the correlation analysis showed a moderate positive relationship between HbA1c and glycated albumin in prediabetes individuals (r = 0.612), indicating that glycated albumin levels increased as HbA1c levels increased. This suggests that both biomarkers reflect worsening glycemic status and impaired glucose metabolism in prediabetes. Since

HbA1c indicates long-term glucose control and glycated albumin reflects short-term changes, their positive association supports the usefulness of glycated albumin as an additional marker for early glycemic assessment. The statistically significant result ($p < 0.001$) confirms that this relationship is reliable and not due to chance.

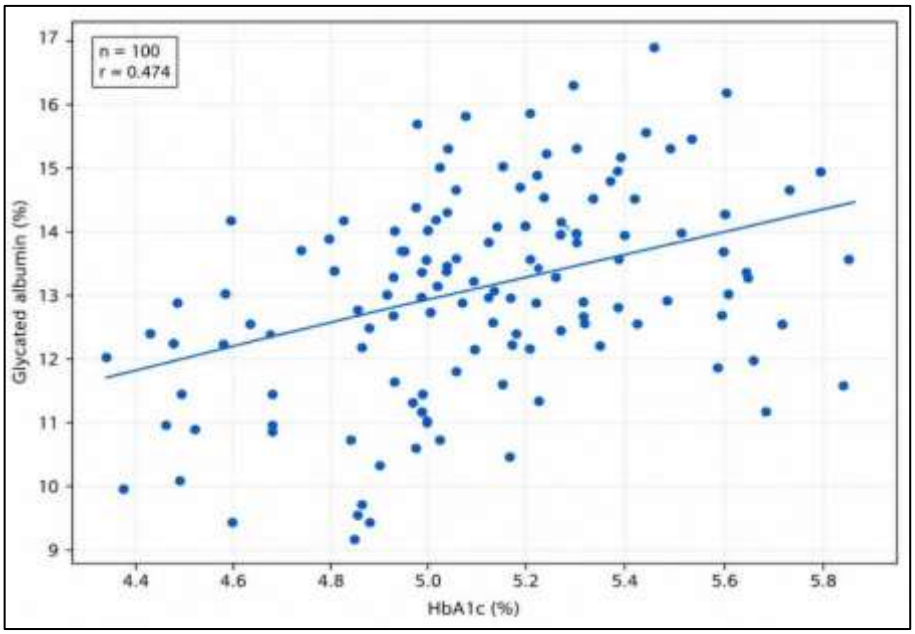

Figure-4: Correlation between HbA1c (%) and Glycated Albumin (%) in Healthy Controls

Figure-4: Showsthe correlation between HbA1c (%) and glycated albumin (%) in healthy control subjects. HbA1c values are represented on the x-axis, while glycated albumin levels are plotted on the y-axis. Each point in the scatter plot represents an individual participant, showing the relationship between long-term glycemic status (HbA1c) and short-term glycemic exposure (glycated albumin).

The scatter distribution demonstrates a positive correlation between HbA1c and glycated albumin, indicating that individuals with relatively higher HbA1c values also tend to have higher glycated albumin levels. Although the participants belong to the healthy control group and exhibit glucose values within the normal physiological range, a proportional increase in glycated albumin with HbA1c can still be observed. The upward trend-line further supports this positive association, suggesting consistency between short-term and long-term glycemic biomarkers even in normoglycemic individuals. This finding indicates that glycated albumin may complement HbA1c in assessing glycemic status and metabolic regulation.

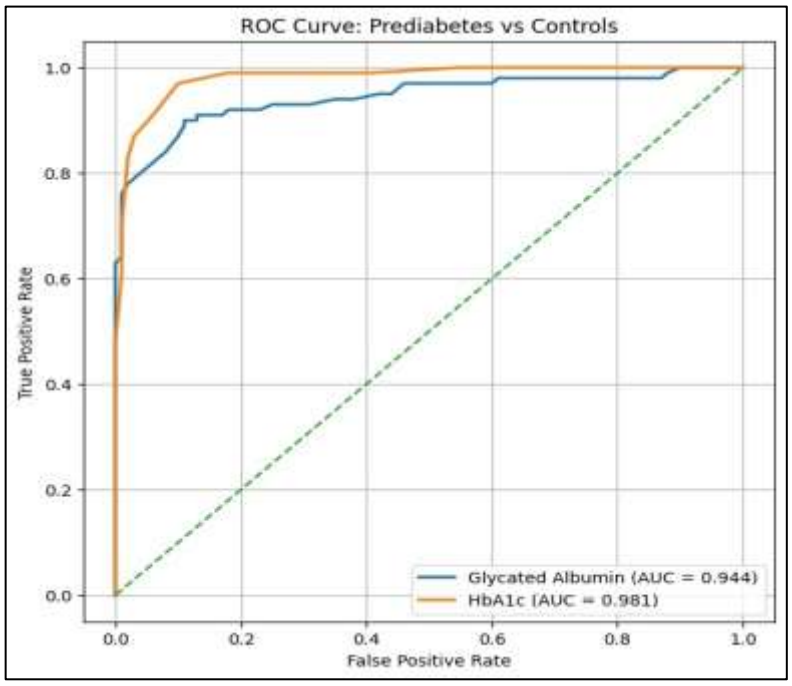

Figure 5: The ROC curve comparing Glycated Albumin and HbA1c for distinguishing Prediabetes from Controls.

Figure-5: Explains the ROC curve demonstrates the diagnostic performance of glycated albumin (GA) and HbA1c in distinguishing prediabetes individuals from healthy controls. A receiver operating characteristic (ROC) curve evaluates

the ability of a biomarker to correctly classify diseased and non-diseased individuals by plotting sensitivity (true positive rate) against 1-specificity (false positive rate). The diagonal dashed green line represents random classification (AUC = 0.5), whereas curves positioned closer to the upper left corner indicate better diagnostic accuracy.
In the present analysis, both glycated albumin and HbA1c showed excellent discriminatory ability, as their curves remain far above the diagonal reference line. Glycated albumin demonstrated an area under the curve (AUC) of 0.944, indicating very high diagnostic performance in differentiating prediabetes individuals from healthy controls. This suggests that glycated albumin has excellent sensitivity and specificity and may be a useful biomarker for detecting early glycemic abnormalities.

DISCUSSION

The present study evaluated glycated albumin as an additional biomarker of glycemic status in individuals with prediabetes and demonstrated significantly elevated glycemic parameters among affected individuals compared with healthy controls. The findings suggest that glycated albumin may have considerable diagnostic utility in the identification of early glycemic abnormalities and may complement conventional biomarkers of glycemic assessment [9].
In the present investigation, fasting blood sugar and post-lunch blood sugar levels were significantly elevated in individuals with prediabetes compared with controls. These observations are in agreement with previous studies that reported worsening glycemic parameters among individuals with impaired glucose metabolism and emphasized the need for early detection to prevent progression toward overt diabetes mellitus [10,11].
HbA1c levels in the present study were significantly increased among prediabetes participants (6.11 ± 0.31%) compared with healthy controls (5.12 ± 0.34%). Similar findings have been documented in earlier investigations demonstrating that HbA1c reflects chronic glucose exposure and remains an important biomarker for long-term glycemic monitoring [12]. However, HbA1c has certain limitations because it is affected by red blood cell lifespan, anemia, chronic renal disease, blood transfusions, and hemoglobin disorders, potentially leading to underestimation or overestimation of glycemic status [13].
A major finding of the present study was the statistically significant elevation of glycated albumin levels among prediabetes individuals (18.14 ± 2.68%) compared with healthy controls (13.10 ± 1.88%, $p<0.001$). This observation is consistent with previous reports demonstrating that glycated albumin reflects recent glycemic fluctuations and may identify dysglycemia earlier than traditional markers [14, 15]. Since albumin has a biological half-life of approximately 2–3 weeks, glycated albumin provides information regarding short-term glucose control and may be particularly useful in clinical situations requiring rapid assessment of glycemic changes [16]. Earlier investigators have reported strong correlations between glycated albumin, fasting blood glucose, postprandial glucose, and insulin resistance markers, supporting its role in glycemic monitoring [17]. Receiver operating characteristic analysis in the present study demonstrated excellent diagnostic performance of both HbA1c and glycated albumin. HbA1c exhibited an AUC of 0.981, whereas glycated albumin demonstrated an AUC of 0.944, indicating strong discriminatory power for identifying prediabetes. Similar studies have reported high sensitivity and specificity of glycated albumin for early dysglycemia detection and glycemic variability assessment [18, 19]. An additional advantage of glycated albumin is its relative independence from hemoglobin metabolism and erythrocyte turnover. Consequently, glycated albumin may provide more reliable glycemic information in patients affected by anemia, hemoglobinopathies, and chronic renal disease where HbA1c estimation may be misleading [20,21].The findings of the present study indicate that glycated albumin should not necessarily replace HbA1c but rather act as an additional biomarker that complements conventional glycemic assessment. Combining HbA1c with glycated albumin may improve diagnostic precision and facilitate early recognition of dysglycemia in high-risk populations [22].
However, the study had certain limitations including a single-center design, relatively limited sample size, and cross-sectional methodology, which prevented long-term follow-up and generalization of findings. Further multicenter prospective studies are needed to establish standardized glycated albumin cut-off values and validate its usefulness in routine clinical practice [23].

CONCLUSION

The present study demonstrated that glycated albumin levels were significantly elevated in individuals with prediabetes compared with healthy controls, indicating its potential usefulness as an additional biomarker for evaluating glycemic status. Significant increases in fasting blood glucose, post-lunch blood sugar, HbA1c, and glycated albumin observed among prediabetes individuals highlight the presence of altered glucose metabolism during the early stages of dysglycemia. Glycated albumin showed strong diagnostic performance in receiver operating characteristic analysis, suggesting excellent discriminatory ability for identifying prediabetes.
Although HbA1c remains an established marker for long-term glycemic monitoring, its interpretation may be influenced by conditions affecting red blood cell lifespan and hemoglobin metabolism. In contrast, glycated albumin reflects short-term glycemic changes and remains relatively unaffected by erythrocyte-related factors, making it a valuable complementary biomarker, particularly in situations where HbA1c measurements may be unreliable. Therefore, glycated albumin may be considered an effective additional diagnostic marker for early detection and monitoring of glycemic abnormalities in prediabetes.

Acknowledgement: I would like to express my sincere gratitude and heartfelt appreciation to my guide and supervisor for their valuable guidance, continuous encouragement,and constant support throughout the completion of this research work. I am also thankful to the management of Chaitanya Deemed to be University, Moinabad, Hyderabad, for their constant support and encouragement in the successful completion of this study.

Conflict of Interest: None

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