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ORIGINAL ARTICLE

Glycated albumin as a surrogate marker for prediabetes: a cross-sectional study

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Abstract

Objective Oral glucose tolerance test (OGTT) and glycated haemoglobin (HbA1c) have many limitations in diagnosing prediabetes. Glycated albumin (GA) estimation can be a potential tool for its early diagnosis. The present study aims to analyze the diagnostic efficacy of GA to identify prediabetes.

Methods Prediabetics (n = 406) and healthy (n = 406) subjects were included. OGTT was used as the diagnostic standard for identifying prediabetes. HbA1c was estimated in a Bio-Rad D-10 analyzer based on the High-Performance Liquid Chromatography (HPLC) method. GA was measured using the enzyme-linked immunosorbent assay (ELISA) technique and was expressed as a percent of total albumin. Total albumin was measured by the modified bromocresol Purple (BCP) dye-binding method in Siemen's autoanalyzer.

Results HbA1c ($5.83 \pm 0.57\%$) and GA ($14.43 \pm 1.92\%$) were significantly higher ($p < 0.05$) in the prediabetics as compared to healthy individuals. Both HbA1c and GA showed a significantly positive correlation with fasting plasma glucose (FPG) and 2-h plasma glucose. However, the correlation was stronger with 2-h plasma glucose for both parameters. GA and HbA1c also showed a significant positive correlation with each other. HbA1c, at 5.7% cut-off, predicted prediabetes with 74% sensitivity and 90% specificity. At the cut-off of 13.5%, GA showed 66% sensitivity and 85% specificity to identify pre-diabetes. The sensitivity of the combined tests was significantly greater than that for HbA1c alone (84% combined versus 74% HbA1c).

Conclusion GA, combined with HbA1c, can be used as a screening test for identifying pre-diabetes. Early diagnosis and interventions could prevent disease progression and limit dreadful complications.

Keywords Prediabetes · Glycated albumin · Diabetes mellitus · Marker · HbA1c

Introduction

Pre-diabetes is a state of hyperglycemia with raised blood glucose levels. It is not high enough to be considered type 2 diabetes mellitus (T2DM) yet, but persons with pre-diabetes are more likely to develop T2DM [1].

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The burden of diabetes continues to rise without effective prevention and control programs and it has been approaching epidemic proportions globally [2]. The prevalence of diabetes is increasing at a rapid rate, such that by 2045, there would be almost 629 million diabetic adults present in the world. Therefore, these alarming levels raise a matter of concern. Therefore, to reduce the chances of diabetes and also the complications associated with it, diabetes should be screened at the stage of prediabetes and an attempt should be made to delay or prevent the transition from prediabetes to diabetes [3, 4].

The Oral glucose tolerance test (OGTT) has been the diagnostic standard since 1979 to evaluate the ability to regulate glucose metabolism. However, this test is associated with many limitations. Within the past 10 years, for making the diagnosis of prediabetes or diabetes, American Diabetes Association (ADA) has adopted HbA1c in its diagnostic criteria. Although, HbA1c is a very simple and inexpensive test

it also has many disadvantages. HbA1c is associated with several limitations including poor specificity in pregnant women,, elderly population, and non-Hispanic blacks along with the risk of over-diagnosis of diabetes mellitus in patients with iron deficiency, RBCs loss, and its related anomalies. Moreover, alcohol consumption, chronic-end stage renal disease, and haemoglobin variants including genetic variants such as haemoglobin S and C traits can lead to an abnormal interpretation of HbA1c levels. These limitations can be overcome by implementing glycated albumin (GA) as a diagnostic marker. GA can demonstrate the glycemic status in a time period of approximately 14–21 days due to the short half-life of GA protein. GA was reported to show9-to-tenfold higher rate of non-enzymatic glycation compared to HbA1c.. Haemoglobin and iron-related anomalies do not affect the glycated albumin and hence can be used as reliable markers in such conditions [5–7]. Therefore, markers such as glycated albumin (GA), fructosamine, etc. could overcome these challenges. [5–7]. Thus, for the patients in whom the measurement of HbA1c may be unreliable, GA could be an attractive alternative option [8]. Therefore, the urgent need arises to introduce a surrogate marker such as GA which may be superior to or complement the existing glycemic control markers [9]. Therefore, we have taken this study to analyze the diagnostic efficacy of GA and correlate it with HbA1c in diagnosing prediabetes (Flowchart).

Materials and methods

Study design

Hospital-based observational, cross-sectional study. The present study was conducted at the HAHC Hospital, Jamia Hamdard University, New Delhi and Maharani Laxmi Bai Medical College, Jhansi, Uttar Pradesh.

Study inclusion criteria

Prediabetic subjects attended the outpatients' department (OPD) of a tertiary hospital of Hakeem Abdul Hameed Centenary Hospital (HAHC) and Maharani Laxmi Bai Medical College, Jhansi aged between 25–60 years, of either sex with a known history of prediabetes (based on the screening recommendation of the American Diabetes Association) along with healthy controls were chosen of the same age and sex-matched population among the escorts coming with patients attending OPD.

Study exclusion criteria

Diabetic patients who wereon anti-diabetic medication, presented albumin level ≤ 3.0 g/dL, anaemic patients, pregnant females, persons with, haemoglobinopathy rheumatic disorder, hepatic cirrhosis, chronic kidney disease, nephrotic syndrome, hypertension, hemodialysis, Cushing syndrome, and untreated thyroid dysfunction were excluded from the study as these disorders are known to influence the GA levels.

Study population

The study population consisted of 812 study subjects including 406 pre-diabetics and 406 healthy in the age group of 25–60 years (Fig. 1). Both males and females fulfilled the OGTT criteria for diagnosing pre-diabetes [10]. 406 healthy volunteers were taken as a comparison arm. The study subjects were matched for age, gender, and socio-economic conditions. Based on the assumption of 80% sensitivity for detecting prediabetes by using HbA1c and GA and 10% relative precision, the sample size estimated was 812. However, because of limited resources and feasibility, a sample size of 406 prediabetics and 406 controls were taken.

OGTT

A standard 75-g OGTT was performed after fasting for at least 8 h. Patients having FPG of 100 mg/dL to 125 mg/dL or 2-h plasma glucose of 140 mg/dL to 199 mg/dL after ingestion of 75 g of oral glucose load were included. The patients satisfied the screening criteria of ADA for diagnosing prediabetes [10]. Glucose concentrations during the OGTT were used as the diagnostic standard for identifying prediabetes.

Analysis of plasma glucose (FPG, 2-h plasma glucose)

3 mL of blood was withdrawn from study subjects under the sterile condition for glucose analysis. Blood was collected in a vacuum tube containing the glycolytic inhibitors potassium oxalate and sodium fluoride. Plasma glucose analysis was done by the hexokinase method using Siemens Healthineers, auto-analyzer Germany [11].

Estimation of HbA1c

For estimation of HbA1c, 2 mL of whole blood was collected in a vacutainer containing ethylene diamine tetraacetic acid (EDTA) as an anticoagulant. HbA1c was estimated by the HPLC method on Bio-Rad D-10 analyzer, Hercules, California, USA, and correlated to the reference assay of the Diabetes Control and Complications Trial (DCCT). For detecting prediabetes by HbA1c, the recommended threshold of 5.7–6.4% was used [7].

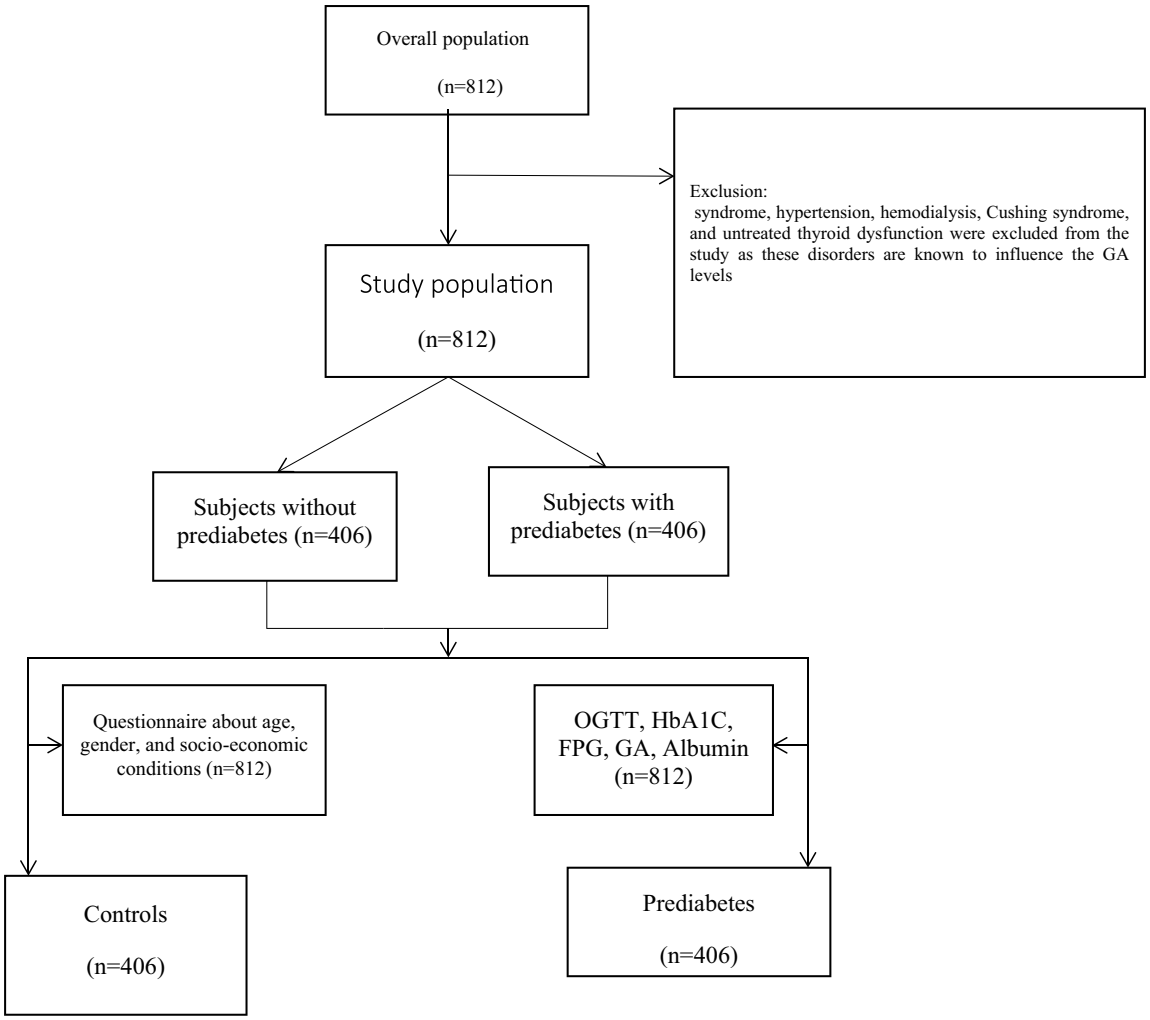

Fig. 1 Flow chart for the Study design

Estimation of albumin

2 mL venous blood was collected in a plain vacutainer under sterile conditions from the study subjects. Sera were separated for estimating albumin. Total albumin was measured by the method which is an adaptation of the bromocresol purple (BCP) dye-binding method in Siemen's autoanalyzer, Germany by using standard reagents and calibrators [12].

Estimation of GA

GA was measured by using an Enzyme-linked immunosorbent assay (ELISA) kit from Krishgen Biosystem, Mumbai, India. The ELISA procedure was performed as per standard protocol provided with the ELISA Kit from Krishgen Biosystem. Briefly, 100µL of each sample, blank (water), and controls (provided within the kit) were added to the appropriate wells followed by incubation for 1 h at 37^0C after covering wells with a plate sealer. Post incubation, the liquid from each well was removed followed by the addition of detection reagent A (100µL) in each well. Post addition, the plate was incubated again for 1 h at 37^0C. Post incubation, the liquid was aspirated followed by washing (3 times/2 min each) with 1 × wash solution (350µL) provided within the kit. Post washing the plate was placed inverted on absorbent pads for removing extra traces of wash solution. 100µL of the detection reagent B was added to each well followed by incubation for 30 min at 37^0C after covering the wells with a plastic sealer. The washing procedure was repeated as performed previously followed by the addition of 90µL substrate to each well and incubation for 15 min at 37^0C in dark. 50µL of stop solution (provided within the kit) was added to each well followed by measuring absorbance at 450 nm immediately. It was expressed as a percent of total albumin which was calculated by the formula [13]:

$$\text{GA (\%)} = 2.9\left\{\left[\text{GA(g/dL)}/\text{Total Albumin (g/dL)}\right] \div 1.4\right\} \times 100$$

Quality checks of all the routine blood assays were routinely performed by participation in internal quality-control programs provided by Bio-Rad (Hercules, CA, USA). The lab was also participating in the external quality control program namely the "CMC External Quality Assurance Scheme" from the Department of Clinical Biochemistry, Vellore, Tamil Nadu, India.

Statistical analysis

It was performed using Statistical Package for the Social Sciences (SPSS), 21st version, International Business Machines (IBM), New York (NY). The Sample size was calculated by Open Epi software, Atlanta, USA. The data were presented as mean ± standard deviation (SD). The statistical significance of the data was determined by Student's t-test. A value of $p < 0.05$ was considered to be statistically significant. Correlation analysis was done to determine the strength and degree of association among study variables. The Receiver operating characteristic (ROC) curve was used to compare the diagnostic value of study parameters and it was used to find the cut-off of parameters in diagnosing prediabetes.

Results

Comparison of OGTT with HbA1c and GA

Based on OGTT results, patients were selected. FPG values were 102.5 ± 11.49 mg/dL in prediabetic subjects as compared to healthy individuals 84.78 ± 9.89 mg/dL. Also, 2-h plasma glucose values were 163.92 ± 21.32 mg/dL in prediabetics as compared to 117.64 ± 14.88 mg/dL in healthy subjects. It was observed that mean HbA1c values were 5.83 ± 0.57% in prediabetes subjects as compared to 4.88 ± 0.60%in healthy subjects. Similarly, it was seen that GA was 14.43 ± 1.92% in prediabetics as compared to 11.15 ± 1.96% in healthy subjects. For all these parameters, the difference was statistically significant ($p < 0.05$) (Table 1).

Correlation among GA and HbA1c with blood plasma values

Pearson's correlation coefficients were used for studying correlation. In prediabetic subjects, a positive and statistically significant correlation was observed between FPG and HbA1c levels (r = 0.656) (p-value = 0.005) as well as between HbA1c and 2-h plasma glucose (r = 0.727) (p-value = 0.005) Correlation was stronger between HbA1c and 2-h plasma glucose as compared to FPG. The results of the present study also showed that the correlation of GA was positive and statistically significant (p-value = 0.01) with both FPG (r = 0.548) and 2-h plasma glucose (r = 0.647) (Table 2). Similar to HbA1c, the correlation of GA with 2-h plasma glucose was stronger as compared to FPG, although HbA1c showed a stronger positive correlation than GA. When GA was compared with HbA1c, a positive and statistically significant (p-value = 0.01) correlation (r = 0.787) was also seen. A scatter plot was made depicting the correlations between HbA1c and FPG**,** HbA1c and 2-h plasma glucose, GA and FPG**,** GA and 2-h plasma, and between HbA1c and GA and found significant**.**

Sensitivity and specificity of GA and HbA1c

ROC curve analysis showed that HbA1c, at a 5.7% cut-off, predicted prediabetes with 74% sensitivity and 90% specificity. Also, when GA was used, at 13.0% cut-off, sensitivity was 72% specificity was 80%, at 14% cut-off, sensitivity was 60%, specificity was 90% and at 13.5%

Table 2 Correlation of HbA1c and GA with FPG and 2-h plasma glucose levels

Parameters	Fasting plasma glucose		2-h plasma glucose	
	r value	R^2 value	*r* value	R^2 value
HbA1c	0.656	0.43	0.727	0.53
GA	0.548	0.30	0.647	0.42

Table 1 Comparison of FPG, 2-h plasma glucose, HbA1c, and GA between controls and prediabetes. Analysis was done using an independent t-test. *$p < 0.05$

Parameters	Control ($n = 406$) Mean ± SD	Pre-diabetes ($n = 406$) Mean ± SD	*p* value
FPG (mg/dL)	84.78 ± 9.89	102.5 ± 11.49 *	0.001
OGTT 2-h plasma glucose (mg/dL)	117.64 ± 14.88	163.92 ± 21.32 *	0.001
HbA1c (%)	4.88 ± 0.60	5.83 ± 0.57 *	0.01
Glycated Albumin (%)	11.15 ± 1.96	14.43 ± 1.92 *	0.02

cut-off, sensitivity was 66%, specificity was 85%, The sensitivity and specificity of both tests combined (HbA1c at 5.7% cut-off and GA at 13.5% cut-off) i.e. patients fulfilling both the criteria were: 84% and 72%, respectively (Table 3). To identify prediabetes, at the cut-off point of GA ≥ 13.5%, good sensitivity, and specificity (66%, 85% respectively) were seen using FPG and/or 2-h plasma glucose as reference values. The sensitivity of HbA1c and GA did not differ much (74% versus 66%, p-value < 0.05). However, the sensitivity of the combined tests was greater than that for HbA1c alone (84% versus 74%, p-value < 0.05). Specifically, 74% people were detected by HbA1c only, 66% people were detected by GA only, and 84% people were detected by both HbA1c and GA. Therefore, there was a substantial increase in the number of subjects because of the use of GA. However, the increase in sensitivity for the combined tests was associated with a decrease in specificity. The specificities for HbA1c (at cut-off 5.7%) and GA (at cut-off 13.5%) independently and in combination were: 90%, 85%, and 72% respectively. The areas under the ROC curves (AUC) for the identification of prediabetes for HbA1c and GA were (AUC: 0.864 for HbA1c, AUC: 0.831 for GA) respectively. General clinical characteristics of recruited study subjects are mentioned in Table 4. Significant changes were observed between HbA1c (%), FPG (mg/dL), PPG (mg/dL) and GA (%) in control and prediabetes study participants ($p < 0.001$).

Table 3 Sensitivity and specificity of HbA1c, GA, and both tests combined in predicting prediabetes

Diagnostic Parameters	Sensitivity	Specificity
HbA1c (cut-off 5.7%)	74%	90%
GA (cut-off 13.0%)	72%	80%
GA (cut-off 13.5%)	66%	85%
GA (cut-off 14.0%)	60%	90%
HbA1c (5.7%) + GA (13.5%) combined	84%	72%

Table 4 General characteristics of study subjects

	Control	Pre-diabetes
Total, *n* (%)	406 (50)	406 (50)
Men, *n* (%)	286 (49)	302 (51)
Women, *n* (%)	120 (54)	104 (46)
Age (years)	43.1 ± 6.6	42.9 ± 6.3
BMI (kg/m^2)	24.1 ± 3.6	25.9 ± 2.9
HbA1c (%)	4.88 ± 0.60	5.83 ± 0.57
FPG (mg/dL)	84.78 ± 9.89	102.5 ± 11.49
PPG (mg/dL)	117.64 ± 14.88	163.92 ± 21.32
GA (%)	11.15 ± 1.96	14.43 ± 1.92

BMI, body mass index; *FBG*, fasting blood glucose; *PPG*, Postprandial blood glucose; *GA*, Glycated Albumin. Continuous variables are presented as mean ± SD. Categorical variables are presented as number and percentage. Continuous variables were compared using student's t test

Discussion

OGTT has been the diagnostic standard for diagnosing diabetes for ages with associated limitations like more consumption of time, lack of reproducibility, and difficulty in taking samples. HbA1c, GA, and fructosamine can overcome these challenges. [5–7]. Albumin, being an abundant plasma protein readily participates in the non-enzymatic glycation process with a rate of 9-to 10 times higher than that of haemoglobin [14–17]. Recently, published studies demonstrated the utility of GA in the diagnosis of diabetes, renal, cerebral, and cardio-metabolic disorders [18, 19]. GA exhibits a broader fluctuation, thus rapid changes in blood glucose can be detected earlier [20]. Moreover, studies have suggested that GA is an intermediate-term glycation index for determining short-term glycemic changes over 2 weeks due to its lower half-life of 14–21 days [21]. HbA1c levels are also affected in conditions like reticulocytosis, transfusion, hyperbilirubinemia, hypertriglyceridemia, administration of drugs like dapsone, ribavirin, and uremia [20–28]. GA is a good biomarker in conditions potentially associated with an alteration of HbA1C, such as pregnancy and anaemia [29–31]. Therefore, because of these advantages of GA over HbA1c, GA could emerge as a possible marker and studies have suggested that it would represent an excellent index for monitoring short-term variations of glycemic control, pregnancy, liver diseases, chronic kidney disease undergoing dialysis, anaemia, haemoglobinopathies, and those receiving blood transfusions and microvascular complications of diabetes [32–35]. Our findings were supported by earlier studies which suggest that GA levels were raised in prediabetes [9, 36].

In the present study, prediabetic subjects showed a significant positive and stronger correlation between FPG and HbA1c levels and between HbA1c and 2-h plasma glucose. HbA1c gives an idea of overall glucose exposure which incorporates both fasting and postprandial hyperglycemia [37]. The present study also revealed an interesting finding that GA significantly and positively correlated strongly with 2-h plasma glucose as compared to FPG. Studies have shown that an independent variable for predicting cardiovascular complications and mortality in diabetes is 2-h plasma glucose, this is not the case with FPG, and therefore detection of these glucose variations is very important. Therefore, GA may reflect postprandial glucose levels and glycemic

variability more adequately than HbA1c [21, 38, 39]. Furthermore, it has been detected in our study that the correlation between GA and HbA1c was statistically significant and positive. This finding was supported by other studies which also showed a positive correlation between GA and HbA1c [40, 41]. According to a study conducted in Japan by Furusyo et al. in 2011, GA at a cut-off point of ≥ 15.5% identifies DM with both sensitivity and specificity of 83.3% [42]. Hwang et al. described a cut-off point of GA ≥ 14.3% for identifying prediabetes (sensitivity: 77.5%; specificity: 89.9%) in Korea [43]. Another study, conducted in Taiwan by Hsu et al., reported a cut-off point of 14.9% for diagnosing DM with a sensitivity of 78.5% and specificity of 80% [41]. A study conducted by Sumner et al. on 236 African Americans reported a cut-off point of GA ≥ 13.77% for diagnosing prediabetes. In the present study, we found that when HbA1c was used as a single diagnostic test to identify prediabetes, at a cut-off of 5.7%, sensitivity was 74%**,** and specificity was 90%. The cut-off point of GA ≥ 13.5% presented a good sensitivity and specificity (66%, 85% respectively) to identify prediabetes using FPG and/or 2-h plasma glucose as reference tests [6]. However, in the present study, it has been observed that diagnostic sensitivity might improve if HbA1c is combined with GA. After combining HbA1c with GA (at a cut-off of 13.5%), it was seen that sensitivity increased to 84% (combined test) from 74% (HbA1c) but the specificity decreased (HbA1c: 90%, versus combined test:72%) as seen in other studies also [9, 27]. In one of the previously published study it was also reported that GA had low sensitivity and higher specificity as it with complete agreement with our observations. The reasons behind the lower sensitivity are contributed by several factors including ethnicity that is independent of glycemia.

GA can be a better diagnostic and prognostic biomarker for the diagnosis of diabetes and its associated complications because it is associated with several advantages over glycosylated haemoglobin. In an anaemic condition, where there is a disorder of red blood cells, the rate of glycated in haemoglobin protein gets severely affected, thereby giving a false reading of glycemic index. Because GA is not affected by the red cell turnover and therefore reflects more accurate information. Similarly, in cases of iron deficiency with anaemia and without anaemia, GA can be an accurate marker compared to HbA1c [21]. Studies also support that GA is a good predictor marker of glycemic control in monitoring diabetes during pregnancy. A published study showed that the estimated glomerular filtration rate (GFR) in patients with CKD showed an inverse association with HbA1c rather than GA [44]. GA measurement can also be advantageous in conditions like nephrotic syndrome, liver, and thyroid disease [45]. Moreover, GA can predict accurately in conditions like HIV, tuberculosis, and other conditions where medication of nucleoside reverses transcriptase inhibitors were given [46]. GA assessment is also not affected by ethnicity and BMI as suggested by the previous literature [47, 48].

The finding that GA when combined with HbA1c could improve diagnostic sensitivity by detecting more cases of prediabetes would be very beneficial. Therefore, at this stage, preventive measures could be implemented and progression to diabetes could be curbed. Limitations of the present study include small sample size, cross-sectional study design, single centric study, and many unknown confounding factors that may affect the result. The strengths of this study were, age and sex-matched, standard techniques were used to measure study variables, recruited characterized study population. Further follow-up studies may be conducted on large scale to validate the results of the present study which might help in early patient management.

Conclusion

The need of the hour is to introduce a surrogate maker for detecting prediabetes so that early intervention could be done which could slow down the burden of disease and maximize health care resources. GA could be more than the missing link in controlling the diabetic epidemic. Also, additional comparison studies are to be carried out to ascertain its clinical utility. It is of utmost importance to curb progression to dysglycemic states when βcell function is still relatively more optimal and responsive to lifestyle modifications. Outstanding research would be to gain unequivocal evidence that GA could be a reasonable alternative and/or adjuvant to HbA1c in the diagnosis of prediabetes and hence diabetes.

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Data availability The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation, to any qualified researcher.

Declarations

Conflict of interest The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethical approval Informed and written consent from prediabetics as well as healthy subjects was obtained before taking blood samples. An Ethical clearance certificate was obtained from the institutional ethical committee before the conduction of the study (No. JHIEC 08/2018). The present study followed the principles of the declaration of Helsinki.

References

1. Sacks DB, Arnold M, Bakris GL, Bruns DE, Horvath AR, Kirkman MS. Guidelines and Recommendations for Laboratory Analysis in the Diagnosis and Management of Diabetes Mellitus. Diabetes Care. 2011;34:61–99.
2. Atlas D. International diabetes federation. IDF Diabetes Atlas, 7th edn. Brussels, Belgium: International Diabetes Federation. 2015;33(2).
3. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, Malanda B. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract. 2018;138:271–81.
4. Balk EM, Earley A, Raman G, Avendano EA, Pittas AG, Remington PL. Combined diet and physical activity promotion programs to prevent type 2 diabetes among persons at increased risk: A systematic review for the Community Preventive Services Task Force. Ann Intern Med. 2015;163:437–51.
5. Li HY, Ma WY, Wei JN, Lin MS, Shih SR, Hung CS. Hemoglobin A1c for the diagnosis of diabetes: To replace or to guide oral glucose tolerance tests. J Diabetes Investig. 2012;3:259–65.
6. Diabetes Association of The Republic of China Taiwan. Executive summary of the DAROC clinical practice guidelines for diabetes care- 2018. J Formos Med Assoc. 2020;119(2):577–86. https://doi.org/10.1016/j.jfma.2019.02.016.
7. Summary of revisions for the 2010 Clinical practice recommendations. Diabetes Care. 2010;33 Suppl 1(Suppl 1):S3. https://doi.org/10.2337/dc10-S003.
8. Ueda Y, Matsumoto H. Recent topics in chemical and clinical research on glycated albumin. J Diabetes Sci Technol. 2015;9:177–82.
9. Sumner AE, Duong MT, Aldana PC, Ricks M, Tulloch-Reid MK, Lozier JN, Chung ST, Sacks DB. A1C Combined With Glycated Albumin Improves Detection of Prediabetes in Africans: The Africans in America Study. Diabetes Care. 2016;39(2):271–7. https://doi.org/10.2337/dc15-1699.
10. American Diabetes Association. 2. Classification and diagnosis of diabetes: Standards of medical care in diabetes-2018. Diabetes Care. 2018;41(Suppl 1):S13–27. https://doi.org/10.2337/dc18-S002.
11. Jagannathan R, Weber MB, Anjana RM, Ranjani H, Staimez LR, Ali MK, et al. Clinical utility of 30-min plasma glucose for prediction of type 2 diabetes among people with prediabetes: Ancillary analysis of the diabetes community lifestyle improvement program. Diabetes Res Clin Pract. 2020;161:108075.
12. Louderback A, Mealey EH, Taylor NA. A new dye-binding technic using bromocresol purple for determination of albumin in serum. Clin Chem. 1968;14:793–4.
13. Summer CM. Glycated Albumin Identifies Prediabetes Not Detected by Hemoglobin A1c: The Africans in America Study. Clin Chem. 2016;62:1524–32.
14. Raghav A, Ahmad J. Glycated albumin in chronic kidney disease: Pathophysiologic connections. Diabetes Metab Syndr. 2018;12(3):463–8.
15. Raghav A, Ahmad J, Noor S, Alam K, Mishra BK. Glycated albumin and the risk of chronic kidney disease in subjects with Type 2 Diabetes: A study in North Indian Population. Diabetes Metab Syndr. 2018;12(3):381–5.
16. Raghav A, Ahmad J, Alam K. Preferential recognition of advanced glycation end products by serum antibodies and low-grade systemic inflammation in diabetes mellitus and its complications. Int J Biol Macromol. 2018;118(Pt B):1884–91.
17. Raghav A, Ahmad J, Alam K. Nonenzymatic glycosylation of human serum albumin and its effect on antibodies profile in patients with diabetes mellitus. PLoS ONE. 2017;12(5):e0176970.
18. Giglio RV, Lo Sasso B, Agnello L, Bivona G, Maniscalco R, Ligi D, Mannello F, Ciaccio M. Recent updates and advances in the use of glycated albumin for the diagnosis and monitoring of diabetes and renal, cerebro- and cardio-metabolic diseases. J Clin Med. 2020;9(11):3634. https://doi.org/10.3390/jcm9113634.
19. Bellia C, Zaninotto M, Cosma C, Agnello L, Bivona G, Marinova M, Lo Sasso B, Plebani M, Ciaccio M. Clinical usefulness of Glycated Albumin in the diagnosis of diabetes: Results from an Italian study. Clin Biochem. 2018;54:68–72.
20. Rondeau P, Bourdon E. The glycation of albumin: structural and functional impacts. Biochimie. 2011;93:645–58.
21 Koga M, Kaayama S. Clinical impact of glycated albumin as another glycemic control marker. Endocr J. 2010;57:751–62.
22. WHO, Use of glycated hemoglobin (HbA1c) in the diagnosis of diabetes mellitus: abbreviated report of a WHO consultation. Available at: http://www.who.int/cardiovascular_diseases/report-hba1c_2011_edited.pdf, Accessed on 28th April 2021.
23. Uzu T, Hatta T, Deji N, Izumiya T, Ueda H, Miyazawa I, et al. Target for glycemic control in type 2 diabetic patients on hemodialysis: effects of anemia and erythropoietin injection on hemoglobinA(1c). Ther Apher Dial. 2009;13:89–94.
24. Spencer DH, Grossman BJ, Scott MG. Red cell transfusion decreases hemoglobin A1c in patients with diabetes. Clin Chem. 2011;57:344–6.
25. Welsh KJ, Kirkman MS, Sacks DB. Role of glycated proteins in the diagnosis and management of diabetes: research gaps and future directions. Diabetes Care. 2016;39:1299–306.
26. Kim C, Bullard KM, Herman WH. Association between iron deficiency and A1c Levels among adults without diabetes in the National Health and Nutrition Examination Survey. Diabetes Care. 2013;33:780–5.
27. Suzuki S, Koga M, Amamiya S, Nakao A, Wada K, Okuhara K. Glycated albumin but not HbA1c reflects glycaemic control in patients with neonatal diabetes mellitus. Diabetologia. 2015;54:2247–53.
28. Albright ES, Ovalle F, Bell DS. Artificially low hemoglobin A1c caused by use of dapsone. Endocr Pract. 2002;8:370–2.
29. Agnello L, Lo Sasso B, Scazzone C, Giglio RV, Gambino CM, Bivona G, Pantuso M, Ciaccio AM, Venezia R, Vidali M, Ciaccio M. Preliminary reference intervals of Glycated Albumin in healthy Caucasian pregnant women. Clin Chim Acta. 2021;519:227–30.
30. Zendjabil M. Glycated albumin. Clin Chim Acta. 2020;502:240–4.
31. Bellia C, Cosma C, Lo Sasso B, Bivona G, Agnello L, Zaninotto M, Ciaccio M. Glycated albumin as a glycaemic marker in patients with advanced chronic kidney disease and anaemia: a preliminary report. Scand J Clin Lab Invest. 2019;79(5):293–7.
32. Yoshiuchi K, Matsuhisa M, Katakami N. Glycated albumin is a better indicator for glucose excursion than glycated hemoglobin in type 1 and type 2. Endocr J. 2008;55:503–7.
33. Correa Freitas PA, Ehlert LR, Camarg JL. Glycated albumin: a potential biomarker in diabetes. Arch Endocrinol Metab. 2017;61:3.
34. Sany D, Elshahawy Y, Anwar W. Glycated albumin versus glycated hemoglobin as a glycemic indicator in hemodialysis patients with diabetes mellitus: variables that influence. Saudi J Kidney Dis Transpl. 2013;24:260–73.

35. Raghav A, Ahmad J. Glycated serum albumin: a potential disease marker and an intermediate index of diabetes control. Diabetes Metab Syndr. 2014;8:245–51.
36. Arasteh A, Farahi S, Habibi-Rezaei M, Moosavi-Movahedi AA. Glycated albumin: an overview of the In Vitro models of an In Vivo potential disease marker. J Diabetes Metab Disord. 2014;13:49.
37. Dorcely B, Katz K, Jagannathan R. Novel biomarkers for prediabetes, diabetes and associated complications. Diabetes Metab Syndr Obes Targets Ther. 2017;10:345–61.
38. Rosediani M, Azidah AK, Mafauzy M. Correlation between Fasting Plasma Glucose, Post Prandial Glucose and Glycated Hemoglobin andFructosamine. Med J Malaysia. 2016;61:67–71.
39. Koga M. Glycated albumin: clinical usefulness. Clin Chim Acta. 2014;433:96–104.
40. Paroni R, Ceriotti F, Galanello R, Battista Leoni G, Panico A, Scurati A. Performance characteristics and clinical utility of an enzymatic method for the measurement of glycated albumin in plasma. Clin Biochem. 2007;40:1398–405.
41 Hsu P, Ai M, Kanda E, Yu NC, Chen HL, Chen HW. A comparison of glycated albumin and glycosylated hemoglobin for the screening of diabetes mellitus in Taiwan. Atherosclerosis. 2015;242:327–33.
42. Furusyo N, Ali KTM, Otokozawa S, Kohzuma T, Ikezaki H, Schaefer EJ, et al. Utility of glycated albumin for the diagnosis of diabetes mellitus in a Japanese population study: results from the Kyushu and Okinawa Population Study (KOPS). Diabetologia. 2011;54:3028–36.
43. Hwang YC, Jung CH, Ahn HY, Jeon WS, Jin SM, Woo JT, Cha BS, Kim JH, Park CY, Lee BW. Optimal glycated albumin cutoff value to diagnose diabetes in Korean adults: a retrospective study based on the oral glucose tolerance test. Clin Chim Acta. 2014;437:1–5. https://doi.org/10.1016/j.cca.2014.06.027.
44. Freedman BI, Shihabi ZK, Andries L, Cardona CY, Peacock TP, Byers JR, et al. Relationship between assays of glycemia in diabetic subjects with advanced chronic kidney disease. Am J Nephrol. 2010;31:375–9.
45. Danese E, Montagnana M, Nouvenne A, Lippi G. Advantages and pitfalls of fructosamine and glycated albumin in the diagnosis and treatment of diabetes. J Diabetes Sci Technol. 2015;9:169–76.
46. Duran L, Rodriguez C, Drozd D, Nance RM, Delaney JA, Burkholder G, Mugavero MJ, Willig JH, Warriner AH, Crane PK, Atkinson BE, Harrington RD, Dhanireddy S, Saag MS, Kitahata MM, Crane HM. Fructosamine and hemoglobin A1c correlations in HIV-infected adults in routine clinical care: impact of anemia and albumin levels. AIDS Res Treat. 2015;2015:478750. https://doi.org/10.1155/2015/478750.
47. Koga M, Matsumoto S, Saito H, Kasayama S. Body mass index negatively influences glycated albumin, but not glycated hemoglobin, in diabetic patients. Endocr J. 2006;53:387–91.
48. Chume FC, Kieling MH, Correa Freitas PA, Cavagnolli G, Camargo JL. Glycated albumin as a diagnostic tool in diabetes: An alternative or an additional test? PLoS One. 2019;14(12):e0227065.