

COMPARISON OF GLYCATED ALBUMIN LEVELS AMONG WOMEN WITH GESTATIONAL DIABETES MELLITUS AND WOMEN WITHOUT GESTATIONAL DIABETES MELLITUS

Abstract

Background: Gestational diabetes mellitus is a common endocrine disorder in pregnancy and a known cause of maternal and fetal morbidities and mortalities. The diagnosis of gestational diabetes mellitus is made using the oral glucose tolerance test. Conducting the oral glucose tolerance test requires patient preparation, drinking glucose solution, is time-consuming and multiple samples are collected. Meanwhile, glycated albumin does not require the patient to be prepared, no glucose solution is taken and a single sample is collected. Glycated albumin is affected by ethnicity and black Americans have higher glycated albumin levels than Caucasians. This study determined the use of glycated albumin in diagnosing gestational diabetes mellitus among pregnant women.

Materials and method: The study was a prospective study of 200 pregnant women at the University of Port Harcourt Teaching Hospital. The diagnosis of GDM was based on the World Health Organization 2013 diagnostic criteria. The diagnostic cut-off of glycated albumin was determined using the receiver operator characteristic (ROC) curve. The comparison of means was done using the Student's T-test.

Results: The area under the receiver operator characteristic curve for glycated albumin was 0.8 and the optimal cut-off value of glycated albumin in the diagnosis of gestational diabetes mellitus was 19%. Glycated albumin was significantly elevated in women with gestational diabetes mellitus compared to women without gestational diabetes mellitus at $P < 0.001$.

Conclusion: Glycated albumin can be used in the diagnosis of gestational diabetes mellitus.

Keywords

Glycated albumin, Gestational diabetes mellitus, Oral glucose tolerance test, University of Port Harcourt Teaching Hospital.

1. Introduction

Gestational diabetes mellitus (GDM) is a common pregnancy complication seen in about 5% of all pregnancies [1]. Gestational diabetes mellitus is varying degrees of glucose intolerance first diagnosed in pregnancy [2,3]. There is a variation in the prevalence of GDM in different regions of the world. The prevalence of GDM in Europe is 5.4% [4] while the prevalence in the Middle East and Asian region is 11.5% [5]. The prevalence in the Sub-Saharan Africa region is 14.3% [6]. The prevalence of GDM in Port Harcourt, southern Nigeria, is 10.5% [7].

Gestational diabetes puts the baby at risk of prematurity, growth restriction, fetal macrosomia, intra-uterine fetal death, shoulder dystocia, instrumental vaginal delivery, birth injuries, and stillbirth [8,9]. Neonatal complications may include electrolyte imbalance, hyperglycemia, hypoglycemia, hyperbilirubinemia, jaundice, respiratory distress syndrome, and early neonatal death [8,10]. The child is at risk of obesity, type II diabetes mellitus, and cardiovascular disease later in life [11,12]. The mother may develop hypertension, pre-eclampsia, preterm rupture of membranes, perineal injuries at delivery, and an increased risk of cesarean section [6,10]. Obesity and type II diabetes mellitus may also occur after puerperium [12,13].

Gestational diabetes mellitus occurs when the body fails to regulate the hyperglycemic effects of hormones produced during pregnancy [13]. Most women with GDM may not have any symptoms or risk factors, [14] therefore, the World Health Organization recommends universal screening for GDM using OGTT [15]. However, screening women based on risk factors is the practice in some countries. For example, the National Institute for Health and Care Excellence recommends a selective screening for GDM for women with the following risk factors: a history of a first-degree relation with diabetes mellitus, Body mass index $\geq 30 \text{ kg/m}^2$, a history of delivery of a baby weighing $\geq 4.5 \text{ kg}$, belongs to an ethnicity with a high rate of diabetes mellitus [16]. Maternal age, previous unexplained stillbirth, and previous GDM are other risk factors for GDM [2,3].

The diagnosis of GDM is usually made following a one-hour 75g oral glucose tolerance test (OGTT): fasting plasma glucose (FPG) value of ≥ 5.1 mmol/L but ≤ 6.9 mmol/L, one-hour OGTT value of ≥ 10.0 mmol/L, or two-hour OGTT value of ≥ 8.5 mmol/L but ≤ 11.1 mmol/L [15,17]. The drawbacks of OGTT are patient preparation before the test, drinking of a glucose solution, and multiple sample collections. The patient preparation requires the woman to have her normal diet for three days and to have an overnight fast of 8 to 15 hours [18,19]. Some health workers don't know how to prepare women for the procedure and some women are not motivated to fast [18,20]. Oral Glucose Tolerance Test may also be affected by exercise, physical stress, acute illness, and medication. [18,19]. Nausea and vomiting, a side effect of drinking the glucose solution during OGTT, have been indicated as a reason some women withdraw from the test [21]. The cumbersome nature of the OGTT procedure has led to the search for other methods of screening and diagnosis of GDM. Glycemic markers that have been evaluated for diagnosis of GDM are glycated hemoglobin, glycated albumin, B-cell activating factor, tumor necrosis factor, platelet-activating factor, and methylglyoxal [22,23].

Glycated albumin is produced by a non-enzymatic reaction between albumin and reducing sugars [24]. Albumin has a high content of glycine and lysine which makes it susceptible to a non-enzymatic reaction with reducing sugars in plasma [24,25]. Since albumin is an abundant extracellular plasma protein, it is glycated 9 to 10 times more than other proteins [22,24]. The amount of glucose attached to the albumin during this reaction is dependent on the degree and duration of hyperglycemia, therefore, serum glycated albumin is a reflection of the degree and duration of hyperglycemia for a period of 14 to 20 days [22,26]. Fasting is not required before the measurement of glycated albumin, it is not affected by abnormal hemoglobin metabolism, insulin use, and renal failure [25,27]. Disease conditions that affect albumin metabolism, age, ethnicity, and body mass index may influence the level of glycated albumin [24,28]. Most studies on glycated albumin use in the diagnosis of hyperglycemic states were done among Asians and Caucasians [29,30], however, studies have shown that blacks have higher glycated albumin levels than Caucasians [28].

2. Objectives

The objective of this study was to determine the diagnostic cut-off of glycated albumin in the diagnosis of GDM. It also compared the levels of glycated albumin among women with GDM and women without GDM.

3. Methodology

This was a prospective cross-sectional study of pregnant women between 24 to 28 weeks of gestation, conducted at the antenatal clinic of the University of Port Harcourt Teaching Hospital from February 2021 to March 2022. The hospital is a referral center for Rivers State Nigeria and neighboring states. Exclusion criteria: 1.) Women with diabetes mellitus, chronic liver disease, or chronic kidney disease. 2.) Women with unsure last menstrual period and no early ultrasound scan determination of their gestational age. The simple random sampling technique was used to select 200 participants. The participants were told to have their usual diet for at least three days, and they fasted for 8 to 16 hours from the previous day before blood sample collection the next morning. The blood samples for glucose analysis were collected into fluoride oxalate bottles and samples for glycated albumin were collected into ethylenediamine tetra-acetic acid bottles. The plasma glucose was analyzed with the glucose oxidase method and the glycated albumin was analyzed with the Enzyme-Linked Immunosorbent Assay technique. The diagnosis of GDM was based on the WHO 2013 diagnostic criteria. The analysis of the data was done using the Statistical Product and Services Solutions version 25.0. The diagnostic cut-off of glycated albumin was determined using the receiver operator characteristic (ROC) curve. The comparison of means was done using the Student's T-test. The confidence interval was at 95% and the significance was at a p-value of <0.05.

4. Results

4.1. Demographic characteristics

Table 1 shows the demographic characteristics of the women. The mean age of the women was 31.08 (± 5.12) years. Almost half (42.5%) of the women were nulliparous and most of the women (52.0%) were overweight.

Table I: Demographic characteristics of the study population

	Frequency (n=200)	Percentage (%)
Age (years)		
≤19	3	1.5
20 - 34	148	74.0
≥35	49	24.5

Parity		
P0	85	42.5
P1	53	26.5
P2	37	18.5
P3	10	5.0
P4	12	6.0
≥P5	3	1.5
Body Mass Index		
18.5 - 24.9	18	9.0
25 - 29.9	104	52.0
≥ 30	78	39.0

4.2. Optimal cut-off of glycated albumin in the diagnosis of GDM

Figure 1 shows the ROC curve with the area under the curve (AUC) above the diagonal line. Table 2 shows the AUC value of the ROC curve and glycated albumin cut-off value. Table 3 shows the cross-tabulation for the determination of the sensitivity and specificity of glycated albumin using an optimal cut-off of 19.0%.

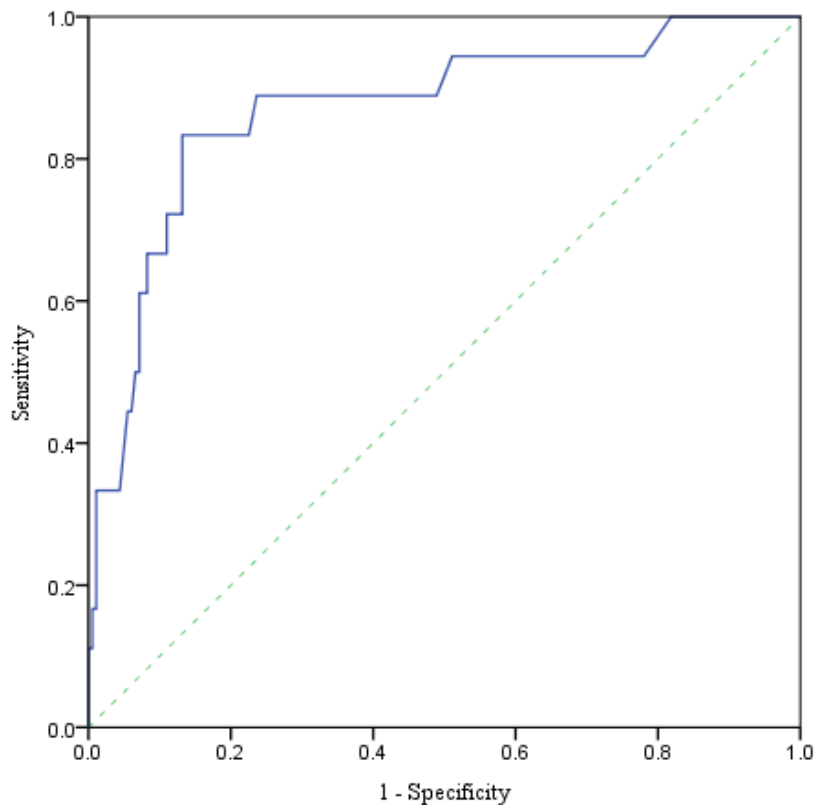


Figure 1: ROC curve showing the different cut-offs of glycated albumin in the diagnosis of GDM.

Table 2: Summary of ROC findings on Glycated albumin in the diagnosis of GDM

ROC findings	Values
AUC (95% CI)	0.8 (0.7 – 0.9)
p-value	<0.0001*
Optimal cut-off value of GA	19.0%

AUC – Area under the Curve; CI – Confidence intervals; *Statistically significant.

Table 3: Cross-tabulation for determination of sensitivity and specificity of glycated albumin

		OGTT (Gold standard)		Total
		Yes	No	
Glycated Albumin (screening test)	Elevated GA ($\geq 19.0\%$)	15 True positive	24 False positive	39
	Normal GA ($< 19.0\%$)	3 False-negative	158 True negative	161
	Total	18	182	200

4.3. Comparison of glycated albumin level among women with GDM and women without GDM

Figure 2 is a bar chart showing the percentage of the study population who has elevated glycated albumin (value $\geq 19.0\%$). **Table 4** shows that women with GDM have a significantly elevated glycated albumin level compared to women without GDM.

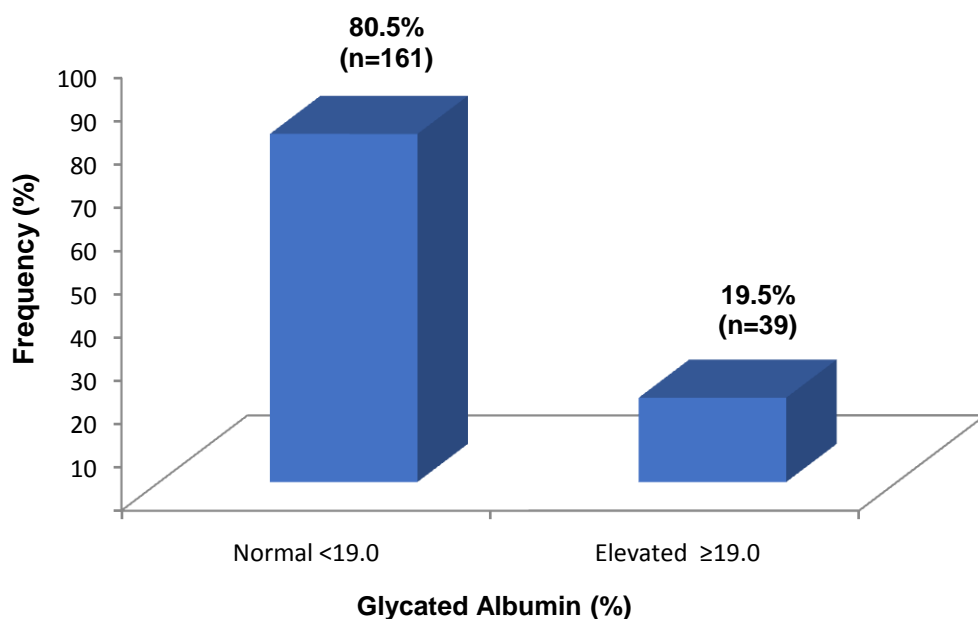


Figure 2: Glycated albumin level among women with GDM and women without GDM

Table 4: Comparison of glycated albumin levels among women with GDM and women without GDM

	With GDM Mean \pmSD	Without GDM Mean \pmSD	p-value	95% CI
Glycated albumin	21.4 \pm3.2	16.5 \pm2.3	<0.0001*	3.7 - 6.5

SD-Standard deviation; *=Statistically significant at $p < 0.05$

5. Discussion

The mean glycated for women with GDM in this study was higher than the values reported in studies done among Caucasians and Asians[30,31]. A Report from China showed that the mean glycated albumin level of women with GDM was 11.7% (± 1.5) [30] which is lower compared to the mean value of 21.4% (± 1.5) obtained in this study. This may be due to racial differences associated with glycated albumin. A study that compared the mean glycated albumin among Black Americans and Caucasians reported that Black Americans had significantly higher glycated albumin levels in participants without diabetes mellitus and participants with diabetes mellitus[28].

The optimal cut-off can be determined from the area under the ROC curve: it is the point along the curve where the diagnostic test has the best sensitivity and specificity[32,33]. The Optimal cut-off is chosen based on the need for a diagnostic test to have a higher sensitivity and lower specificity or vice versa[33,34]. In our study, the diagnostic cut-off of glycated albumin was chosen to be at $\geq 19.0\%$. This cut-off value was chosen because it is the point where the sensitivity and specificity of glycated albumin have a fair balance in diagnosing GDM. A value above this cut-off will reduce sensitivity and increase specificity, while a point below this cut-off will increase sensitivity and reduce specificity. The calculated sensitivity and specificity based on the glycated albumin diagnostic cut-off value of $\geq 19.0\%$ were 83.3% and 86.8% respectively. The diagnostic cut-off in this study was higher than the values reported in some studies. In Shanghai a diagnostic cut-off value of $\geq 11.6\%$ was gotten and for a sensitivity of 75.9% and specificity of 86.4%[30].

Dong et al report that women with GDM had a higher GA level than women without GDM, but the difference was not significant [35]. In this study, the glycated albumin level was significantly higher in women with GDM than in women without GDM. The method used in the analysis of glycated albumin levels may explain the difference in the findings between these studies. While glycated albumin was analyzed by an enzymatic method in this study, Dong et al used the peroxidase analysis method. The finding in our study is in keeping

with other studies where analysis of glycated albumin was done using an enzymatic method. The glycated albumin of women with GDM and women without GDM were analyzed by Li et al using an enzymatic method, they found that women with GDM had significantly higher GA levels [30]. Findings by Dong et al may also be different from our findings because of the difference in the method of patient selection. Dong et al recruited pregnant women in all trimesters of pregnancy and they excluded women who had a BMI of $\geq 25\text{kg}/\text{M}^2$. A high body mass index is a known risk factor for GDM[22,27]. Women with a BMI of $\geq 25\text{kg}/\text{M}$ were not excluded in our study and participants were between 24 to 28 weeks of gestation.

Conclusion

Gestational diabetes mellitus causes maternal and fetal morbidities and mortalities. Oral glucose tolerance test which is used for diagnosis of GDM requires patient preparation, drinking glucose solution, and multiple sample collection, therefore is cumbersome. Glycated albumin has an area under the ROC curve of 0.85 with an optimal cut-off value of 19.0%. Glycated albumin is significantly elevated in women with GDM than in women without GDM with a sensitivity of 83.3% and a specificity of 86.8%. Therefore glycated albumin can be used to diagnose GDM.

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