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Indian Journal of Obstetrics and Gynecology Research

Journal homepage: www.ijogr.org

Original Research Article

Test characteristics of glycated albumin in the diagnosis of gestational diabetes mellitus

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ARTICLE INFO

Article history:
Received 27-12-2023
Accepted 03-02-2024
Available online 11-05-2024

Keywords:
Glycated albumin
Gestational diabetes mellitus
Test characteristics

ABSTRACT

Aims and Objectives: This study determined the test characteristics of glycated albumin in the diagnosis of gestational diabetes mellitus.

Background: The gold standard for diagnosing gestational diabetes mellitus is the oral glucose tolerance test which requires patient preparation, drinking of glucose solution, and multiple sample collections. A possible alternative biomarker for the diagnosis of gestational diabetes is glycated albumin does not require patient preparation and only one sample is collected. Glycated albumin levels are higher among Black Americans than in Caucasians.

Materials and Methods: The study involved 200 pregnant women attending the antenatal clinic at the University of Port Harcourt Teaching Hospital. The diagnosis of gestational diabetes mellitus was made using the World Health Organization 2013 diagnostic criteria. The test characteristics of glycated albumin were determined using the area under the curve of the receiver operator characteristic curve, sensitivity, specificity, positive predictive value, and negative predictive value.

Results: The prevalence of gestational diabetes mellitus was 9.0%. The area under the receiver operator characteristic curve for glycated albumin was 0.8 (95% CI 0.7-0.9; p=0.0001). The sensitivity and specificity of glycated albumin were 83.3% and 86.8% respectively. The positive predictive value was 38.5% and the negative predictive value was 98.1%.

Conclusion: Glycated albumin has high sensitivity, specificity, and negative predictive values and therefore, can be used as a preliminary test for gestational diabetes mellitus.

1. Introduction

The number of young women of childbearing age diagnosed with Type II diabetes mellitus has increased globally, and many more women will present with hyperglycemia first identified in pregnancy.[1,2] There is a global rise in the prevalence of gestational diabetes mellitus (GDM). Over 80% of women with hyperglycemia in pregnancy have GDM.[1] Hyperglycemia first identified in pregnancy can be classified as either GDM ordiabetes mellitus in pregnancy.[2,3] Gestational diabetes mellitus is defined as different levels of glucose intolerance first identified in pregnancy.[1,3] The diagnosis of GDM is made when hyperglycemia first detected in pregnancy does not meet the criteria for the diagnosis of diabetes mellitus in the non-pregnant state: Gestational diabetes mellitus is fasting plasma glucose (FPG) value between 5.1 to 6.9 mmol/L, or one-hour 75g oral glucose tolerance test (OGTT) of

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https://doi.org/10.18231/j.ijogr.2024.054

10.0mmol/l or more, or two-hour 75g OGTT value between 8.5 to 11.1mmol/L.[1]

The prevalence of GDM varies from country to country and from region to region in the same country. The prevalence of women with hyperglycemia in pregnancy in developing countries has been reported to be higher than the prevalence in Western countries.[4] The global prevalence of GDM is 4.4%[5], which is less than the Sub-Saharan Africa prevalence of 14.28%[6] and the prevalence of 11.5% in the Middle East and Asia.[7] In Nigeria, a prevalence of 7.7% has been reported GDM in Sokoto, Northern Nigeria[8] and a prevalence of 10.5% has been reported in Port Harcourt, Southern Nigeria.[9]

The babies of women with GDM may be premature, growth-restricted, or large-for-date.[10] They may suddenly die in utero or have birth injuries from shoulder dystocia and instrumental delivery.[11] These babies may be admitted into the special care baby unit for hyperglycemia, hypoglycemia, hyperbilirubinemia, electrolyte imbalance, necrotizing enterocolitis, intra-ventricular hemorrhage, or respiratory distress syndrome.[10,11] Some babies may die from the complications of GDM. In later life, babies who survive are at risk of type II diabetes mellitus, obesity, hypertension, cardiovascular disease, delayed developmental milestones, eating disorders, sleep apnea, and pediatric ophthalmic disorders.[12,13]

Women with GDM are at increased risk of hypertensive disorders in pregnancy, induction of labor, perineal injuries, and cesarean section.[11] They are also at risk of developing Type II diabetes mellitus, obesity, cardiovascular disease, renal disease, and glaucoma later in life.[13] Other associated problems of GDM in later life are an increased risk of ovarian and endometrial malignancy, a higher risk of depression, and the recurrence of GDM in subsequent pregnancies.[13,14]

Gestational diabetes mellitus occurs due to the failure of the body to regulate the hyperglycemic effects of hormones produced in pregnancy.[14] Most women who develop GDM are asymptomatic and may not have any risk factors,[15] therefore, universal screening for GDM with OGTT is being advocated by the World Health Organization.[2] However, some countries only screen women based on risk factors. The National Institute for Health and Care Excellence recommends a selective screening for GDM if the woman has a first-degree relation with diabetes mellitus, if her BMI is ≥30kg/m^2, if she has a history of previous delivery of a baby weighing ≥4.5 kg, or if she belongs to an ethnicity with a high rate of diabetes mellitus.[16] Other risk factors for GDM are maternal age, previous unexplained stillbirth, and previous GDM.[9,17]

The morbidities associated with GDM can be significantly reduced if the women are diagnosed with GDM early and appropriate treatment is instituted. The Oral glucose tolerance test is the gold standard for GDM screening in pregnant women.[1] The OGTT requires a stable carbohydrate diet for about three days and an overnight fast of at least eight hours.[14,18] The OGTT is also affected by medications, acute illness, exercise, and stress.[14,19] Most women do not meet these pre-analytical conditions before they are screened for GDM using the OGTT. The OGTT procedure requires drinking a glucose solution that may cause nausea and vomiting and also requires multiple sample collections.[20,21] Therefore, the OGTT procedure is cumbersome.

Studies have been conducted to find alternative biomarkers for hyperglycemic states. Some biomarkers that have been studied are B-cell activating factor, tumor necrosis factor, platelet-activating factor, methylglyoxal, glycated hemoglobin, and glycated albumin.[22,23] Glycated albumin is formed when albumin undergoes a non-enzymatic glycation reaction with blood sugar.[24,25] Unlike OGTT which can be affected by fasting and type of food, glycated albumin is not affected by fasting or type of carbohydrate intake.[26] The half-life of glycated albumin is about 20 days, therefore can be used to assess glycemic control for up to three weeks with a single sample collection irrespective of fasting or type of food eaten by the woman.[24,26] Glycated albumin concentration in plasma is not affected by iron deficiency anemia, sickle cell disease, and sickle cell disease traits,[26] however, it can be affected by disease conditions that affect albumin metabolism, age, and body mass index.[24] Glycated albumin is also affected by ethnicity and race. Black Americans have higher glycated albumin levels than Caucasians.[27]

2. Materials and Methods

The study participants were 200 pregnant women between the gestational ages of 24 to 28 weeks who were attending the antenatal clinic at the University of Port Harcourt Teaching Hospital, Choba Port Harcourt. The Teaching Hospital provides all levels of health care services and also serves as a reference hospital for Rivers State and other states in Southern Nigeria. Simple random sampling was used to select 200 participants from February 2021 to March 2022. Exclusion criteria include women with diabetes mellitus, chronic liver disease, and chronic kidney disease.

The participants were counseled on the need to be on a normal diet, and they overnight fasting from 10:00 PM the previous day. The time of arrival was 8:00 am and sample collection commenced by 8:30 am. The samples for glucose analysis were collected in a Fluoride Oxalate sample container and were analyzed within 4 to 6 hours of sample collection using the oxidase method. The blood samples for glycated were collected alongside the fasting blood glucose sample into an Ethylene diamine tetra-acetic acid (EDTA) bottle. The analysis of glycated albumin was done by the Enzyme-Linked Immunosorbent Assay

(ELISA) technique. The diagnosis of GDM was based on the WHO 2013 diagnostic criteria.

The Statistical Package of the Social Sciences version 25.0 was used for data analysis. For statistical significance, the p-value was set at < 0.05 and the confidence interval was at 95%. The test characteristics of glycated albumin were analyzed using the area under the receiver operator characteristic (ROC) curve specificity, sensitivity, positive predictive value, and negative predictive value.

3. Results

3.1. Demographic characteristics of the study population

Table 1 shows the demographic characteristics of the study population. Most of the women were between 20 to 34 years old, and 113 women (56.5%) were multiparous. More than half (52%) were overweight.

3.2. Validity of glycated albumin in the diagnosis of GDM

Figure 1 shows the receiver operator characteristic curve of glycated in the diagnosis of GDM. The area under the curve was 0.8 (p=0.0001; 95% CI 0.7 – 0.9). Table 2 is a summary of the receiver operator characteristic curve.

Table 1: 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		
Nulliparous	85	42.5
Multiparous	113	56.5
Grand multiparous	2	1
Body Mass Index		
18.5 - 24.9	18	9.0
25 – 29.9	104	52.0
≥ 30	78	39.0

Table 2: Summary of the receiver operator characteristic curve

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.

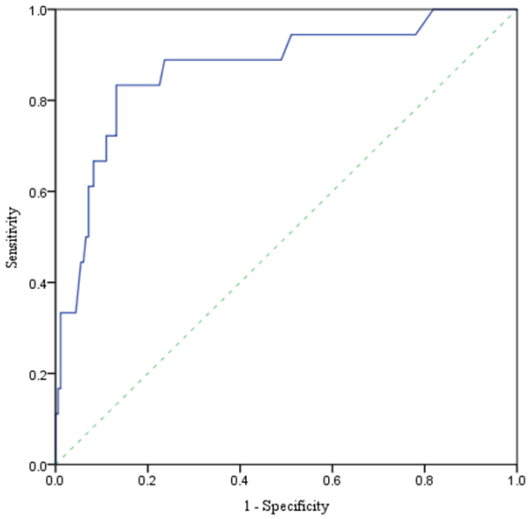

Figure 1: Receiver operator characteristic of glycated in the diagnosis of GDP

3.3. Determination of the test characteristics of glycated albumin

Table 3 is a cross-tabulation of glycated albumin at a diagnostic cut-off of 19.0% and OGTT as the gold standard. The calculated sensitivity and specificity were 83.3% and 86.8%, respectively (Equations 1 and 2). The calculated PPV was 38.5%, and the NPV was 98.1% (Equations 3 and 4).

Equation 1: Calculation of the sensitivity of Glycated albumin

$$Sensitivity = \frac{True\ Positive}{True\ Positive + False\ Negative} \times 100$$
$$= \frac{15}{15+3} = 83.3\%$$

Equation 2: Calculation of the specificity of Glycated albumin

$$Sensitivity = \frac{True\ Positive}{True\ Positive + False\ Negative} \times 100$$
$$= \frac{15}{15+3} = 83.3\%$$

Equation 3: Calculation of positive predictive value of Glycated albumin

$$Positive\ Predictive\ Value\ (PPV) = \frac{True\ Positive}{True\ Positive + False\ Positive} \times 100$$

$$= \frac{15}{15+24} = 38.5\%$$

Equation 4: Calculation of the negative predictive value of Glycated albumin

$$Negative\ Predictive\ Value = \frac{True\ Negative}{True\ Negative + False\ Negative} \times 100$$

$$= \frac{158}{158+3} = 98.1\%$$

Table 3: Cross-tabulation of glycated albumin and OGTT for determination of test characteristics

		OGTT (Gold standard)		
		Yes	No	Total
Glycated Albumin (screening test)	Elevated GA (≥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. Discussion

Gestational diabetes mellitus complicates about 16 million pregnancies worldwide.[1] The majority of these women will not have any obvious symptoms during pregnancy and will only present when they already have complications. All healthy pregnant women should have screening for GDM, and all women who are diagnosed with GDM should have appropriate management of their blood glucose in other to prevent the complications of GDM.

A systematic review and meta-analysis of 23 studies on the prevalence of GDM in Africa gave a prevalence of 14.3% in the Sub-Saharan Africa region.[6] In this study, the prevalence of GDM was 9%. While our study was a single-center study with one screening method and a single diagnostic criterion, the systematic review and meta-analysis included studies with different screening methods and different diagnostic criteria. The difference in the methodology of the study may explain the variation in the prevalence. In another systematic review and meta-analysis, Natamba et al reported a GDM prevalence of 9% in the Sub-Saharan Africa region[28] which is the same as the prevalence in our study. This similarity is possible because most of the studies in their review were done in Nigeria.

A diagnostic test can only be useful if it can correctly differentiate people with a disease from people without a disease. A test will only have a diagnostic value when the area under the ROC curve is more than 0.5.[29] The area under the ROC curve in this study was 0.8 (95% CI 0.7 – 0.9). This means glycated albumin can correctly differentiate women with GDM from women without GDM. Irrespective of the racial difference, our finding was similar to the results of studies done in Asia.[30,31] In a study of 2118 pregnant women in Shanghai using an enzymatic method of glycated albumin analysis, the area under the ROC curve was 0.8 (95% CI 0.8- 0.9), therefore GA was reported to significantly differentiate women with GDM from women without GDM.[30] Some studies have reported a lower area under the ROC curve value for glycated albumin using a non-enzymatic method of GA analysis. A study by Zhu et al using the chromatography method of GA analysis reported a value of 0.56 (95% CI 0.53 – 0.61).[31] A possible explanation for the lower value may be attributed to the method of glycated albumin analysis.

Test characteristics assessed in the study were sensitivity, specificity, positive predictive value, and negative predictive value. The sensitivity and specificity of glycated albumin in this study were 83.3% and 86.8% respectively. Despite racial differences, similar sensitivity and specificity values have been reported in some studies. A study in Shanghai reported that glycated albumin has a sensitivity of 75.9% and a specificity of 86.4% in the diagnosis of GDM[30].

The positive predictive value (PPV) and the negative predictive value (NPV) evaluate the positivity or negativity of a diagnostic test and are more useful in the clinical application of a diagnostic test[29,32]. The PPV (and NPV) will help the clinician know the probability that a patient with a positive result (or negative result) has the disease (or does not have the disease)[32]. The PPV of GA in this study was 38.5% and this low value implies that GA has a high false positive. The NPV of GA was 98.1% which implies that almost all pregnant women with a negative test result do not have GDM (low false negative). This low false negative result means that women with GDM are less likely to be missed during screening with glycated albumin. This is particularly important for GDM because most women with the condition are asymptomatic and will require early diagnosis and treatment to prevent complications of GDM.

The pregnant women selected for the study did not carry out a liver or kidney function test. Therefore, an underlying metabolic abnormality may affect the levels of plasma proteins including glycated albumin. It is recommended that screening for GDM should be done at first contact with a pregnant woman,[3] but this study was restricted to pregnant women between 24 to 28 weeks of gestation because the maximal effect of hyperglycemic hormones in pregnancy is experienced during this period.

5. Conclusion

The prevalence of GDM in this study is 9.0% which is higher than the values reported in a systematic review and meta-analysis of other studies in Africa. Glycated albumin measured between 24 to 28 weeks of gestation at a diagnostic cut-off value of 19% has a sensitivity of 83.3%, a specificity of 86.8%, a positive predictive value of 38.5%, and a negative predictive value of 98.1%. Therefore, can be used as a preliminary test in determining who will be screened for GDM using OGTT.

6. Source of Funding

None.

7. Conflict of Interest

None.

Acknowledgment

Special thanks to Dr Korubo I.F., Dr Nkoyo N., Otokunefor O., and Dr Okafor C.U.

References

1. IDF Diabetes Atlas 9th edition. Available from: https://diabetesatlas.org/atlas/ninth-edition/.
2. Diagnostic Criteria and Classification of Hyperglycaemia First Detected in Pregnancy. World Health Organization; 2013. Available from: https://iris.who.int/bitstream/handle/10665/85975/WHO_NMH_MND_13.2_eng.pdf?sequence=1.
3. Hod M, Kapur A, Sacks DA, Hadar E, Agarwal M, Renzo GCD, et al. The International Federation of Gynecology and Obstetrics (FIGO) Initiative on gestational diabetes mellitus: A pragmatic guide for diagnosis, management, and care. *Int J Gynaecol Obstet*. 2015;131(Suppl 3):S173–211.
4. Guariguata L, Linnenkamp U, Makaroff LE, Ogurtsova K, Colagiuri S. Global Estimates of Hyperglycaemia in Pregnancy: Determinants and Trends. In: Rajendram R, Preedy V, Patel V, editors. Nutrition and Diet in Maternal Diabetes. Nutrition and Health. Cham: Humana Press; 2018.
5. Behboudi-Gandevani S, Amiri M, Yarandi RB, Tehrani FR. The Impact of Diagnostic Criteria for Gestational Diabetes on its Prevalence: A Systematic Review and Meta-analysis. *Diabetol Metab Syndr*. 2019;11:11.
6. Muche AA, Olayemi OO, Gete YK. Prevalence and determinants of gestational diabetes mellitus in Africa based on the updated international diagnostic criteria: a systematic review and meta-analysis. *Arch Public Health*. 2019;77:36. doi:10.1186/s13690-019-0362-0.
7. Lee KW, Ching SM, Ramachandran V, Yee A, Hoo FK, Chia Y, et al. Prevalence and risk factors of gestational diabetes mellitus in Asia: a systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2018;18(1):494.
8. Adoke AU, Shehu CE, Nwobodo EI, Ekele BA, Sabir A, Umar AG. Gestational Diabetes Mellitus and Outcome of Pregnancy Among Women Attending Antenatal Care Clinic in North Western Nigeria. *J Middle East North Afr Sci*. 2018;4:27–32.
9. John DH, Awoyesuku PA, Macpepple DA, Kwosah NJ. Prevalence of Gestational Diabetes Mellitus and Maternal and Fetal Outcomes at the Rivers State University Teaching Hospital (RSUTH). *J Adv Med Med Res*. 2019;31:1–16.
10. Billionnet C, Mitanchez D, Weill A, Nizard J, Alla F, Hartemann A, et al. Gestational Diabetes and Adverse Perinatal Outcomes from 716,152 Births in France in 2012. *Diabetologia*. 2017;60(4):636–44.
11. Sathiamma PK, Lalithambica KA. Prospective Study on Maternal and Perinatal Outcome of Gestational Diabetes Mellitus. *Int J Reprod Contracept Obstet Gynecol*. 2017;6:2933–8.
12. Bianco ME, Josefson JL. Hyperglycemia During Pregnancy and Long-Term Offspring Outcomes. *Curr Diab Rep*. 2019;19(12):143.
13. Farahvar S, Walfisch A, Sheiner E. Gestational Diabetes Risk Factors and Long-term Consequences for Both Mother and Offspring: A Literature Review. *Expert Rev Endocrinol Metab*. 2019;14:63–74.
14. Mcintyre HD, Catalano P, Zhang C, Desoye G, Mathiesen ER, Damm P. Gestational Diabetes Mellitus. *Nat Rev Dis Primers*. 2019;5:47. doi:10.1038/s41572-019-0098-8.
15. Hymavathi K, Tadisetti S, Polisetty K, Gottipatti MD. Gestational diabetes mellitus-universal versus selective screening. *Int J Reprod Contracept Obstet Gynecol*. 2016;5:2155–60.
16. Diabetes in pregnancy: management from preconception to the postnatal period. NICE; 2020. Available from: https://www.ncbi.nlm.nih.gov/books/NBK555331/.
17. Ogu RN, John CO, Maduka O, Chinenye S. Screening for Gestational Diabetes Mellitus: Findings from a Resource Limited Setting of Nigeria. *Br J Med Med Res*. 2017;20:1–8.
18. Kumar V, Gill KD. To Perform Glucose Tolerance Test. In: Basic Concepts in Clinical Biochemistry: A Practical Guide. Singapore: Springer; 2018.
19. Sareen R, Kapil M, Gupta GN. Blood Glucose Fasting – Harmonization of Variables Affecting Pre Analytical Phase. *J Fam Med Forecast*. 2019;2(1):1014.
20. Bogdanet D, O'shea P, Lyons C, Shafat A, Dunne F. The Oral Glucose Tolerance Test-Is It Time for a Change?-A Literature Review with an Emphasis on Pregnancy. *J Clin Med*. 2020;9(11):3451.
21. Nanda R, Patel S, Sahoo S, Mohapatra E. Review of Pre-Analytical Errors in Oral Glucose Tolerance Testing in a Tertiary Care Hospital. *J Nepal Health Res Counc*. 2018;16(1):6–10.
22. Rodrigo N, Glastras SJ. The emerging role of biomarkers in the diagnosis of gestational diabetes mellitus. *J Clin Med*. 2018;7(6):120.
23. Piuri G, Basello K, Rossi G, Soldavini CM, Duiella S, Privitera G, et al. Methylglyoxal, Glycated Albumin, PAF, and TNF-Possible Inflammatory and Metabolic Biomarkers for Management of Gestational Diabetes. *Nutrients*. 2020;12(2):479.
24. Zendjabil M. Glycated albumin. *Clin Chim Acta*. 2019;502:240–4.
25. Neelofar N, Ahmad J. An overview of in vitro and in vivo glycation of albumin: a potential disease marker in diabetes mellitus. *Glycoconj J*. 2017;34(5):575–84.
26. Freitas PAC, Ehlert LR, Camargo JL. Glycated albumin: a potential biomarker in diabetes. *Arch Endocrinol Metab*. 2017;61(3):296–304.
27. Selvin E, Steffes MW, Ballantyne CM, Hoogeveen RC, Coresh J, Brancati FL. Racial Differences in Glycemic Markers: A Cross-sectional Analysis of Community-Based Data. *Ann Intern Med*. 2011;154(5):303–9.
28. Natamba BK, Namara AA, Nyirenda MJ. Burden, risk factors and maternal and offspring outcomes of gestational diabetes mellitus (GDM) in sub-Saharan Africa (SSA): a systematic review and meta-analysis. *BMC Pregnancy Child B*. 2019;19:1–11.
29. Chikere CMU, Wilson K, Graziadio S, Vale L, Allen AJ. Diagnostic test evaluation methodology: A systematic review of methods employed to evaluate diagnostic tests in the absence of gold standard - An update. *PLoS One*. 2019;14:e0223832.
30. Li H, Li H, Wang F, Tao M, Huang Y, Jia W. Association between glycemic control and birthweight with glycated albumin in Chinese women with gestational diabetes mellitus. *J Diabetes Investig*. 2016;7(1):48–55.
31. Zhu J, Chen Y, Li C, Tao M, Teng Y. The diagnostic value of glycated albumin in gestational diabetes mellitus. *J Endocrinol Invest*. 2018;41(1):121–8.
32. Trevethan R. Sensitivity, Specificity, and Predictive Values: Foundations, Pliabilities, and Pitfalls in Research and Practice. *Front Public Health*. 2017;5:307.

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Cite this article: Woruka AP, John CO, Akhidue K, Ogu R. Test characteristics of glycated albumin in the diagnosis of gestational diabetes mellitus. *Indian J Obstet Gynecol Res* 2024;11(2):281-286.