Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Obstetrics & Gynecology

Prediction of Adverse Fetal Outcome among Women with Gestational Diabetes Mellitus Using Glycated Albumin Measured in the Third Trimester

Atochi Prince Woruka[1], Simeon Amadi[2], Ochuko Otokunefor[3*], Terhemen Kasso[1]

[1]Department of Obstetrics and Gynecology, University of Port Harcourt, Rivers State, Nigeria
[2]Department Obstetrics and Gynecology, Rivers State University Teaching Hospital, Rivers State, Nigeria
[3]Department Chemical Pathology Department, University of Port Harcourt, Rivers State, Nigeria

DOI: https://doi.org/10.36347/sjmcr.2025.v13i02.017 | **Received:** 08.01.2025 | **Accepted:** 13.02.2025 | **Published:** 24.02.2025

***Corresponding author:** Ochuko Otokunefor
Department Chemical Pathology Department, University of Port Harcourt, Rivers State, Nigeria

Abstract **Original Research Article**

Background*:** There is a rising trend of gestational diabetes mellitus (GDM) in our environment and it is a major cause of complications in pregnancy, delivery, and puerperium. Fetal complications of GDM are prematurity, fetal macrosomia, hypoglycemia, respiratory distress syndrome etc. Glycated albumin (GA) is a biomarker for hyperglycemic states, and unlike the oral glucose tolerance test, it does not require patient preparation, intake of glucose, or multiple sample collection. Black women have been shown to have a higher GA level than Caucasian women. ***Objectives*:** This study determined the association between glycated albumin and fetal outcomes among pregnant women attending the antenatal clinic at the University of Port Harcourt Teaching Hospital. ***Methodology: The research work was a longitudinal study at the University of Port Harcourt Teaching Hospital from the 15th February 2021 to the 10th March 2023. Two hundred pregnant women between 34 to 38 weeks gestation were selected by simple random sampling method. The diagnosis of gestational diabetes mellitus was made using the World Health Organisation 2016 diagnostic criteria. Fetal outcome studied were prematurity (delivery before 37 completed weeks of gestation), fetal macrosomia (birth weight of ≥4.0kg at delivery), and fetal hypoglycemia (cord blood glucose of ≤3.0mmol/L). All data were analyzed with Statistical Product and Services Solutions version 25.0. The test of significant association between GA levels and fetal outcome was done using the student's T-test the statistical significance was at $p < 0.05$ at 95% confidence interval. ***Results:*** More than half of the women were obese. Prematurity was seen in 6.7% of cases, macrosomia in 10.1% of cases and neonatal hypoglycemia in 5.1% of cases. Glycated albumin was only significantly associated with fetal macrosomia (p=0.012; 95% CI 0.3−3.1). ***Conclusion*:** Elevated glycated albumin at 34 to 36 weeks of gestation is significantly associated with fetal macrosomia.

Keywords: Glycated albumin, Gestational diabetes mellitus, adverse fetal outcome, fetal macrosomia, University of Port Harcourt Teaching Hospital.

1. INTRODUCTION

Gestational diabetes mellitus is defined as varying levels of glucose intolerance in pregnancy [1]. There is a global rise in the prevalence of gestational diabetes mellitus (GDM), over 80% of women with hyperglycemia in pregnancy have GDM [2]. A substantial number of these cases are reported in low-income countries [3]. The Sub-Saharan Africa prevalence of 14.28% was reported in a systematic review and meta-analysis of GDM in 23 studies conducted in Africa [4]. In Nigeria, a study on the prevalence of GDM in Sokoto reported a prevalence of 7.7% [5] while in Port Harcourt, the prevalence of 10.5% has been reported [6]. The values are higher than the global prevalence of 4.4% reported in a systematic review and meta-analysis of 51 population-based studies on GDM [7].

The babies of women with GDM may be born premature, growth-restricted, large-for-date, may suddenly die in-utero, or have birth injuries from shoulder dystocia and instrumental delivery [8]. Infants of GDM mothers may be admitted into the special care baby unit for hyperglycemia, hypoglycemia, hyperbilirubinemia, electrolyte imbalance, necrotizing enterocolitis, intra-ventricular haemorrhage, or respiratory distress syndrome [9, 10]. While some neonates die from these complications, those who

survive may develop Type II diabetes mellitus, obesity, hypertension, or cardiovascular disease in the future [11, 12]. Other long-term consequences reported in children born to a GDM mother are delayed developmental milestones, eating disorders, sleep apnea, and pediatric ophthalmic disorders [12]. The Women with GDM may have hypertensive diseases, perineal injuries, and have an increased risk of induction of labor and cesarean section [10]. About half of the women diagnosed with GDM may develop Type II diabetes mellitus, become obese later in life, or have a recurrence of GDM in subsequent pregnancies [12, 13]. Other long-term complications of GDM are cardiovascular disease, renal disease, ophthalmic diseases such as glaucoma, increased risk of ovarian and endometrial malignancies, and a higher risk of depression later in life [12]. The morbidities associated with this condition can be significantly reduced if women with GDM are treated.

In the past decade, some studies have been conducted to find alternative biomarkers for hyperglycemic states. Glycated albumin (GA) has gained significant attention and has become a promising marker for hyperglycemic states. Glycated albumin is formed when albumin undergoes a non-enzymatic glycation reaction with blood sugar [14, 15].

Serum albumin reacts with plasma glucose in a non-enzymatic reaction to produce glycated albumin [14]. Albumin has a high content of glycine and lysine which makes it susceptible to a non-enzymatic reaction with reducing sugars in plasma [14, 15]. Since albumin is an abundant extracellular plasma protein, it is glycated 9 to 10 times more than other proteins [14, 16]. The amount of glucose attached to the albumin during this reaction is dependent on the degree and duration of hyperglycemia, therefore serum GA is a reflection of the degree and duration of hyperglycemia [16, 17]. The half-life of GA is about 20 days, therefore can be used to assess glycemic control for up to three weeks with a single sample collection [14, 16].

Glycated albumin concentration in plasma is not affected by fasting or type of carbohydrate intake [16], iron deficiency anemia, sickle cell disease, and sickle cell disease traits [16]. The level of GA in plasma can be affected by disease conditions that affect albumin metabolism, age, and body mass index [14]. GA is also affected by ethnicity. In a cross-sectional community-based study in the United States of America, a total of 1295 Caucasians and 424 African Americans were studied. Caucasians without diabetes mellitus had a mean GA of 13.4% while African Americans without diabetes mellitus had a mean of 14.5%. The study group diagnosed with diabetes mellitus had means of 16.5% and 20.1% for Caucasian and African Americans respectively. The group concluded that GA is higher in the black population [18]. Most studies on GA in pregnancy were carried out among the non-African population.

Studies in China have shown that GA level in pregnant women with GDM is significantly higher than in pregnant women without GDM when GA is assayed using the enzymatic method [19]. In Zhejiang, the GA levels of 893 pregnant women with GDM and 661 healthy pregnant women without GDM were assayed using the enzymatic method. The GA level of the pregnant women with GDM was significantly higher than the GA level of the control group. GA levels also correlated with FPG at all gestational ages [19]. A similar finding was reported by Li *et al.*, [20]. in Shanghai: they used the enzymatic method in the analysis of the GA levels of 639 pregnant women with GDM and 1,479 women without GDM in the first, second and third trimesters. The GDM group had significantly higher GA levels than the control group in all trimesters and the level of GA correlated with the FPG, 1-hour plasma glucose, and 2-hour plasma glucose of OGTT. Using an optimal cut-off GA value of ≥11.6%, the sensitivity and specificity of GA in the diagnosis of GDM were 75.93% and 86.36% respectively. However, Zhu *et al.*, [21] in Shanghai used the chromatography method in the analysis of GA level in pregnant women and healthy age-matched women. In their study, they found significantly lower GA values among pregnant women compared to healthy age-matched women.

Using Pearson's correlation, a study in Japan reported an association between GA levels and fetal outcomes: hypoglycemia, neonatal respiratory disorders, hypocalcemia, polycythemia, myocardial hypertrophy, and large-for-date [22]. Researchers in China [20] and Portugal [23] applied logistic regression models in their studies and found a significant association between GA level and increasing birth weight. However, in a study where the relative risk and odds ratio was applied, the GA level was only significantly associated with postpartum hemorrhage and not increasing fetal weight [24].

2. MATERIALS AND METHOD

The study participants were recruited from the antenatal clinic of the Department of Obstetrics and Gynaecology at the University of Port Harcourt Teaching Hospital, Port Harcourt. The University of Port Harcourt Teaching Hospital provides all levels of health care services and is one of the reference hospitals in southern Nigeria. The study was a longitudinal study conducted between 15th February 2021 to the 10th March 2023. The participants were pregnant women between the gestational ages of 34 to 36 weeks diagnosed with GDM. The following category of women were excluded from the study: women with pre-gestational diabetes mellitus, women not sure of their last menstrual period (LMP), and had no early ultrasound scan determination of gestational age, and women with conditions that can affect the metabolism of albumin such as lipid disorders, nephrotic syndrome, Cushing's syndrome, thyroid diseases, and liver diseases.

The sample size was 200 and the sampling technique was a simple random sampling technique. The outcome measures in this study were: Glycated albumin level, gestational age at delivery, birth weight of the baby, and fetal cord blood glucose. The blood samples for GA were collected into an EDTA bottle and the analysis was done by ELISA technique. The fetal cord blood samples were collected in a Fluoride Oxalate sample container and the analysis was done using the oxidase method. Fetal outcomes studied were prematurity, macrosomia, and hypoglycemia, Prematurity was defined as delivery before 37 completed weeks of gestation, fetal macrosomia was defined as a birth weight of ≥4.0kg at delivery, and fetal hypoglycemia was defined as fetal cord blood glucose of ≤2.6mmol/L. The diagnosis of GDM was based on the WHO 2016 diagnostic criteria. The Statistical Product and Services Solutions version 25.0 was used for data analysis. The test of significant association between GA levels and fetal outcome was done using the student's T-test the statistical significance was at $p < 0.05$ at 95% confidence interval. Ethical approval was issued by the University of Port Harcourt Teaching Hospital's ethical review board.

3. RESULTS

3.1. Demographic characteristics of the study population

Two hundred pregnant women between 34 to 36 weeks of gestation were studied. Their mean age was 31.1 (±5.0) years. Table I shows that more than half of the women were multiparous, and more than half of the women had obesity.

Table I: Demographic characteristics of the study population

	Frequency (n=200)	Percentage (%)
Age (years)		
≤19	5	2.5
20 - 34	121	60.5
≥35	74	37.0
Parity		
One delivery	86	43.0
Two to four deliveries	106	53.0
Five deliveries and more	8	4.0
Body Mass Index (Kg/M^2)		
18.5 - 24.9	12	6.0
25 – 29.9	86	43.0
≥ 30	102	51.0

3.2. Pregnancy outcome of the study population

Of the 200 women who participated in the study, 178 women delivered at UPTH. Twelve (6.7%) women gave birth before 37 weeks of gestation, and 18 (10.1%) babies weighed ≥4.0kg. Nine babies (5.1%) had a blood glucose level ≤3.0mmol/L (Table II).

Table II: Pregnancy outcome of the study population

	Frequency (n=178)	Percentage
Prematurity (<37 weeks)		
Yes	12	6.7
No	166	93.3
Macrosomia (≥4.0kg)		
Yes	18	10.1
No	160	89.9
Neonatal hypoglycaemia (≤3.0mmol/l)		
Yes	9	5.1
No	169	94.9

3.3. Glycated albumin and pregnancy outcome.

Tables III to V show the association between GA and fetal outcomes. The GA level among women who had babies with fetal macrosomia was significantly higher than in women who had normal-weight babies (p=0.012; 95% CI 0.3−3.1).

Table III: Comparison of Glycated albumin level among women who had preterm delivery and women who had term delivery

	Prematurity		p-value	95% CI
	Yes (Mean ±SD)	No (Mean ±SD)		
Glycated albumin	18.2 (±3.8)	16.8 (±2.70)	0.093	0.2−3.0

SD-Standard Deviation; Statistically significant at $p<0.05$

Table IV: Comparison of Glycated albumin level among women who had babies with macrosomia and women who had babies with normal birth weight

	Macrosomia		p-value	95% CI
	Yes (Mean ±SD)	No (Mean ±SD)		
Glycated albumin	18.4(±3.2)	16.7(±2.7)	**0.012***	0.3–3.1

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

Table V: Glycated albumin level among women who had babies with hypoglycemia and women who had babies without hypoglycemia

	Hypoglycemia		p-value	95% CI
	Yes (Mean ±SD)	No (Mean ±SD)		
Glycated albumin	18.4(±4.7)	16.8 (±2.7)	0.082	0.2– 3.5

SD-Standard Deviation; Statistically significant at p<0.05

4. DISCUSSION

Gestational diabetes mellitus complicates about 16 million pregnancies worldwide [2]. 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 order to prevent the complications of GDM. In the University of Port Harcourt Teaching Hospital, the 2-hour 75g OGTT is used to screen every pregnant woman for GDM and the diagnosis of GDM is based on the WHO 2016 criteria.

Adverse pregnancy outcomes in GDM are dependent on the extent of hyperglycemia. The serum levels of GA are a reflection of the extent of hyperglycemia and have been linked to adverse pregnancy outcomes in women with GDM [22, 24]. In this study, GA was significantly associated with fetal macrosomia. The association of GA with macrosomia has been reported. In a study in Japan evaluating the GA level in women with diabetes mellitus in pregnancy, GA was significantly associated with macrosomia [22]. Another study in China also found a correlation between GA level and fetal weight [20]. Elevated GA albumin is also associated with a high Body Mass Index (BMI) [25]. More than half of the participants in this study had a BMI of ≥30kg/m^2.

We defined neonatal hypoglycemia as a cord blood glucose level of ≤3.0mmol/l, and GA was not significantly associated with fetal hypoglycemia. The finding in our study is not in keeping with a study by Sugawara *et al.*, which showed that elevated GA was significantly associated with neonatal hypoglycemia [26]. The difference may be due to the definition of neonatal hypoglycemia used by Sugawara *et al.*, which was < 1.9 mmol/L. Although prematurity is a complication of GDM, our study found no association between elevated GA and prematurity.

5. CONCLUSION

Glycated albumin measured between 34 to 36 weeks of gestation was significantly associated with fetal macrosomia.

REFERENCES

1. World Health Organization. Diagnostic Criteria and Classification of Hyperglycaemia First Detected in Pregnancy. 2013. http://apps.who.int/iris/bitstream/10665/85975/1/WHO_NMH_MND_13.2_eng.pdf [Last assessed 18/07/2024].
2. IDF Diabetes Atlas, 9th edition Available at https://www.diabetesatlas.org/upload/resources/2019/IDF_Atlas_9th_Edition_2019.pdf [Last accessed 18/07/2024].
3. Guariguata L, Linnenkamp U, Makaroff LM, Ogurtsova K, Colagiuri S. Global Estimates of Hyperglycaemia in Pregnancy: Determinants and Trends. https://www.researchgate.net/publication/320333784_Global_Estimates_of_Hyperglycaemia_in_Pregnancy_Determinants_and_TrendsGuariguata 2017 [last assessed 18/07/2024].
4. Muche, A. A., Olayemi, O. O., & Gete, Y. K. (2019). 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*, *77*(36), 1-20.
5. Adoke, A. U., Shehu, C. E., Nwobodo, E. I., Ekele, B. A., Sabir, A., Umar, A. G. (2018). Gestational Diabetes Mellitus and Outcome of Pregnancy among Women Attending Antenatal Care Clinic in North Western Nigeria. *J Middle East North Afr Sci*, *4*(6), 27-32.
6. John, D. H., Awoyesuku, P. A., MacPepple, D. A., & Kwosah, N. J. (2019). Prevalence of gestational diabetes mellitus and maternal and fetal outcomes at the Rivers State University Teaching Hospital (RSUTH), Port Harcourt, Nigeria. *J Adv Med Med Res*, *31*(9), 1-16.
7. Behboudi-Gandevani, S., Amiri, M., Bidhendi Yarandi, R., & Ramezani Tehrani, F. (2019). The

impact of diagnostic criteria for gestational diabetes on its prevalence: a systematic review and meta-analysis. *Diabetology & metabolic syndrome*, *11*, 1-18.

8. Billionnet, C., Mitanchez, D., Weill, A., Nizard, J., Alla, F., Hartemann, A., & Jacqueminet, S. (2017). Gestational diabetes and adverse perinatal outcomes from 716,152 births in France in 2012. *Diabetologia*, *60*, 636-644.
9. Battarbee, A. N., Venkatesh, K. K., Aliaga, S., & Boggess, K. A. (2020). The association of pregestational and gestational diabetes with severe neonatal morbidity and mortality. *Journal of Perinatology*, *40*(2), 232-239.
10. Sathiamma, P. K., & Karunakaran, L. (2017). A prospective study on maternal and perinatal outcome of gestational diabetes mellitus. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, *6*(7), 2933-2939.
11. Bianco, M. E., & Josefson, J. L. (2019). Hyperglycemia during pregnancy and long-term offspring outcomes. *Current diabetes reports*, *19*, 1-8.
12. Farahvar, S., Walfisch, A., & Sheiner, E. (2019). Gestational diabetes risk factors and long-term consequences for both mother and offspring: a literature review. *Expert review of endocrinology & metabolism*, *14*(1), 63-74.
13. McIntyre, H. D., Catalano, P., Zhang, C., Desoye, G., Mathiesen, E. R., & Damm, P. (2019). Gestational diabetes mellitus. *Nature reviews Disease primers*, *5*(1), 47.
14. Zendjabil, M. (2019). Glycated albumin. *Clinica Chimica Acta*, *502*(1), 240-244.
15. Neelofar, K., & Ahmad, J. (2017). An overview of in vitro and in vivo glycation of albumin: a potential disease marker in diabetes mellitus. *Glycoconjugate journal*, *34*, 575-584.
16. Freitas, P. A. C., Ehlert, L. R., & Camargo, J. L. (2017). Glycated albumin: a potential biomarker in diabetes. *Archives of endocrinology and metabolism*, *61*, 296-304.
17. Dozio, E., Di Gaetano, N., Findeisen, P., & Corsi Romanelli, M. M. (2017). Glycated albumin: from biochemistry and laboratory medicine to clinical practice. *Endocrine*, *55*, 682-690.
18. Selvin, E., Steffes, M. W., Ballantyne, C. M., Hoogeveen, R. C., Coresh, J., & Brancati, F. L. (2011). Racial differences in glycemic markers: a cross-sectional analysis of community-based data. *Annals of internal medicine*, *154*(5), 303-309.
19. Huang, Y., Hu, Y., Ma, Y. U., & Ye, G. (2015). Glycated albumin is an optimal biomarker for gestational diabetes mellitus. *Experimental and therapeutic medicine*, *10*(6), 2145-2149.
20. Li, H. P., Wang, F. H., Tao, M. F., Huang, Y. J., & Jia, W. P. (2016). Association between glycemic control and birthweight with glycated albumin in C hinese women with gestational diabetes mellitus. *Journal of Diabetes Investigation*, *7*(1), 48-55.
21. Zhu, J., Chen, Y., Li, C., Tao, M., & Teng, Y. (2018). The diagnostic value of glycated albumin in gestational diabetes mellitus. *Journal of Endocrinological Investigation*, *41*, 121-128.
22. Sugawara, D., Sato, H., Ichihashi, K., Nagai, K., & Kawano, A. (2018). Glycated albumin level during late pregnancy as a predictive factor for neonatal outcomes of women with diabetes. *The Journal of Maternal-Fetal & Neonatal Medicine*, *31*(15), 2007-2012.
23. Mendes, N., Alves, M., Andrade, R., Ribeiro, R. T., Papoila, A. L., & Serrano, F. (2019). Association between glycated haemoglobin, glycated albumin and fructosamine with neonatal birthweight and large-for-date status infants in gestational diabetes mellitus: a prospective cohort study. *Journal of Obstetrics and Gynaecology*, *39*(6), 768-773.
24. Dong, Y., Zhai, Y., Wang, J., Chen, Y., Xie, X., Zhang, C., ... & Cao, Z. (2020). Glycated albumin in pregnancy: reference intervals establishment and its predictive value in adverse pregnancy outcomes. *BMC Pregnancy and Childbirth*, *20*, 1-9.
25. Sugawara, D., Makita, E., Matsuura, M., Sato, H., Kuwata, T., & Ichihashi, K. (2023). Prepregnancy body mass index and glycated albumin in the third trimester may predict infant complications in gestational diabetes mellitus: a retrospective cohort study. *Diabetology international*, *14*(3), 280-287.
26. Sugawara, D., Maruyama, A., Imanishi, T., Sugiyama, Y., & Ichihashi, K. (2016). Complications in infants of diabetic mothers related to glycated albumin and hemoglobin levels during pregnancy. *Pediatrics & Neonatology*, *57*(6), 496-500.