

Elevated HBA1C and the Outcomes in Pregnancy

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How to citation this article: Dr. AR Jameela Ponmalar, Dr. Kavya Arja, Dr. Vishnu Priya R S, “Elevated HBA1C and the Outcomes in Pregnancy”, IJMACR- March - 2024, Volume – 7, Issue - 2, P. No. 96 – 100.

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Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Glycosylated Hemoglobin (HbA1c) and fasting blood glucose are commonly used to screen for overt diabetes in the first trimester of pregnancy. The purpose of the study was to determine whether elevated glycosylated hemoglobin (HbA1c) values in the first trimester were associated with the development of gestational diabetes mellitus (GDM) later in pregnancy.

Materials and Methods: All patients underwent first-trimester screening for diabetes mellitus with HbA1c. Patients were followed up and all underwent GTT at 24–28 weeks. All women received regular antenatal visits, regardless of GDM status, were followed up until delivery. The study included several outcome measures such as GDM, pre-eclampsia, polyhydramnios, mode of

delivery, and neonatal measures such as birth weight, LGA, hyperbilirubinemia and hypoglycemia.

Results: Out of 510 subjects, 104 (20.4%) developed GDM. In retrospect, there was a significant difference in HbA1c values, with a p-value of <0.001 with a mean HbA1c of $5.22 \pm 0.34\%$ in patients who developed GDM. There is a positive correlation between HbA1c and large for gestational age with a mean of $5.19 \pm 0.41\%$. No association was noted with polyhydramnios and gestational hypertension, preterm delivery, hyperbilirubinemia. At HbA1c level of 5.15% or higher predicted GDM with 65.4% sensitivity and 64.8% specificity.

Conclusion: Raised level of HbA1c in the first trimester of pregnancy is associated with a higher chance of GDM and macrosomia in pregnancy.

Keywords: Glycosylated Hemoglobin, Gestational Diabetes Mellitus, Macrosomia, Overt Diabetes Mellitus.

Introduction

Gestational diabetes mellitus (GDM) is a pathology that can create a lot of problems in pregnancy. Glycosylated hemoglobin (HbA1c) and fasting blood glucose can be used to screen for overt diabetes in the first trimester of pregnancy. HbA1c level of more than 6.5% is considered as diagnostic of overt diabetes in pregnancy in the first trimester. Fasting blood sugar between 92 and 125 mg/dL were considered as GDM by the International Association of Diabetes and Pregnancy Study Group (IADPSG). Fasting blood sugar values more than 126 mg/dL signifies overt diabetes.¹ There have been studies previously regarding elevated HbA1c and the risk of developing GDM.² Gestational diabetes may occur even before 24 weeks of gestation and hence early screening, detection and treatment would benefit mother and the fetus. Many centers are now using HbA1c as a screening test in first trimester.³ In developed countries, obesity and abnormal glucose metabolism during pregnancy has increased drastically which increases the maternal and neonatal complications rate.⁴ We did a study to determine whether lower HbA1c less than 6.5% detected in the first trimester of pregnancy can predict GDM later in pregnancy. Currently there are no guidelines or effective modalities for prediction and prevention of GDM even before actual diagnosis. Accurate prediction may create a window of opportunity in prevention of GDM and HbA1c may predict the risk of development of GDM later in pregnancy.

Material and Methods

It is a prospective observational study that occurred in the Obstetrics and Gynecology Department at Sree Mookambika institute of medical sciences between June 2022 and December 2023. Women presenting up to 12 weeks of gestation were included in the study. Patients with fasting sugar > 126 mg/dL and HbA1c > 6.5% were excluded from the study. At the first visit, HbA1c was sent for all patients. The patients were followed up with 75 g GTT by IADPSG criteria at 24–28 weeks of gestation. GTT was considered abnormal if it was more than 92 mg/dL after fasting, 180 mg/dL after 1 hour, and 153 mg/dL after 2 hours. GDM was diagnosed if one value was abnormal. The glucose oxidase/peroxidase method was used to estimate glucose from venous blood plasma. All women who received regular antenatal visits, regardless of GDM status, were followed up until delivery. The study includes several outcome measures such as GDM, pre-eclampsia, polyhydramnios, mode of delivery and neonatal measures such as birth weight, LGA, hyperbilirubinemia, hypoglycemia. Done using SPSS version 21.0 statistical analysis software. $p < 0.05$ was considered statistically significant.

Results

The first trimester HbA1c levels (up to 12 weeks) of 689 women were collected. Out of which 56 women underwent missed/incomplete abortion, 32 women underwent medical termination of pregnancy mainly due to contraception failure and very few due to anomalies. 91 women out of 709 lost to follow-up. Finally 510 subjects were available for analysis.

The HbA1c values were significantly higher in the first trimester in women who developed GDM later in pregnancy. Patients with higher values of HbA1c values

in the first trimester are at risk of developing GDM later. Incidences of pre-eclampsia were also higher in women with higher HbA1c values in the first trimester (Table 1). Incidence of large for gestational age (LGA) babies was higher in women with higher HbA1c values. No association between first-trimester HbA1c levels with preterm birth, neonatal hypoglycemia, and neonatal hyperbilirubinemia (Table 2). The incidence of

caesarean section was higher when the HbA1c value was high (Table 3). An ROC curve was constructed with an area under the curve of 0.671 (95% CI 0.610-0.732, p= 0.000) and HbA1c level of 5.15% or higher predicted GDM with 65.4% sensitivity and 64.8% specificity. Higher HbA1c values were associated with a higher chance of development of GDM in pregnancy (Fig. 1).

Table 1: First trimester HbA1c association with adverse maternal outcome (N = 510)

Pregnancy variable	Yes		No		p value
	Number	HbA1c%	Number	HbA1c%	
Gestational diabetes mellitus	104 (20.4%)	5.22 ± 0.34	406 (79.6%)	5.07 ± 0.27	<0.001
Gestational hypertension	26 (5.1%)	5.14 ± 0.34	484 (94.9%)	5.10 ± 0.29	0.49
Pre-eclampsia	15 (3.0%)	5.28 ± 0.29	495 (97%)	5.10 ± 0.28	0.02
Polyhydramnios	6 (1.2%)	5.31 ± 0.26	504 (98.8%)	5.10 ± 0.28	0.07

Table 2: First trimester HbA1c association with adverse neonatal outcome (N = 510)

Variable	Yes		No		p value
	Number	HbA1c%	Number	HbA1c%	
Large for gestational age	36 (7.10%)	5.19 ± 0.41	474 (92.9%)	5.09 ± 0.28	0.04
Small for gestational age	53 (10.4%)	5.07 ± 0.25	457 (89.6%)	5.10 ± 0.29	0.52
Preterm birth <37 weeks	41 (8.0%)	5.12 ± 0.31	471 (92%)	5.10 ± 0.29	0.68
Neonatal hypoglycemia	4 (0.8%)	4.90 ± 0.49	506 (99.2%)	5.10 ± 0.28	0.15
Neonatal hyperbilirubinemia	216 (42.3%)	5.12 ± 0.28	294 (57.7%)	5.095 ± 0.27	0.27

Table 3: Association of HbA1c level with the mode of delivery

Mode of delivery	Number(510)	Mean HbA1c	p value
Spontaneous delivery	197 (38.6%)	5.062 ± 0.254	0.02
Caesarean section	298 (58.4%)	5.120 ± 0.319	
Instrumental delivery	15 (3%)	5.136 ± 0.303	

Discussion

One of the most serious health issues in pregnancy is gestational diabetes mellitus. If it is not identified and treated early enough, it can lead to serious perinatal problems that are preventable. An “oral glucose tolerance test (OGTT)” between 24 and 28 weeks of pregnancy is the most prevalent screening tool used around the world. The universal first-trimester screening is not done in all places. The first-trimester screening is done in women with a high-risk category, such as the elderly, high BMI, history of GDM, and family history of GDM. Although the debate over universal versus selective GDM screening continues, GDM screening in pregnancy is currently recommended by most medical organizations.⁵ HbA1c is a screening biochemical measure that shows the mean blood glucose level during the previous 2 to 3 months. The efficacy of HbA1c testing during the first trimester of pregnancy for GDM screening is still up for dispute. HbA1c readings of 6.5% are considered diagnostic for diabetes mellitus, according to WHO criteria.⁶ The typical range for first trimester HbA1c was 4.3–5.4%.⁷ We decided to do a study on the level of HbA1c and the risk of subsequent GDM in pregnancy. Out of 510 cases, 104 developed GDM. The mean HbA1c in the cases that developed GDM was 5.22 ± 0.34%. This was statistically significant when compared to women who

did not develop GDM. Thus, first trimester HbA1c may be an important predictor for the development of GDM subsequently in pregnancy. We created an ROC curve and a value of 5.15% had a 65.4% sensitivity and 64.8% specificity in predicting GDM. A higher value of HbA1c in the first trimester was also associated with macrosomia and increased chances of caesarean section in our study. Thus, elevated value of HbA1c in early pregnancy is a useful marker of the development of GDM and macrosomia in pregnancy. David Benaiges et al. did a study to determine the ideal HbA1c values to predict GDM in pregnancy. According to them, a value of 4.8% had 96.7% sensitivity (95%CI 93.9–99.5), 10.1% specificity to diagnose GDM. A value of 5.6% had 89.3% specificity and 32.9% sensitivity (95%CI 25.4–40.4). A value of 4.6% had higher sensitivity but very poor specificity. A value of 5.6% had very low sensitivity. They suggested that HbA1c does not have adequate sensitivity or specificity to diagnose GDM subsequently in pregnancy.⁸ However, in our study, a value of 5.15% had higher sensitivity and specificity. In 2019, a study by Arbib N et al. found a higher sensitivity of 83.3% and a specificity of 69% for HbA1c value 5.45% to detect GDM later in pregnancy.⁹ In our study, we found higher first-trimester HbA1c values were associated with more incidence of large babies and higher chances of caesarean section. In the current

study, it is clear that higher HbA1c values are a predictor of GDM later in pregnancy. There may be a variety of other factors like family history and obesity that may be playing a part in the development of GDM. We found a value of 5.15% had a sensitivity of 65.4% in predicting GDM later in pregnancy. Many people nowadays routinely do HbA1c in the first trimester to detect overt diabetes. If they accidentally find a higher value, you can predict that these higher values are associated with the risk of developing GDM later in pregnancy. GDM is widespread among Asian women. If we find a high HbA1c value in the first trimester, they may be warned that their risk of developing GDM is higher later in pregnancy.

Conclusion

Elevated HbA1c in the first trimester of pregnancy is associated with a risk of development of GDM later in pregnancy. Thus it can be used as a screening test for prevention or early detection of GDM and thereby preventing the risks and harms associated with GDM to mother as well as fetus.

References

1. Punnose J, Malhotra RK, Sukhija K, et al. Glycated hemoglobin in the first trimester: A predictor of gestational diabetes mellitus in pregnant Asian Indian women. *Diabetes Res Clin Pract.* 2020;159:107953.
2. Fong A, Serra AE, Gabby L, et al. Use of hemoglobin A1c as an early predictor of gestational diabetes mellitus. *Am J Obstet Gynecol.* 2014;211(6):641.e1-7.
3. Valadan M, Bahramnezhad Z, Golshahi F, et al. The role of first-trimester HbA1c in the early detection of gestational diabetes. *BMC Pregnancy Childbirth.* 2022;22(1):71.
4. Lapolla A, Dalfrà MG, Lencioni C, et al.

Epidemiology of diabetes in pregnancy: a review of Italian data. *Diabetes Nutr Metab.* 2004;17(6):358-67.

5. American Diabetes Association. 2. Classification and Diagnosis of Diabetes. *Diabetes Care.* 2017;40(Suppl 1):S11-24.
6. Use of Glycated Hemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus: Abbreviated Report of a WHO Consultation. Geneva: World Health Organization; 2011.
7. Hughes RC, Rowan J, Florkowski CM. Is There a Role for HbA1c in Pregnancy? *Curr Diab Rep.* 2016;16(1):5.
8. Benaiges D, Flores-Le Roux JA, Marcelo I, et al. Is first- trimester HbA1c useful in the diagnosis of gestational diabetes? *Diabetes Res Clin Pract.* 2017;133:85-91.
9. Arbib N, Shmueli A, Salman L, et al. First trimester glycosylated hemoglobin as a predictor of gestational diabetes mellitus. *Int J Gynaecol Obstet.* 2019;145(2):158-63.