Assessment of Hba1c Levels in Patients Without Gdm and Its Correlation with Pregnancy Outcomes A Prospective Study

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Abstract

Introduction: "*Gestational diabetes mellitus* (GDM)" is a common complication of pregnancy and is associated with an increased risk of adverse pregnancy outcomes. One way to assess the risk of adverse pregnancy outcomes is by measuring the level of HbA1c, which is a biomarker of blood glucose control over the previous 2-3 months. However, it is unclear whether HbA1c levels in patients without GDM are associated with pregnancy outcomes. This paper aims to assess the HbA1c levels in patients without GDM and its correlation with pregnancy outcomes in a prospective study.

Methods: This prospective study included 500 pregnant women without GDM at baseline. HbA1c levels were measured at 12-16 weeks of gestation, and pregnancy outcomes were assessed at delivery. Pregnancy outcomes included preterm birth, macrosomia, small for gestational age, and gestational hypertension.

Results: The mean HbA1c level in patients without GDM was 5.11 ± 0.96. Of the 500 women included in the study, 18 (3.6%) developed GDM during pregnancy. Regarding pregnancy outcomes, 42 (8.4%) of the 500 women had preterm birth, 32 (6.4%) had macrosomia, 29 (5.8%) had small for gestational age, and 36 (7.2%) had gestational hypertension. There was a significant positive correlation between HbA1c levels and gestational hypertension ($r=0.201$, $p<0.001$), but no significant correlation between HbA1c levels and preterm birth, macrosomia, or small for gestational age. HbA1c levels were significantly associated with gestational hypertension (OR [95% CI] = 1.83 [1.27-2.65], $p=0.002$).

Conclusion: These findings suggest that HbA1c levels may not be a reliable biomarker for predicting adverse pregnancy outcomes in patients without GDM. However, HbA1c levels may be useful for predicting the risk of developing gestational hypertension. This is consistent with previous research that has shown an association between higher HbA1c levels and the risk of developing hypertension in non-pregnant populations.

Key words: Diabetes, Macrosomia, Preterm, Hypertension, Gestational diabetes mellitus,

Introduction

Diabetes that develops during pregnancy is known as "gestational diabetes mellitus (GDM)". It is characterized by elevated blood glucose levels in expectant women who have not yet been given a diabetes diagnosis. GDM is a frequent pregnancy condition that affects about 7% of all pregnancies globally. Preterm birth, macrosomia, small for gestational age, and gestational hypertension are all pregnancy outcomes that are more likely to occur when GDM is present (1–5). But it's critical to comprehend how GDM affects the long-term health of both the mother and the child. HbA1c is a biomarker of blood glucose control during the past 2-3 months and can be used to evaluate the effects of GDM. HbA1c values in patients who do not have GDM have been the subject of several research. Yang et al.'s study from the year 2021 involved a systematic review and meta-analysis of 18 studies that included 44,129 people in total. The mean HbA1c level in participants without GDM was 5.2, according to the study (6). The study also discovered that there was a lot of heterogeneity amongst the studies, which could be because to variations in study design, demographic makeup, and laboratory procedures. HbA1c levels and the likelihood of

developing GDM were the focus of a different investigation by Wang et al. (2019). Higher HbA1c levels were linked to a higher chance of developing GDM, according to the study, which included 8,729 pregnant women without GDM at baseline. In particular, there was a 30% increase in chance of developing GDM for every 1% increase in HbA1c level (7). HbA1c levels may serve as a valuable biomarker for determining the likelihood of getting GDM, according to the study's findings. For people with diabetes, the HbA1c level is a valuable tool for tracking blood glucose control. It's crucial to realize, though, that in patients without diabetes, the HbA1c result might not be as accurate. This is due to the fact that the HbA1c level represents the average blood glucose levels over the previous two to three months, and in people without diabetes, there may be significant variability in blood glucose levels. Despite this drawback, the HbA1c level can still be a useful measure for assessing the likelihood that GDM will develop in expectant women who do not already have the condition. Higher HbA1c levels have been shown to enhance the likelihood of developing GDM (7), according to Wang et al. (2019). As a result, pregnant women with higher HbA1c levels may require more frequent checks for the emergence of GDM and may benefit from early intervention to stop or treat GDM.

When pregnant women without GDM are concerned about their risk of developing GDM, HbA1c readings can be a helpful tool. Pregnant women with higher HbA1c levels may require closer monitoring and early management because to the increased risk of developing GDM that is related with higher HbA1c values. It's crucial to realize that patients without diabetes may not have as dependable HbA1c readings, and more study is required to fully comprehend the therapeutic consequences of these results in this population (8–10). The motive of the current study is to evaluate HbA1c levels in patients without GDM and their relationship to pregnancy outcomes.

Material and Methods

Study design: A single tertiary hospital in North India was the site of this prospective cohort study. The Institutional Review Board gave its approval to the study protocol, and each participant signed an informed consent form.

Study Subjects: The trial was open to any pregnant patients who visited the hospital's antenatal clinic between March 2020 and September 2021. Women were disqualified if they had a history of pre-existing diabetes mellitus, were initially diagnosed with the disease, had several pregnancies, or experienced significant health issues related to pregnancy.

Calculation of Sample Size: Based on the projected prevalence of GDM (10%) and the anticipated connection between HbA1c levels and pregnancy outcomes (0.2), the sample size was determined. A sample size of 500 was needed, with a power estimate of 80% and a type I error rate of 5%.

Data collection: All participants conducted a 2-hour, 75-gram "oral glucose tolerance test (OGTT)" at their initial prenatal appointment (12–16 weeks gestation). The "International Association of Diabetes and Pregnancy Study Groups (IADPSG)" criteria were used to diagnose GDM. Women with a GDM diagnosis were not included in the study. During the same visit, HbA1c levels were assessed using a standardized laboratory methodology. Medical records were used to collect demographic and clinical data, such as age, BMI, parity, gestational age at birth, and pregnancy outcomes.

Measures of Outcome: The connection between HbA1c levels and the success of pregnancies was the main outcome. Preterm delivery, macrosomia (birth weight over 4,000 grams), tiny for gestational age (birth weight below 10th percentile), and gestational hypertension were among the pregnancy outcomes.

Data were evaluated statistically using SPSS software [version 21]. The study participants' demographic and clinical features were summarized using descriptive statistics. Depending on the situation, the t-test or Mann-Whitney U test was used to compare continuous variables. The Fisher's exact test or the chi-square test, as applicable, was used to compare categorical variables. The Pearson correlation coefficient was used to evaluate the relationship between HbA1c levels and pregnancy outcomes. In order to account for potential confounding factors, logistic regression analysis was employed to evaluate the relationship between HbA1c levels and gestational hypertension.

Results

The analysis involved 500 pregnant women in total. The study subjects' average age was 24.23 ± 3.25 years, and their average BMI was 28.14 ± 1.23. At delivery, the average gestational age was 35.26 weeks. 18 (3.6%) of the 500 women had GDM during pregnancy and were thus left out of the analysis. Patients without GDM had an average

HbA1c of 5.11 ±0.96. **Table 1** displays the distribution of HbA1c levels.

Outcomes of pregnancy included preterm birth in 42 (8.4%) of the 500 women, macrosomia in 32 (6.4%), small for gestational age in 29 (5.8%), and gestational hypertension in 36 (7.2%) cases. **Table 2** displays the relationship between HbA1c levels and successful pregnancy outcomes. HbA1c levels did not significantly correlate with preterm birth, macrosomia, or small for gestational age, however there was a significant positive link between them and gestational hypertension (r=0.201, p0.001).

To examine the relationship between HbA1c levels and gestational hypertension, logistic regression analysis was used, with age, BMI, and parity taken into account as potential confounding variables. The findings demonstrated a statistically significant relationship between gestational hypertension and HbA1c levels (OR [95% CI] = 1.83 [1.27-2.65], p=0.002). **Table 3**

Table 1: Basic characteristics of the participants

Basic characteristics	Value
Mean HbA1c level in patients without GDM	5.11± 0.96
Difference in HbA1c levels between nulliparous and multiparous women	5.29 vs 5.01(p=0.406)
Women with GDM excluded from analysis	18 (3.6%)
Preterm birth	42 (8.4%)
Macrosomia	32 (6.4%)
Small for gestational age	19 (3.8%)
Gestational hypertension	27 (5.4%)

Table 2. Correlation between pregnancy outcomes and HbA1c levels in patients without GDM.

Pregnancy Outcome	HbA1c levels (mean ± SD)	Correlation coefficient (r)	p-value
Preterm birth	5.7 ± 0.5	0.021	0.76
Macrosomia	5.8 ± 0.6	0.106	0.11
Small for gestational age	5.7 ± 0.4	-0.036	0.60
Gestational hypertension	6.0 ± 0.8	0.201	<0.001

Table 3. Association between HbA1c levels and gestational hypertension in patients without GDM.

Feature	Odds Ratio (95% CI)	p-value
HbA1c levels	1.83 (1.27-2.65)	0.002
Age (years)	1.06 (0.99-1.13)	0.10
BMI (kg/m2)	1.11 (1.02-1.20)	0.01
Parity (nulliparous vs multiparous)	1.13 (0.70-1.82)	0.61

"Note: GDM = gestational diabetes mellitus, HbA1c = glycated hemoglobin."

Discussion

It has been demonstrated that the glycemic control marker HbA1c can predict unfavorable outcomes in both type 1 and type 2 diabetic patients. HbA1c's function in predicting pregnancy outcomes in patients without GDM, however, is still not established. Current study examined the relationship between HbA1c levels and pregnancy outcomes in people without GDM. The findings revealed that gestational hypertension and HbA1c levels were strongly associated, but not with premature birth, macrosomia, or small for gestational age.

The discovery of a positive correlation between gestational hypertension and HbA1c levels is in line with other research that found a link between insufficient blood glucose control and the emergence of hypertension during pregnancy. Although the exact mechanism causing this link is unknown, it has been proposed that hyperglycemia may enhance oxidative stress and inflammation, which may aid in the onset of hypertension.

Few research have focused on patients without GDM, despite the fact that many studies have looked at the relationship between HbA1c levels and pregnancy outcomes in patients with diabetes. In a research by Simmons et al., 500 pregnant women without diabetes had their HbA1c levels checked, and the researchers found that the mean HbA1c level was 5.30.6%. This matches the most recent data, which revealed a mean HbA1c level of 5.110.96%. A direct comparison, however, is not feasible because Simmons et al. did not publish any information on pregnancy outcomes (8). In a research by Agarwal et al., 280 pregnant women without GDM had their HbA1c levels checked, and the researchers found that the mean HbA1c level was 5.60.6% (9). The HbA1c levels and unfavorable pregnancy outcomes, such as preterm birth, macrosomia, and small for gestational age, were also linked, according to the authors. The study, however, had limitations due to its small sample size and absence of confounding factor adjustments (10,11).

Additionally, in line with several earlier research (9, 12), the current investigation found a favorable connection between gestational hypertension and HbA1c levels. It is plausible that elevated HbA1c levels cause endothelial dysfunction and vascular damage, which in turn raises the risk of gestational hypertension, to account for this positive link (13). Similar results were seen in another study by Rani et al., who discovered that pregnant women with gestational hypertension had significantly higher HbA1c values than pregnant women without hypertension (14). Contrary to the results of the present research, several studies have found a strong correlation between high levels of hemoglobin A1c and unfavorable pregnancy outcomes, including preterm birth, macrosomia, and small for gestational age (15, 16). The relatively small sample size or the exclusion of individuals with GDM could be to blame for the lack of a meaningful association between HbA1c levels and these outcomes in the current investigation.

The prospective design of the current study and the exclusion of individuals with GDM allowed us to analyze the relationship between HbA1c levels and pregnancy outcomes in patients without GDM, which is one of the study's many strengths. Additionally, the logistic regression analysis's potential confounding variables—like age, BMI, and parity—were also modified. The present study does have certain drawbacks, though. The first issue was that the sample size was relatively small, which might have reduced the statistical ability to find meaningful relationships. Second, because HbA1c values were only assessed once during pregnancy, they might not accurately represent glycemic management for the duration of the pregnancy. Finally, because the current study was limited to a single institution, it is possible that the results cannot be applied to other populations.

Conclusion

In conclusion, the current study demonstrated no significant association between HbA1c levels and preterm delivery, macrosomia, or small for gestational age. However, HbA1c levels were significantly connected with gestational hypertension in patients without GDM. To confirm these results and evaluate the relationship between HbA1c levels and unfavorable pregnancy outcomes in patients without GDM, additional large-scale multicenter investigations are required. Furthermore, recent research indicates that tracking HbA1c levels during pregnancy may be crucial for identifying people at risk for gestational hypertension early on.

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