Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2023i1.251
*Biol. Clin. Sci. Res. J., Volume, **2023**: 251*
Original Research Article

RELATIONSHIP BETWEEN HEMOGLOBIN A1C LEVELS IN EARLY PREGNANCY AND ADVERSE OUTCOMES AMONG NON-DIABETIC PATIENTS

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(Received, 02nd November 2022, Revised 27th February 2023, Published 21st April 2023)

Abstract: *This study was designed to assess the effects of increased hemoglobin A1c in the first trimester on adverse perinatal outcomes in patients without gestational diabetes mellitus. A prospective study was conducted in the Obstetrics and Gynecology Department of Buch International Hospital Multan from January 2022- January 2023. A total of 160 women with singleton pregnancies in their first trimester and elevated hemoglobin A1c were included in the study. The following outcomes were evaluated in patients: miscarriage, shoulder dystocia, preterm delivery <37 weeks, macrosomia, small or large for gestational age, hypertensive disorders of pregnancy, third- or fourth-degree lacerations, operative vaginal delivery, cesarean delivery, neonatal hypoglycemia, neonatal jaundice, NICU admission, and intrauterine fetal demise. The multivariate analysis evaluated the relationship between hemoglobin A1c and adverse outcomes. The Hb1Ac level in patients ranged from 5.7-6.4%. Elevated levels were noted in elderly patients who were multiparous, obese, and diagnosed with chronic hypertension. 5.6% of patients had a preterm delivery, and 31.2% had a c-section delivery. 7.5% had a likelihood of hypertensive pregnancy disorder, and 10.6% were likely to deliver a macrosomic infant. Based on the results, it can be concluded that elevated hemoglobin A1c levels are significantly associated with preterm birth in patients without gestational diabetes.*

Keywords: Hemoglobin Hba1c, First Trimester, Pregnant Women, Gestation Diabetes

Introduction

Pregnant women with glucose intolerance are at high risk of developing adverse perinatal outcomes (Valadan et al., 2022; Wu et al., 2018). Pregnant women with diabetes have high levels of HbA1c in the first trimester, especially which may lead to abortion, preeclampsia, preterm birth, and congenital abnormalities (Mellitus, 2018). This high hemoglobin A1c also increases the risk of gestational diabetes in early pregnancy. The gestation of diabetes mellitus leads to adverse perinatal and maternal outcomes. However, very little data is available on perinatal outcomes in pregnant women without gestational diabetes.

A study of the New Zealand population with high hemoglobin A1c levels, i.e., more than 5.9%, showed that such patients presented a high probability of preterm delivery, shoulder dystocia, perinatal death, high birth weight infants, and hypertensive disorders. These results are inconsistent with subsequent studies after this (Fong et al., 2014; Osmundson et al., 2016; Rasmussen et al., 2020). This may be due to a difference in patients' data about gestation age, ethnicity, and gestational diabetes mellitus. This study assessed the effects of increased hemoglobin A1c in the first trimester on adverse perinatal outcomes in patients without gestational diabetes mellitus

Methodology

A prospective study was conducted in the Obstetrics and Gynecology Department of Buch International Hospital Multan from January 2022- January 2023. The study included 160 women with singleton pregnancies in their first trimester and elevated hemoglobin A1c (5.7-6.4%). The patients with diabetes mellitus, hemoglobin A1c levels at 6.5%, HbA1c screening done after completion of the 16th week, and multigravida were excluded from the study. Patients were included after their informed consent. The ethical board of the hospital approved the study.

All the patients underwent hemoglobin A1c screening, and patient data regarding demographic, obstetric, and pregnancy outcomes was noted. Pregnancy outcomes including miscarriage, shoulder dystocia, preterm delivery <37 weeks, macrosomia, small or large for gestational age, hypertensive disorders of pregnancy, third- or fourth-degree

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lacerations, operative vaginal delivery, cesarean delivery, neonatal hypoglycemia, neonatal jaundice, NICU admission, and intrauterine fetal demise.

SPSS version 23 was used for data analysis. The chi-squared test was performed for categorical variables, while continuous variables were assessed by t-test. The multivariate analysis assessed the relation between hemoglobin A1c and adverse perinatal outcomes.

Results

A total of 160 pregnant women were analyzed for this study. The average gestation age at the time of screening was 9.9 weeks. The patients were mostly older, obese, multiparous, and had hypertensive disorders. The clinical features of patients are shown in Table I.

Similarly, the women with elevated hemoglobin HbA1c mostly had a preterm delivery, macrosomic neonate, hypertensive disorders, and underwent C-sections. However, these patients had less possibility of third- or fourth-degree lacerations. Pregnancy and delivery outcomes of patients are presented in Table II. The multivariate analysis of the effect of HbA1c on the adverse outcome is shown in Table III.

Table I: Clinical features among pregnant women with elevated hemoglobin A1c

	Patients with elevated HbA1c (n= 160)	Probability
Maternal age (mean, years)	28.2 (5.4)	0.003
Gestation age at screening	9.9 (2.1)	0.50
Nulliparous	55 (34.3%)	<0.001
BMI at first prenatal visit (mean)	31.8 (7.6)	<0.001
BMI at the first prenatal visit		<0.001
Underweight/ Normal	32 (20%)	
Overweight	40 (25%)	
Obese	88 (55%)	
Chronic hypertension	12 (7.5%)	0.010

Table II: Pregnancy and delivery outcomes in patients

	Patients with elevated HbA1c (n= 160)	P value
Birth outcome		0.005
Spontaneous preterm birth	9 (5.6%)	
Predicted term	10 (6.2%)	
Actual term	141 (88.1%)	
Gestation age at delivery (SD, weeks)	37.4 (2.1)	0.001
Mode of delivery		0.035
Cesarean	50 (31.2%)	
Spontaneous vaginal	100 (62.5%)	
Operative vaginal	10 (6.2%)	
Indication of cesarean		0.629
Planned repeat	62 (38.7%)	
Malpresentation	7 (4.3%)	
Nonreassuring fetal status	37 (23.1%)	
Labor arrest	22 (13.7%)	
Other	32 (20%)	
Shoulder dystocia	7 (4.3%)	0.25
Third/fourth-degree laceration	3 (1.8%)	0.002
Preeclampsia	50 (31.2%)	0.001
Maternal hospital stay (Median, days)	2 (2,3)	0.17
Birth weight (mean, g)	3,198.4 (578.4)	0.22
Large for gestation age infant	9 (5.6%)	0.50
Small for gestation age infant	48 (30%)	0.24
Macrosomia	17 (10.6%)	0.012
Neonatal data		

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ICU admission	18 (11.2%)	0.43
Hypoglycemia	9 (5.6%)	0.61
Hyperbilirubinemia	10 (6.2%)	0.35
Hospital stay (median, days)	2 (2,3)	0.52

Table III: **Multivariate analysis**

	Crude OR (95% CI)	**aOR (95% CI)**
Preterm birth	1.76 (1.20-2.55)	1.45 (0.98-2.14)
Spontaneous preterm delivery	1.65 (0.95-2.80)	1.72 (0.97-3.06)
Medically indicated preterm birth	1.85 (1.10-3.00)	1.20 (0.72-2.08)
Cesarean delivery	1.25 (0.96-1.60)	0.90 (0.68-1.19)
Hypertensive disorders	1.52 (1.18-1.15)	1.21 (0.92-1.63)

Discussion

We conducted a study to assess the relationship between high HbA1c and adverse perinatal outcomes in non-diabetic women. We found that high values of HbA1c in the first trimester were associated with preterm delivery. After adjusting for confounders like age, nulliparity, and maternal BMI, this risk remained significant. These results highlight the association between metabolic abnormalities and diabetes diagnosis that, in turn, impacts obstetric outcomes (Chen et al., 2019; Hughes et al., 2014; Siricharoenthai and Phupong, 2020).

Another study conducted in New Zealand which conducted HbA1c screening in patients with elevated levels, found that it was associated with shoulder dystocia, large for gestation age, early birth, preeclampsia, congenital disorders, and fetal death (Hughes et al., 2014). However, this study included patients with only one ethnic background and did not adjust for confounders associated with perinatal outcomes. Additionally, they considered an HbA1c level of 5.9%, limiting the results.

The confounders in our study remained significant after adjustment but predicted preterm delivery, hypertension disorder, and C-section delivery were not significant after adjustment of factors.

Mane et al. also used a 5.7% HbA1c and concluded that patients with hemoglobin A1c levels less than 5.9% were at high risk of preeclampsia and macrosomia(Mañé et al., 2019). In comparison, Rasmussen et al. found that a less than 5.7% HbA1c level was not associated with birth weight (Rasmussen et al., 2020). This difference may be due to inclusion criteria and study population.

A HAPO study found that elevated hemoglobin A1c levels were significantly related to preeclampsia, C-section delivery, preterm delivery, and birth weight in more than 90% of patients without diabetes (Lowe et al., 2012). HbA1c screening was done at 24-32 weeks; hence this study does not contain early pregnancy results. This study does not specify the number of patients having an elevated hemoglobin A1c level. On the other hand, our study focuses on first-trimester women and states the exact number of patients suffering adverse outcomes.

Another study in Washington was conducted to analyze the outcomes in pregnant women by HbA1c screening >20 weeks (Chen et al., 2019). After adjusting the cofounders, they concluded that no significant difference of association was noted between HbA1c levels and preeclampsia, preterm birth, and C-section delivery in comparison with normal patients. Only 3.4% of patients in this reached the HbA1c cut-off level.

Our study has some limitations. The study period was smaller, so no results were found for the later pregnancy period, and a small population of the same ethnicity was selected for the study.

Conclusion

Elevated hemoglobin A1c levels are significantly related to preterm delivery in patients without gestational diabetes.

Conflict of interest

The authors declared absence of conflict of interest.

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