

Original Article

Relationship Between HbA1c in 3rd Trimester & Pregnancy Outcome of Patients with Gestational Diabetes Mellitus (GDM)

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Abstract

Background: Gestational Diabetes Mellitus (GDM) is a condition characterized by glucose intolerance with onset or first recognition during pregnancy. It affects approximately 7% of all pregnancies and is primarily associated with increased insulin resistance and inadequate compensatory insulin secretion. GDM poses significant risks for both maternal and neonatal health, including complications such as preeclampsia, macrosomia, neonatal hypoglycemia, and an increased likelihood of developing type 2 diabetes mellitus later in life. Elevated maternal HbA1c levels in the third trimester have been linked to increased risks of complications such as preterm delivery, vulvovaginitis, polyhydramnios, and neonatal issues including hypoglycemia and macrosomia. Monitoring HbA1c levels during pregnancy, alongside blood glucose, may provide valuable insights into managing euglycemia and reducing the risks of these complications. This study aims to evaluate the impact of third-trimester HbA1c levels on pregnancy outcomes, focusing on both maternal and fetal health in women with controlled and uncontrolled serum HbA1c levels. **Methods:** This cohort-type observational study was conducted at the Department of Gynaecology and Obstetrics, BIRDEM-II General Hospital, Dhaka, from July 2019 to June 2020. The study included pregnant women diagnosed with Gestational Diabetes Mellitus (GDM) attending the outpatient department or admitted to the hospital. Participants were categorized into two groups based on third-trimester HbA1c levels: those with HbA1c >6.0% (uncontrolled group) and those with HbA1c ≤ 6.0% (controlled group). A sample size of 100 was determined by consecutive purposive sampling, with 50 participants in each group. During the third trimester, 5 cc of venous blood was collected from each participant for HbA1c and blood glucose level testing. Participants were monitored for fetomaternal outcomes during the follow-up period, which lasted until the puerperium. Data were collected using a pre-structured form, and the researcher personally gathered all information to ensure accuracy. After data collection, the information was carefully reviewed, and inconsistencies were corrected. **Results:** This prospective cohort study conducted at BIRDEM-II General Hospital, Dhaka, aimed to investigate the impact of third-trimester HbA1c levels on pregnancy outcomes in Gestational Diabetes Mellitus (GDM) patients. The study included 100 participants, categorized into controlled (HbA1c ≤ 6%) and uncontrolled (HbA1c > 6%) groups. The results demonstrated that poor glycemic control was significantly linked to increased rates of polyhydramnios, preterm delivery, macrosomia, and neonatal complications including hypoglycemia, hyperbilirubinemia, and respiratory distress syndrome (RDS). Additionally, newborns in the poorly controlled group had significantly higher rates of NICU admission, incubator care, and resuscitation at birth. However, there was no significant difference in mode of delivery or maternal complications between the two groups. These findings suggest that poor HbA1c control in the third trimester is linked to adverse maternal and fetal outcomes in GDM pregnancies. **Conclusion:** The study found that GDM patients with HbA1c >6.0% in the third trimester had higher rates of complications such as polyhydramnios, preterm delivery, macrosomia, hypoglycemia, hyperbilirubinemia, RDS, NICU admissions, incubator care, and resuscitation at birth, compared to those with HbA1c ≤6.0%. However, differences in vulvovaginitis, oligohydramnios, PPH, and UTIs were not statistically significant.

Key Words: Gestational Diabetes Mellitus (GDM), HbA1c, Characterized, Preeclampsia.

Introduction: Gestational Diabetes Mellitus (GDM) currently defined as any degree of glucose intolerance with an onset or first recognition during current pregnancy.^{1,2} Women with gestational diabetes are characterized by relatively diminished insulin secretion and pregnancy-induced insulin resistance, which is

primarily observed in skeletal muscle tissue (Matouleibi *et al.*, 2015). About 7% of all pregnancies are complicated by GDM³. The incidence of vulvovaginitis, preterm delivery, and polyhydramnios was significantly higher in the third trimester among women with elevated HbA1c levels. The rate of normal vaginal delivery was higher

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in patients with normal HbA1c levels compared to those with elevated (uncontrolled) HbA1c levels. The incidence of postpartum hemorrhage (PPH) was significantly greater in the elevated HbA1c group, both in cases of normal vaginal delivery and caesarean section. Neonatal complications were also more frequent in the uncontrolled HbA1c group, with higher rates of hypoglycemia, hyperbilirubinemia, respiratory distress syndrome (RDS), macrosomia, and birth asphyxia.⁴

Hemoglobin A (HbA) is the predominant form of adult hemoglobin, accounting for approximately 90% of the total hemoglobin content. When hemoglobin A (HbA) binds with glucose in the bloodstream, it forms glycated hemoglobin, known as HbA1c. Increasing evidence suggests that elevated maternal serum HbA1c levels during the antenatal period are associated with a higher risk of both maternal and neonatal complications.⁵ HbA1c is a specific glycated fraction formed by the non-enzymatic binding of glucose to the N-terminal valine of the β -chain of hemoglobin A (HbA). This process occurs over the lifespan of red blood cells and reflects the average blood glucose concentration over the preceding 8 to 10 weeks. Unlike daily blood glucose levels, HbA1c is not influenced by short-term fluctuations, making it a reliable marker for long-term glycemic control.⁶ HbA1c levels tend to be lower across all three trimesters of a normal pregnancy. However, there is currently no consensus on the reference range of HbA1c for pregnant women at different stages of gestation. To reduce the risk of adverse pregnancy outcomes in women with Gestational Diabetes Mellitus (GDM), it is essential to maintain strict euglycemic control through appropriate treatment and monitoring. Daily self-monitoring of blood glucose is recommended for all patients with Diabetes in Pregnancy (DIP) and Gestational Diabetes Mellitus (GDM) to achieve and maintain euglycemic control. However, isolated measurements of fasting and postprandial blood glucose may not accurately reflect

the overall glycemic status. Therefore, glycated hemoglobin (HbA1c) can serve as a valuable adjunctive parameter, providing an estimate of average blood glucose levels over the preceding two to three months.⁷

The role of HbA1c in pregnancies complicated by pre-gestational diabetes is well established. According to the 2015 guidelines from the National Institute for Health and Care Excellence (NICE), HbA1c measurement is recommended at the first antenatal visit for all pregnant women with pre-existing diabetes. Additionally, it is advised to consider measuring HbA1c during the second and third trimesters to help assess the level of risk throughout the pregnancy.^{8, 4}

Therefore, the present study designed to assess third-trimester HbA1c levels & their impact on pregnancy outcomes from our clinical perspective. This study was undertaken to evaluate maternal and fetal outcomes in gestational diabetes mellitus based on controlled versus uncontrolled serum HbA1c levels.

Materials & Method

This cohort-type observational study was conducted in the Department of Gynaecology and Obstetrics at BIRDEM-II General Hospital, Shegunbagicha, Dhaka, over a one-year period from July 2019 to June 2020. The study included pregnant women diagnosed with gestational diabetes mellitus (GDM), who either attended the outpatient department or were admitted to the hospital. Participants were divided into two groups based on their third-trimester HbA1c levels: those with HbA1c levels greater than 6.0% were categorized as the uncontrolled group (cohort group), and those with HbA1c levels equal to or less than 6.0% were classified as the controlled group (comparison group).

The sample size was calculated using a standard formula for comparing two proportions, based on neonatal hyperbilirubinemia rates reported by Sengupta et al.⁴ (11.76% vs. 33.73%). With 95% confidence and 80% power, 110 participants (55 per

group) were required. However, 100 participants were enrolled using consecutive purposive sampling due to practical constraints.

From each patient, 5 cc of venous blood was collected during the third trimester for laboratory measurement of HbA1c and blood glucose profile. Based on HbA1c levels, patients were allocated to either the uncontrolled or controlled group. All participants were followed up at intervals of 15 to 30 days until the puerperium to monitor and evaluate fetomaternal outcomes.

Data for this study were collected using a pre-structured data collection sheet. Relevant socio-demographic information, clinical findings, and laboratory values were recorded. The researcher herself collected all data to ensure consistency and accuracy. Once data collection was complete, the information was meticulously compiled, edited, and checked for discrepancies. Any omissions or inconsistencies were corrected during the data screening process.

For statistical analysis, all data were entered into a computer and analyzed using the Statistical Package for Social Sciences (SPSS), version 22.0 (SPSS Inc., Chicago, IL, USA). The results were presented in tabular form. Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as means and standard deviations. A p-value of less than 0.05 was considered statistically significant.

Prior to the commencement of the study, the research protocol was reviewed and approved by the Ethical Review Committee of BIRDEM, ensuring that all ethical standards for conducting human research were upheld.

Results

This prospective cohort study was conducted in the Department of Obstetrics and Gynaecology, BIRDEM-II General Hospital, Dhaka to find out the relationship of the HbA1C level in 3rd trimester with pregnancy outcome in GDM patients. The results are as follows:

Table I: Demographic profile of the study subjects (N=100)

	Frequency (n)	Percentage (%)
Age (years)		
≤25	15	15.0
26 – 30	40	40.0
31 – 35	29	29.0
≥36	16	16.0

Mean ± SD	30.55 ± 4.80	
Min – max	19 – 40	
Occupations		
House wife	81	81.0
Service	17	17.0
Others	2	2.0

Table I shows distribution of the study subjects according to age. Most of the study subjects were within 26 to 35 years of age. Mean age was 30.55 ± 4.80 years within the range of 19 – 40 years. Majority of the study subjects were housewife followed by service holder.

Table II: Distribution of the study subjects according to complications of current pregnancy (N=100)

	Total n (%)	Poor control HbA1c >6% (n=53)	Well control HbA1c <6% (n=47)	p-value	RR
Polyhydramnios	18 (18.0)	16 (30.2)	2 (4.3)	.001	7.09
Oligohydramnios	15 (15.0)	10 (18.9)	5 (10.6)	.250	1.77
Vulvovaginitis	16 (16.0)	9 (17.0)	7 (14.9)	.776	1.14

Chi-Square test was done

Table II shows distribution of the study subjects according to history of complications of current pregnancy. Most common complications were Polyhydramnios (18.0%), vulvovaginitis (16.0%) and Oligohydramnios (14.0%). Polyhydramnios was significantly more common in patients with poor control of HbA1c compared to those with well-controlled HbA1c. Vulvovaginitis and oligohydramnios were also found more in poor control HbA1c patients but the differences were not statistically significant between the groups.

Table III: Distribution of the study subjects according to their selected clinical characteristics (N=100)

Obstetric history	Frequency (n)	Percentage (%)
Married for (years)	7.77 ± 5.48	0.50 – 23
Para	1.60 ± 1.30	0 – 5
Gravid	2.57 ± 1.33	1 – 6
ALC	5.68 ± 3.33	1 – 18
Gestational age (weeks)	37.28 ± 1.56	31 – 40
Pre term	19	19.0
Term	81	81.0
Irregular menstrual history	19	19.0
Antenatal care (irregular)	17	17.0
Previous H/O GDM	4	4.0
Family H/O DM	52	52.0

Table III shows obstetric history of the study subjects. Mean para was 1.60 ± 1.30 and gravid was 2.57 ± 1.33 . Mean gestational age was 37.28 ± 1.55 weeks, pre term delivery was 19.0% and term delivery was 81.0%. Irregular menstrual history was in 19.0% case. Irregular antenatal care was observed in 17.0% cases. 4.0% of cases had a previous history of GDM, and 52.0% had a family history of DM.

Table IV: Relationship of HbA1c Level at 3rd trimester with mode of delivery and maternal outcome of the study subjects (N=100)

	Total n (%)	Poor control HbA1c >6% (n=53)	Well control HbA1c <6% (n=47)	p-value	RR
Mode of delivery					
NVD	12 (12.0)	8 (15.1)	4 (8.5)	.312	1.30
CS	88 (88.0)	45 (84.9)	43 (91.5)		
Maternal complications					
PPH	9 (9.0)	7 (13.2)	2 (4.3)	.161	1.54
UTI	5 (5.0)	4 (7.5)	1 (2.1)	.363	1.55

Fisher's Exact test was done

Table IV shows mode of delivery of the study subjects. Majority of the delivery was done in caesarean section (88.0%). There was no significant difference in mode of delivery between well and poor glycemic control. PPH was found in 9 (9.0%) cases and UTI in 5 (5.0%) cases. There was no statistically significant difference in the mode of delivery between well-controlled and poorly controlled HbA1c groups.

Table V: Relationship of HbA1c level with Fetal complications (N=100)

Foetal complication	Total	Poor controlled HbA1c > 6% (n=53)	Well controlled HbA1c ≤ 6% (n=47)	p-value	RR
IUGR	21 (21.0)	15 (28.3)	6 (12.8)	^a .057	1.48
Congenital anomalies	5 (5.0)	4 (7.5)	1 (2.1)	^b .367	1.55
Preterm	19 (19.0)	14 (26.4)	5 (10.6)	^a .045	1.53
Macrosomia	6 (6.0)	6 (11.3)	0 (0.0)	^b .028	

^aChi-Square test and ^bFisher's Exact test was done

Table V shows fetal complication. IUGR was found in 21 (21.0%) cases, congenital anomalies in 5 (5.0%) cases, preterm in 19 (19.0%) cases and macrosomia in 6(6.0%) cases. There was no significant difference in IUGR and congenital anomalies between well and poor controlled HbA1c. Preterm delivery and macrosomia were significantly more common in patients with poorly controlled HbA1c than in those with well-controlled HbA1c.

Table VI: Newborn outcome according to 3rd trimester glycemic status (N=100)

New born outcome	Total	HbA1c > 6% (n=53)	HbA1c ≤ 6% (n=47)	p-value	RR
Birth weight	2.78±0.68	2.85±0.8	2.69±0.53	^a .248	
≤2.5	32 (32.0)	16 (30.2)	16 (34.0)	^b .830	0.92
2.6 - 3.9	62 (62.0)	31 (58.5)	31 (66.0)		
≥4.0	6 (6.0)	6 (11.3)	0 (0.0)	^c .028	
New born complications					
Hypoglycemia	8 (8.0)	8 (15.1)	0 (0.0)	^c .005	
Hyperbilirubinaemia	6 (6.0)	6 (11.3)	0 (0.0)	^c .028	
RDS	14 (14.0)	11 (20.8)	3 (6.4)	^c .046	1.61
Jaundice	12 (12.0)	8 (15.1)	4 (8.5)	^c .312	1.30
NICU admission	31 (31.0)	25 (47.2)	6 (12.8)	^b .001	1.99
Incubator care (required)	38 (38.0)	29 (54.7)	9 (19.6)	^b .001	1.97
Phototherapy (required)	22 (22.0)	14 (26.4)	8 (17.0)	^b .258	1.27
Blood transfusion (required)	11 (11.0)	8 (15.1)	3 (6.4)	^c .165	1.44
Resuscitation at birth	50 (50.0)	36 (69.2)	14 (29.8)	^b .001	2.12
Neonatal death	8 (8.0)	6 (11.3)	2 (4.3)	^c .276	1.47

^aUnpaired t test, ^bChi-Square test and ^cFisher's Exact test was done

Table VI shows New born outcome according to 3rd trimester glycemic status. Mean weight was 2.78 ± 0.68 kg. LBW was 32.0% and overweight was 6.0%. Regarding complications, 8.0% new born had hypoglycaemia, 6.0% had Hyperbilirubinaemia, 14.0% had RDS, 12.0% had jaundice and 31.0% were needed NICU admission. Hypoglycemia, hyperbilirubinemia, and RDS were significantly more common in poor controlled group than good controlled group. NICU admission required significantly higher number of poor controlled group than good controlled group. Incubator care required significantly more in poor controlled group than good controlled group. Resuscitation at birth significantly more in poor controlled group than good controlled group. It shows that GDM patients with Poor control of blood sugar (HbA1c > 6%) had relative risk of developing different newborn complications such as RDS (RR 1.61; p =0.046); Jaundice (RR 1.30; p=0.312); NICU admission (RR 1.99; p= 0.001); Incubator care (required) (RR 1.97; p=0.001); Phototherapy (RR 1.27; p=0.258); blood transfusion (required) (RR 1.44; p=0.165), Resuscitation at birth (RR 2.12, p=0.001). Although the relative risk for newborn death was greater than one, it was not statistically significant

Discussion

The highest incidence of GDM occurred in the 26-35 years age group, with a mean age of 30.55 ± 4.80 years, ranging from 19 to 40 years. Similar finding was observed in the study of Shingala et al. (2019), Seshiah et al. (2008), Groof et al. (2019) and Wahabi et al., (2014).^{9, 10, 11, 12}

HbA1c level 6.0% was considered normal. In the third trimester, 47.0% of patients had well-controlled HbA1c, while 53.0% had poorly controlled HbA1c. Kaur *et al.* (2019) revealed that 54.7% had HbA1c levels <5.8% and 45.3% had HbA1c $\geq$ 5.8% done at 28-32 weeks. Also when HbA1c levels done at 37-39 weeks period of gestation at the time of delivery, 52.8% patients had <5.8% and 47.2% had HbA1c $\geq$ 5.8%.¹³

In this study, polyhydramnios was found significantly higher in poor control HbA1c patients comparing well control HbA1c patients (30.2% vs 4.3% $p=0.001$). Vulvovaginitis (17.0% vs 14.5% $p=0.776$) and oligohydramnios (18.9% vs 10.6% $p=0.250$) were also found more in poor control HbA1c patients but the differences were not statistically significant between the groups. Similar findings were observed in Kaur *et al.* (2019), where polyhydramnios was significantly more common in patients with poorly controlled HbA1c. (28.0% vs 3.6% $p=0.020$). Vulvovaginitis (21.6% vs 5.88% $p=0.020$) and polyhydramnios (21.7% vs 11.7% $p=0.030$) were found significantly higher in poor control HbA1c patients comparing well control HbA1c patients in the study of Sengupta *et al.*, (2012).^{13, 4}

Majority of the delivery was done in caesarean section (88.0%). There was no significant difference in mode of delivery between well and poor glycemic control at 3rd trimester. Similar finding was observed in the study of Kaur *et al.* (2019); but statistically higher rate of normal vaginal delivery (NVD) in women with controlled HbA1c level than uncontrolled (70.59% vs 10.84%, $p=0.01$). Rate of LUCS was high in women with uncontrolled HbA1c level (29.41% Vs 89.16%, $p=0.23$) which is statistically not significant (Sengupta *et al.*, 2012).^{13, 4}

In this study rate of Caesarean section in poor controlled HbA1c group was 84.9% at 3rd trimester which is equivalent to the study done by Sengupta *et al.*, (2012) (89.16%).⁴

Rate of PPH and UTI was found higher in poor control HbA1c than in well control HbA1c at 3rd trimester but the difference in PPH and UTI was not statistically significant between poor control and well control HbA1c. Similar finding was observed in the study of Kaur *et al.* (2019). In case of UTI similar finding also observed in the study of (Sengupta *et al.*, 2012), but the rate of PPH was significantly higher in uncontrolled HbA1c than that of controlled HbA1c in their study.^{13,4}

IUGR was found in 21 (21.0%) cases and Congenital anomalies in 5 (5.0%) cases in this study. Rate of IUGR and congenital anomalies was found higher in poor control HbA1c than in well control HbA1c at 3rd trimester but the difference in IUGR and congenital anomalies was not statistically significant between poor control HbA1c than in well control HbA1c. Similar finding was observed in the study of Sengupta *et al.* (2012) in case of IUGR.⁴

Hypoglycemia, Hyperbilirubinaemia and RDS were found significantly higher in poor HbA1c controlled mothers' neonates than good HbA1c controlled mothers' neonate at 3rd trimester. Similar finding was observed in the study of Sengupta *et al.* (2012). In the present study, the relative risk of maternal complications (PPH and UTI) associated with an HbA1c cutoff of 6% in the third trimester was greater than one, but these findings were not statistically significant."

New born outcome according to 3rd trimester glycemic status. It shows that GDM patients with Poor control of blood sugar (HbA1c > 6%) had relative risk of developing different newborn complications such as RDS (RR 1.61; $p=0.046$); Jaundice (RR 1.30; $p=0.312$); NICU admission (RR 1.99; $p=0.001$); Incubator care (required) (RR 1.97; $p=0.001$); Phototherapy (RR 1.27; $p=0.258$); blood transfusion (required) (RR 1.44; $p=0.165$), Resuscitation at birth (RR 2.12, $p=0.001$). Though, RR was more than one for newborn death, but that was not statistically significant.

Fetal complications, such as preterm delivery and macrosomia, were significantly higher in patients with poorly controlled HbA1c compared to those with well-controlled HbA1c. Similar findings were reported by Sengupta *et al.* (2012) and Buhary *et al.* (2016).^{4, 14}

Conclusion:

This study demonstrated that GDM patients with third-trimester HbA1c levels >6.0% had a significantly higher incidence of adverse maternal and neonatal outcomes, including polyhydramnios, preterm delivery, macrosomia, neonatal hypoglycemia, hyperbilirubinemia, respiratory distress syndrome (RDS), NICU admission, incubator care, and need for resuscitation at birth, compared to those with HbA1c $\leq$ 6.0%. Although vulvovaginitis, oligohydramnios, postpartum hemorrhage (PPH), and urinary tract infections (UTIs) were more frequent in the poorly controlled group, these differences did not reach statistical significance.

Given these findings, further large-scale, multicenter studies are warranted to validate these results, explore underlying mechanisms, and determine optimal glycemic targets for minimizing adverse outcomes in GDM.

CONFLICT OF INTEREST:

The author declares no conflict of interest in relation to the publication of this article.

FUNDING:

This study was self-funded. No external financial support was received.

ACKNOWLEDGEMENTS

The author gratefully acknowledges the support of the Department of Gynaecology and Obstetrics at BIRDEM-II General Hospital, Shegunbagicha, Dhaka, for providing the necessary facilities and assistance during the study. Sincere thanks to the patients who participated in this research for their cooperation. I deeply appreciate the guidance and encouragement provided by the faculty and staff throughout the study period.

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