BANGLADESH J CHILD HEALTH 2021; VOL 45 (2) : 74-78

Hemoglobin A1c Value of Pregnant Diabetic Women with Their Neonatal Outcome

DEBASHISH SAHA[1], SUMAN SHARKER[2], ISMAT JAHAN[3], MD KAMRUL HASAN SHABUJ[4], SADEKA CHOUDHURY MONI[4], SANJOY KUMER DEY[5], MD SHAHIDULLAH[5], MD ABDUL MANNAN[5]

Abstract

Background: *HbA1c is now accepted as a standard measure for diagnosing type 2 diabetes mellitus. Maternal high HbA1c levels have been associated with increased risk of adverse neonatal outcomes.*

Objective: *To find out the relationship between maternal HbA1c and neonatal outcomes.*

Materials & Methods: *This prospective observational study was conducted from February 2018 to January 2019 in the Department of Neonatology and Department of Gynecology & Obstetrics, BSMMU, Dhaka. Diabetic mothers with known HbA1c Value and their infants who were born in this study period in BSMMU were enrolled. Neonates were divided into two groups. One group that had maternal HbA1c <6% and the other group >6%. Neonatal weights, routine capillary blood glucose were recorded.*

Results: *Among the total 94 mothers, HbA1c level were <6% in 56 mothers and ≥6% in 38 mothers. The mean weight, BMI and previous history of gestational diabetes of mothers were significantly higher in HbA1c ≥6% group. Birth weight and large for gestational age infants was high in ≥6% HbA1c group. Neonatal hypoglycemia developed more in high HbA1c group. Total visible birth defect was 4 and all were in high HbA1c group (p=0.022).*

Conclusion: *Elevated HbA1c level during pregnancy is a predictor for large for gestational age infants as well as neonatal hypoglycemia.*

Key words: *Hemoglobin A1c (HbA1c), Diabetes in Pregnancy, Neonatal Outcome.*

Introduction:

Diabetes mellitus is now one of the most common non-communicable disease globally. Magnitude of diabetes mellitus in Bangladesh is increasing.[1] According to WHO report, 2016, 8% (12.88 million) of total population Bangladesh was affected by diabetes.

Hyperglycemia first detected at any time during pregnancy should be classified as either: Diabetes mellitus in pregnancy or gestational diabetes mellitus. Diabetes mellitus in pregnancy should be diagnosed by if one or more of the following criteria are met: 1) fasting plasma glucose ≥7.0 mmol/l (126 mg/dl) 2) 2-hour plasma glucose ≥11.1 mmol/l (200mg/dl) following a 75g oral glucose load, 3) random plasma glucose ≥11.1 mmol/l (200mg/dl) in the presence of diabetic symptoms.[2] Diabetes during pregnancy is mostly due to Gestational diabetes mellitus (GDM). GDM is glucose intolerance at any degree which starts or is recognized during pregnancy. Gestational diabetes mellitus should be diagnosed at any time in pregnancy if one or more of the following criteria are met: 1) fasting plasma glucose 5.1- 6.9 mmol/l (92-125 mg/dl) 2) 1- hour plasma glucose ≥10.0 mmol/l (180mg/dl) following a 75g oral glucose load. 3) 2-hour plasma glucose 8.5-11.1 mmol/l (153-199 mg/dl) following a 75g oral glucose load.[2] The prevalence of GDM is rising worldwide. The prevalence of gestational diabetes (GDM) ranges from 8.2% in rural Bangladesh to 12.9%.

1. Consultant, Department of Neonatology, BSMMU
2. Specialist, Department of Pediatrics and Neonatology, United Hospital Ltd.
3. Assistant Professor, Department of Neonatology, BSMMU
4. Associate Professor, Department of Neonatology, BSMMU
5. Professor, Department of Neonatology, BSMMU

Correspondence: Dr. Debashish Saha, Consultant, Department of Neonatology, BSMMU. Cell no: 01715667295, email: drdevsaha76@gmail.com

Received: 23/01/2021 **Accepted:** 9/05/2021

The rising prevalence of GDM, along with perinatal complications secondary to GDM, and significant long-term impacts on offspring of women with GDM, is an important concern to Obstetric and Neonatologists at both in individual and population health level. Infant of diabetic mother is defined as baby born to a mother who had existence of diabetes in pregnancy. It is currently estimated that 2-3% all pregnancies are complicated by diabetes.[3] Macrosomia is classic presentation of poorly controlled IDM.[3] HbA1c is widely used as a measure of metabolic control during pregnancy. It has been documented that HbA1c is associated with diabetes-related pregnancy complications. In addition, HbA1c can be measured independently of the patient's compliance with glucose monitoring and it is therefore of special value in women with suboptimal treatment compliance. As there is paucity of information about this aspect in Bangladesh, the study may serve as a baseline information for clinicians and other research workers.The objective of this study was to find out relationship of maternal elevated hemoglobin A1c level with adverse neonatal outcomes.

Materials & Methods:

This observational study was conducted from February 2018 to January 2019 in Department of Neonatology and Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. A written informed consent was taken from parents and assurance about confidentiality was given. Diabetic mothers with known HbA1c Value and their Infants who were born in this study period in Bangabandhu Sheikh Mujib Medical University, Dhaka were recruited in this study. A detailed history was taken from the parents of recruited infants. Infants were divided in two groups. One group who had maternal HbA1c levels less than 6% and the other group maternal HbA1c was 6% and above. Neonates were excluded whose mother had some diseases like hemoglobinopathy, complicated with serious cardiovascular diseases and hepato-renal diseases. Neonates with perinatal asphyxia, sepsis, left hospital within 72 hours after delivery were also excluded from this study. Meticulous history of the individual newborn was taken and physical assessment was done and required information was recorded in a data collection form. Newborns gestational age were calculated on the basis of New Ballard scoring. Anthropometry like weight, length, and head circumference (OFC) were measured at birth. The newborns weight was recorded without clothing within first hour after birth on an electronic scale with a precision of 10 g [Model 914, SALTER]. Length were measured by infantometer in centimeter & OFC were measured by measuring tape in centimeter. All infants were routinely monitored for capillary blood glucose for 72 hours according to the institutional guideline and those babies who had were found low capillary blood glucose level by glucometer were tested for venous blood in Department of Biochemistry, BSMMU to see blood sugar level. Before collecting blood sample chlorhexidine wash was given over the skin of hand and blood was collected from superficial vein of the hand. Mothers weight were taken by an electronic scale (model: SALTER) and height were measured by stadiometer in the postpartum period and BMI (kg/m^2) was calculated.

Data were analyzed using the statistical package for social sciences (SPSS) version 20. Quantitative data were expressed as mean± SD and categorical data were presented as proportion. All quantitative variables were compared by independent t-test; categorical variables were compared by Chi-square test or Fisher's exact test. P value < 0.05 was considered as significant. Pearson's correlation test was done.

To determine independent predictors of outcome logistic regression analysis was performed, using variables found significant on univariate analysis. Odds ratios and 95% confidence intervals were calculated.

Result:

During the study period, total 1159 deliveries occurred in the Department of Obstetrics & Gynecology, BSMMU. Among the total deliveries 242 mothers had diabetes in this pregnancy. Among them only 111 mothers had documented HbA1c report, these women were assigned for eligibility. Figure- 1 shows the enrollment process of the infants.

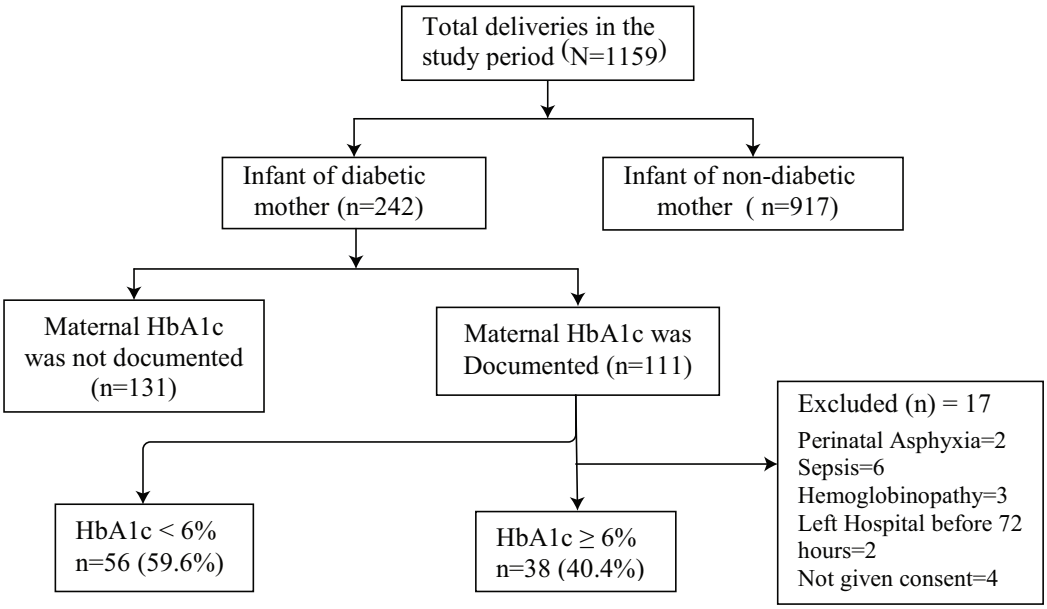

Fig.-1: *Flow chart of enrolment of neonate for study.*

Maternal characteristics of the study group are presented in Table-I. The mean weight and BMI are significantly higher in HbA1c ≥6% group which were 58.32 ± 4.33 vs 62.89 ± 5.06, p=<0.001 and 25.82 ± 2.27 vs 27.66 ± 2.43, p=<0.001 respectively. In previous pregnancy of gestational diabetes between two groups were 23.2% and 50.0% respectively which is statistically significant (p=0.007).

Regarding HbA1c in between two HbA1c group in trimester basis, {(first trimester 3.6% vs 10.5%), (second trimester 60.7% vs 50.0%), (third trimester 35.7% vs 39.5%); p value=0.261} was not statistically significant.

Table I

Comparison of Maternal Characteristics According to Glycated Hemoglobin (HbA1c) Status in Pregnancy

Characteristics	HbA1c <6% n=56	HbA1c ≥6% n=38	P-value
Age (yr) (mean ± SD)	29.04 ± 5.02	29.55± 4.98	0.624
Weight (kg) (mean ± SD)	58.32 ± 4.33	62.89 ± 5.06	<0.001*
BMI (mean ± SD)	25.82 ± 2.27	27.66 ± 2.43	<0.001*
Chronic Hypertension, no (%)	7 (12.5%)	3 (7.9%)	0.477
Pregnancy Induced Hypertension	3 (5.4%)	4 (10.5%)	0.359
Detection of HbA1c in pregnancy (Wk) (mean ± SD)	25.75±6.01	25.68±7.33	0.962
Trimester basis, no(%)			
First Trimester	2 (3.6%)	4 (10.5%)	
Second Trimester	34 (60.7%)	19 (50.0%)	0.261
Third Trimester	20 (35.7%)	15 (39.5%)	
Type of Maternal Diabetes, no (%)			
Gestational Diabetes Mellitus	53 (94.6%)	33 (86.8%)	0.183
Pre-gestational Diabetes Mellitus	3 (5.4%)	5 (13.2%)	
Family History of Diabetes	32(57.1%)	19 (50.0%)	0.495
Previous history of Gestational diabetes Mellitus	13 (23.2%)	19 (50.0%)	0.007

Neonatal characteristics and outcome according to maternal HbA1c status are shown in Table-II. There was no statistical difference between two groups in aspect of gestational age, mode of delivery, small for gestational age or preterm. But there was significant difference between the groups regarding birth weight & BMI, hypoglycemia, Large for gestational age & visible birth defect (0% vs 10.8%, p=0.022)

Table –II

Comparison of Neonatal Characteristics and Neonatal Outcome According to Glycated Hemoglobin (HbA1c) Status of mother in pregnancy

Neonatal Characteristics	HbA1c <6% N= 56	HbA1c ≥6% N= 38	P-value
Gestational Age (Wk)	37± 1.643	37.18± 1.270	0.765
Birth Weight (gm)	2705.5 ± 547.4	3357.1± 713.4	<0.001*
Mode of delivery			
NVD	3 (5.4%)	1 (2.7%)	0.521
LUCS	53 (94.6%)	37 (97.3%)	
Large for Gestational Age	4 (7.1%)	16 (42.1%)	<0.001*
Small for Gestational Age	12 (21.4%)	3 (8.1%)	0.104
Preterm	16 (28.0%)	11 (29.7%)	0.862
Hypoglycemia	4 (7%)	14 (37.8%)	0.001*
Visible Birth Defect	0	4 (10.8%)	0.022*

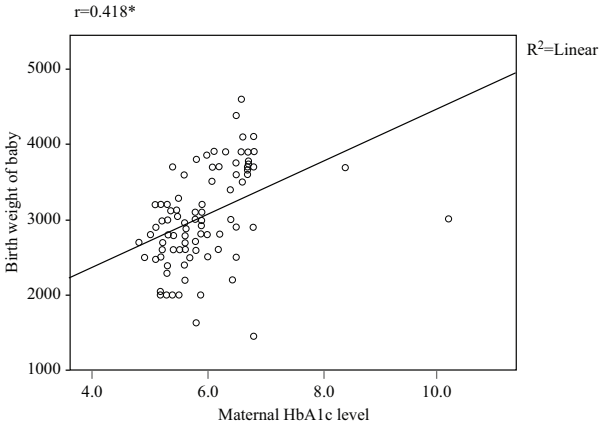

Fig.-2: *Pearson's r Correlation of Maternal HbA1c level with Birth weight of Baby*

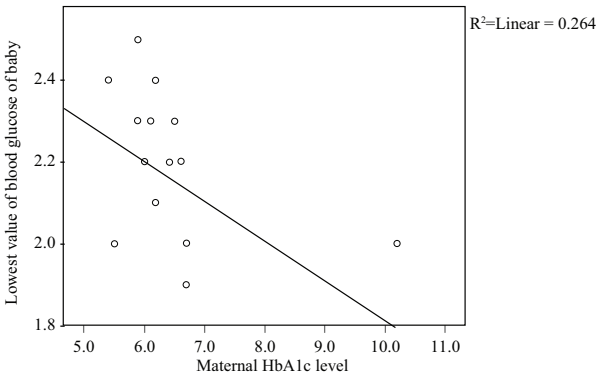

Fig.-3: *Pearson's r Correlation of Maternal HbA1c level with blood glucose level of hypoglycemic infant.*

In logistic regression analysis the independent neonatal adverse outcomes due to high maternal glycated hemoglobin were large for gestational age infant (odd ratio 9.5, 95% CI 2.430 – 37.290, p= 0.001), neonatal hypoglycemia (odd ratio 7.9, 95% CI 1.664 – 37.781, p= 0.009)

Table-III

Binary logistic regression showing risk of adverse neonatal outcome in women with glycated hemoglobin A1c ≥6%

Neonatal Outcome	SE	OR*	95% CI	P value
Large for gestational age	0.697	9.5	2.430- 37.290	0.001*
Neonatal hypoglycemia	0.796	7.9	1.664- 37.781	0.009*
Small for gestational age	0.880	0.558	0.099- 3.135	0.508
Preterm	0.697	0.393	0.100- 1.543	0.181
Visible Birth defect	0.963	2.47	0.518-22.613	0.990

*OR adjusted for maternal BMI, previous history of GDM, treatment of diabetes.

Statistical test: Binary logistic regression. OR = odd ratio, CI= confidence interval, p-value were calculated

Discussion:

Large for gestational age babies were significantly related (P= <0.001) with high maternal hemoglobin A1c concentration in pregnancy in this study. This findings coincides with other styudy.[4]

In this study neonatal hypoglycemia was more common among the HbA1c ≥6% group (p=<0.001). This is accordance with the other studies.[5-7] It suggests that higher maternal level of hemoglobin A1c due to higher glucose load to increase fetal insulin production as mentioned in the Pederson hypothesis.[8] Mikkelson et al.[9] showed there was six fold increased risk of neonatal hypoglycemia with high hemoglobin A1c in pregnancy. Our study also found there was 7.9 times more risk to develop neonatal hypoglycemia in mother with high hemoglobin A1c in their diabetic pregnancy.

Current study shows the significant relationship (P=<0.001) between high HbA1c value and maternal body mass index which was similar with other studies.[10,11]

In this study family history of diabetes was not related to high HbA1c level which differ from the observation of Mikkelsen MR.[9] This may be due to lack of awareness of diabetes checkup among the family members.

Xin et al.[12] found that mothers with normal hemoglobin A1c level had 9.1%, 82.4% and 8.5% of SGA, AGA and LGA infants respectively. Whereas, in those with elevated HbA1c levels 16.2% infants were SGA, 64.9% were AGA and 18.9% were LGA. In this study mothers with hemoglobin <6% level 21.4% infants were SGA, and 7.1% were LGA, where as in those with hemoglobin A1c >6% levels, 8.1% infants were SGA, and 42.1% were large for gestational age infants.

In this study 4 (4.3%) visible birth defect were found. Among them two were meningomyelocele, one had bilateral club foot and another one had imperforated anus. All birth defects were in high hemoglobin A1c group. Congenital heart defects were more in uncontrolled diabetes with high hemoglobin A1c in a study conducted by Lucas et al.[13] In our study congenital heart defects were not identified as echocardiograph was not performed.

Conclusion:

Elevated HbA1c level during pregnancy is a predictor for large for gestational age infants as well as neonatal hypoglycemia. Future multicenter studies with larger samples and trimester basis HbA1c follow up are needed for better understanding the neonatal outcome.

References:

1. Khan AKA, Mahtab H, Grant J, Stewart M, Ahmed T. 'Introduction to diabetes mellitus', 4th (ed.). Diabetes Mellitus. Diabetic association of Bangladesh: Dhaka, Bangladesh 2014; 15
2. World Health Organization. 'Diagnostic Criteria and Classification of Hyperglycemia First Detected in Pregnancy' 2013; 3-5.
3. Gomella TL, Cunnigham MD, Eyal FG. and Tuttle DJ. 'Neonatology: Management, Procedures, On-call problems, Diseases and Drugs, 7th (ed) McGraw Hill education, New York 2013; 711.
4. Bhavadharini B, Mahalakshmi MM, Deepa M, Harish R, Malanda B, Kayal A et al. Elevated glycated hemoglobin predicts macrosomia among Asian Indian pregnant women (WINGS-9). Indian journal of endocrinology and metabolism 2017; 21: 184-89.
5. González-Quintero VH, Istwan NB, Rhea DJ, Rodriguez LI, Cotter A, Carter J, et al. The impact of glycemic control on neonatal outcome in singleton pregnancies complicated by gestational diabetes. Diabetes care 2007; 30: 467-70.
6. Arumugam K and Majeed AN. Glycated haemoglobin is a good predictor of neonatal hypoglycaemia in pregnancies complicated by diabetes. Malaysian J Pathol. 2011; 33: 21-24.
7. Subash S, Sathyamoorthy M, Prasanna R, Karthikeyan P, Sekar P, Reddy R. HbA1c level in last trimester pregnancy in predicting macrosomia and hypoglycemia in neonate. Inter J Contemp Pediatr. 2016; 3: 1334-38.
8. Pedersen j. Weight and length at birth of infants of diabetic mother. Acta endocr. 1954; 16: 330-42.
9. Mikkelsen MR, Nielsen SB, Stage E, Mathiesen ER, Damm P. High maternal HbA1c is associated with overweight in neonates. Danish medical bulletin 2011; 58: A4309.
10. Suhonen L, Hiilesmaa V, Kaaja R, Teramo K. Detection of pregnancies with high risk of fetal macrosomia among women with gestational diabetes mellitus. Acta Obstet Gynaecol Scand. 2008; 87: 940-5.
11. Sweeting AN, Ross GP, Hyett J, Molyneaux L, Tan K, Constantino M, et al. Baseline HbA1c to identify high-risk gestational diabetes: utility in early vs standard gestational diabetes. J Clin Endocrinol Metab. 2016; 102: 150-56.
12. Xin SC, Pravin RR, Rajadurai VS, Chandran S. Elevated glycated hemoglobin during pregnancy in diabetic women as a predictor of large-for-gestational age infants in an Asian cohort. J Clin Neonatol. 2018; 7: 136-40.
13. Lucas MJ, Leveno KJ, Williams ML, Raskin P, Whalley PJ. Early pregnancy glycosylated hemoglobin, severity of diabetes, and fetal malformations. Am J Obstet Gynecol. 1989; 161: 426-31.