ORIGINAL ARTICLE

Observation of HbA1c as a Potential Predictor of Perinatal Outcome in Pregnancy with Diabetes in a Tertiary Care Hospital of Bangladesh

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Abstract

Introduction: *Diabetes Mellitus poses substantial risk for the mother and fetus during pregnancy. Glycosylated HbA1c is increased in chronic hyperglycemia and co-relates closely with an increased risk of fetal and neonatal complications. The present study was undertaken to determine the association of maternal serum HbA1c level with perinatal outcome.*

Methods: *It was a prospective observational study carried out in the department of Obstetrics and Gynaecology in BIRDEM Hospital during the period of January 2019 to December 2019. During this study period, 100 pregnant patients with diabetes who attended or were admitted at BIRDEM Hospital were randomly selected. Estimation of serum HbA1c level was done in all patients in each trimester. From each patient 5 cc blood was taken and HbA1c level was measured by high performance liquid chromatography (HPLC). HbA1c level <6.5% was considered as normal. The perinatal outcomes were studied.*

Results: *In this study serum HbA1c level was found raised in 83% of study subjects. Neonatal complications were higher in study subjects with uncontrolled HbA1c level. Among the complications in uncontrolled group the highest incidence was of neonatal hypoglycaemia (69.6%), followed by hyperbilirubinaemia (60.9%), RDS (21.7%), birth asphyxia (21.7%) and septicemia (10.9%). Perinatal mortality was significantly higher among women who had uncontrolled diabetes (44.6% vs. 11.8%).*

Conclusion: *There is increasing evidence that raised level of maternal serum HbA1c in antenatal period is associated with neonatal complications and by measuring HbA1c level in each trimester, good glycaemic control in diabetic pregnancy can be achieved which can avoid these complications.*

Keywords: *Diabetes, Perinatal outcome, HbA1c*

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Introduction:

Diabetes Mellitus is an important medical disorder in pregnancy, which creates substantial risk for the mother and fetus during current pregnancy and it also has serious implication for their long time well being.[1] Pregnancy and preconception period are of particular importance to women with diabetes as pregnancy puts challenges to the metabolic management in diabetes and, at the same time it increases the risk of diabetes related complications in fetus and neonates. It increases incidence of caesarian section, traumatic vaginal delivery and later development of type 2 diabetes. It also increases the risk of the fetus for abortion, still birth congenital anomalies, macrosomia, and other neonatal problems (e.g. hypoglycaemia, hypocalcaemia, hyperbilirubinaemia and polycythemia). In the long run the baby may develop obesity, diabetes and neurological problems.[2] The discovery of glycosylated Hb has opened a new horizon in all aspects of diabetic research and management.[3] HbA is the major component of adult Hb, comprising approximately 90% of total Hb. This Hb when combines with glucose becomes glycosylated (HbA1c). This glycosylated Hb (HbA1c) are negatively charged and thus migrate quickly than HbA on

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cation exchange chromatography. Glycosylated Hb is increased in diabetes as a consequence of chronic hyperglycaemia[4, 5] and co-relates closely with the blood level and urinary excretion of glucose[6, 7]. Poor glycaemic control is associated with an increased risk of fetal and neonatal complications, suggesting that strict glycaemic control may reduce the rate of fetal and neonatal morbidity.[8] Birth asphyxia and perinatal death showed significant reduction in tight control HbA1c level in previous studies.[9] Glycosylated Hb levels were higher in the spontaneous preterm delivery group in another study.[10] Between 18 and 24 weeks HbA1c was significantly higher in women who delivered large for gestational age (LGA) infants in another one.[11] There is increasing evidence that raised level of maternal serum HbA1c in antenatal period can cause a number of fetal and neonatal complications.[12] HbA1cis proved to be a useful indicator of average long term blood glucose level in diabetic and non pregnant subjects.[13] So by measuring HbA1c in each trimester, blood sugar control can be evaluated. Thus, adequate screening, strict control of hyperglycaemia and careful planning for pregnant diabetic women would ensure a happy outcome. We had undertaken this study to see the fetal outcome in diabetic pregnancy in case of controlled and uncontrolled serum HbA1c level. This study was done to determine the association of maternal serum HbA1c level with perinatal outcome

Methods:

It was a prospective observational study carried out from September 2006 to August 2007 in Department of Obstetrics and Gynaecology at Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic disorder (BIRDEM), Dhaka, Bangladseh. Hundred pregnant women with diabetes mellitus, who attended or were admitted to BIRDEM Hospital during the study period were randomly selected. Pregnant women with preexisting diabetes and with gestational diabetes both were included in this study. Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy.[14]

Multiple pregnancy, pregnancy with other metabolic disorders, heart disease, chronic hypertension were excluded from this study. The variables included in the study were age, status of glycaemic control, fetal complications and neonatal complications. Data collection sheet was formed which included all the variables of interest. Purpose and procedure of the study were discussed with the patients who fulfilled the inclusion criteria. All the variables of interest were collected from history, clinical examination and biochemical investigations and were recorded on the predesigned data collection sheet. Pregnancy was dated by ultrasonography between 6-10 weeks. Some patients were managed initially only by dietary advice and some needed injection Insulin also. From each patient 5 c.c. venous blood was taken and HbA1c was measured by high performance liquid chromatography (HPLC) in each trimester of pregnancy. HbA1c level of 6.5% was considered as normal.[15, 16] Prior to the study ethical clearance was taken from appropriate authority. Informed written consent from patients were duly taken.

Data were processed and analyzed by SPSS 20 version.

Results:

Mean (± SD) age of the study subjects was 29.77 (±4.52) years and most of the subjects were in the 26-30 years age group (Table I). Age range was 20-38 years in study group.

Table I

Age distribution of the study subjects (n = 100)

Age (in years)	Frequency	Percentage
20-25	12	12
26-30	48	48
31-35	26	26
>35	14	14
Mean ± SD	29.77±4.52	

Table II shows the status of glycaemic control in 2ndand 3rd trimester in which 17% women had controlled HbA1c level whereas 83% of women had uncontrolled HbA1c.

Table II

Status of glycaemic control in late trimester of pregnancy in respect with HbA1c level (n = 100)

HbA1c level	Frequency	Percentage
Controlled	17	17
Uncontrolled	83	83

After performing univariate logistic regression test it was found that there is 6 times increased risk of perinatal mortality among women who have uncontrolled diabetes. This is statistically significant ($p < 0.05$)(Table III).

Table III

Association of glycaemic control of diabetic mothers and neonatal mortality

Neonatal mortality	Controlled HbA1c (n=17)	Uncontrolled HbA1c (n=83)	Crude OR (95% CI)	p value
Survived	15 (88.2%)	46 (55.4%)	6.03 (1.3,28.1)	< 0.05
Expired	2 (11.8%)	37(44.6%)		

Table IV shows that regarding septicaemia and birth asphyxia there is no significant difference between two groups but hyperbilirubinaemiaand hypoglycemia of the newborn were significantly higher in uncontrolled group.

Table IV

Association of neonatal morbiditywith controlled and uncontrolled diabetic mothers

Variables		Controlled HbA1c(n=15)		Uncontrolled HbA1c(n=46)		$\chi 2$	* p value
RDS	Present	0	0	10	21.7	3.9	NS
	Absent	15	100	36	78.3		
Septicaemia	Present	1	6.7	5	10.9	0.23	> 0.05
	Absent	14	93.3	41	89.1		
Birth asphyxia	Present	1	6.7	10	21.7	1.74	> 0.05
	Absent	14	93.3	36	78.3		
Bilirubin	Normal	13	86.7	18	39.1	10.23	<0.002
	Hyperbilirubinaemia	2	13.3	28	60.9		
Blood sugar	Hypoglycemia	1	6.7	32	69.6	18.02	<0.001
	Normal	14	93.3	14	30.4		

* Chi-square test was done

* p value < 0.05was considered as the level of significance

There is a positive correlation between raised HbA1c and increasing birth weight and it is statistically significant (p < 0.05)(Table V).

Table-V

Correlation between HbA1c and birth weight

Variable	r	p
Birth weight	0.208	<0.05

* Pearson's correlation test was done

* p value < 0.05was considered as lowest level of significance

Discussion:

Proper screening, diagnosis and management of diabetes in pregnancy can reduce fetal as well as neonatal morbidity and mortality.[8] Diabetes and pregnancy may mutually affect each other over a range of interaction from conception to delivery, and possibly even later.[14] This study was done to evaluate the fetal and neonatal outcome in pregnant women with controlled and uncontrolled diabetes.

The higher incidence of neonatal hypoglycaemia was in uncontrolled group and was found in agreement with the study done by Deorary et al.[17] This incidence is similar with the incidence of Agrawal et al. and Majed et al.[18, 19] Where as in the study of Ferrara et al, the incidence of hypoglycemia is very high, but the study population is also large.[20] The incidence of hypoglycemia is also coincides with the study of Das et al.[21]

The incidence of hyperbilirubinaemia (60.9%) among uncontrolled HbA1c group was higher than the study done by Deorary et al. (26 %)[17], Abdulrahman M. et al[22].

Birth asphyxia and neonatal septicaemiawere high among women who have uncontrolled blood sugar but statistically not significant. These findings also coincide with the findings of Deodary et al,[17] Brooket et al[23] .The incidence of birth asphyxia in uncontrolled HbA1c group was 21% which was almost similar to the study done by Deorary et al.[17]

The incidence of macrosomia in uncontrolled HbA1c group was higher than and this is statistically significant. This finding is similar to the finding, study done by Beard et al.[24] Risk of neonatal mortality is 6 times higher among uncontrolled diabetic women in the present study which is statistically significant and similar to the study of Vitoras et al[25] Ferrara et al[20].

Diabetes Mellitus in pregnancy is one of the leading cause of fetal and neonatal morbidity and mortality. But it is preventable by controlling blood sugar level strictly during pregnancy. There is increasing evidence that the raised level of maternal serum HbA1c in antenatal period is associated with a number of fetal and neonatal complications. By investigating HbA1c level in each trimester blood sugar control can be done, so we can predict the fetal and neonatal outcome.

The main factors that contributed to this reduction were a good control of diabetes periconceptually and throughout pregnancy. Particular attention is needed during the programmed conception, the first trimester, and the selection of the appropriate time for delivery.

Limitations of the study:

The study has few limitations as it was conducted with a small sample size and not representative of the whole country or region. More representative findings can be obtained from large sample size and in different tertiary level hospitals. Also the issue of potential variation of HbA1c levels in subjects with iron deficiency anaemia &/ or haemoglobinopathies was not addressed in this study.

Conflict of interest: Nothing to declare.

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