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HbA_1C Level in 2nd and 3rd Trimester with Pregnancy Outcome in Diabetic Patients

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Abstract

Objective: The present study was undertaken to determine the association of maternal serum HbA_1C level with maternal and fetal outcome. Materials and Methods: It was prospective observational study. The study was carried out in the department of Obstetrics and Gynaecology in BIRDEM Hospital during the period of September 2006 to August 2007. During this study period, 100 pregnant patient with diabetes who attended or admitted at BIRDEM Hospital were studied. Estimation of serum HbA_1C level was done in all patient in each trimester. From each patient 5 c.c blood was taken & HbA_1C level was measured with the help of enzymatic method. HbA_1C level < 6 was considered as normal. .The maternal complications in antenatal period, in postpartum period, during labour & fetal outcome were studied in both cases of controlled & uncontrolled HbA_1C level. Result: In this study serum HbA_1C level was found raised in uncontrolled diabetic patients. The incidence of vulvovaginitis, preterm delivery and polyhydramnios were significantly high in 2nd and 3rd trimester in raised HbA_1C level. The rate of normal vaginal delivery was higher in patient with normal HbA_1C leve uncontrolled HbA_1C level (17.59% Vs 10.84%, p = 0.01), which statistically significant. Post partum haemorrhage (PPH) was significantly higher in raised HbA_1C level than normal (0.00% Vs 22.20%, p =0.01) in NVD and (0.00% Vs 16.22%, p = 0.01) in Caesarean section. Neonatal complications were higher in raised HbA_1C level than normal. The incidence of Hypoglycemia (5.88% Vs 38.55%, p = 0.02); Hyperbilirubinemia (11.76% Vs 33.73%, p = 0.03) ; RDS (0.00% Vs 12.05%, p = 0.02); Macrosomia (0.00% Vs 18.07%,p = 0.01) and Birth asphyxia (5.88% Vs. 12.05%, p = 0.04). These differences are statistically significant. Conclusion: There is increasing evidence that the raised level of maternal serum HbA_1C in antenatal period is associated with maternal & neonatal complications. By investigating HbA_1C level in each trimester, blood sugar control can be done. This study was taken out to evaluate the usefulness of HbA_1C for good glycaemic control in diabetic pregnancy.

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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 people with diabetes as pregnancy challenges to the metabolic management in diabetes and, at the same time it increase risk of diabetes related complications in mother (*e.g.* pre eclampsia, infection, postpartum haemorrhage, increase incidence of ceaserian section, traumatic delivery and later development of type 2 diabetes).It also increases the risk to the fetus for abortion, still birth congenital anomalies, macrosomia, polyhydramnios and other neonatal problems (*e.g.* hypoglycemia, hypocalcaemia, hyperbilirubinemia and polycythemia). In the long run the baby may develop obesity, diabetes and neurological problems[2].

The discovery of glycosylated Hb has opened new horizon in all aspect of diabetic research and management.[3] HbA is the major component of adult Hb, comprising approximately 90% of Hb. This Hb when combines with glucose becomes glycosylated (HbA_1C).This glycosylated Hb (HbA_1C) are negatively charged and thus migrate quickly than HbA on cation exchange chromatography. Glycosylated HbA_1C is increased in diabetes as a consequence of chronic hyperglycemia [4,5] and co-relate closely with their blood level and urinary excretion of glucose [6,7].Poor glycemic

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control is associated with an increased risk of maternal and foetal complications, suggesting that strict glycemic control may reduce the rate of maternal and foetal morbidity [8]. Birth asphyxia, perinatal death and congenital anomalies showed significant reduction in tight control HbA_1C level.[9] Glycosylated haemoglobin HbA_1C levels were higher in the spontaneous preterm delivery group.[10] Between 18 and 24 weeks HbA_1C was significantly higher in women who delivered LGA infants.[11]

There is increasing evidence that raised level of maternal serum HbA_1C in antenatal period can cause maternal and neonatal complications [12] . HbA_1C proved to be a useful indicator of average long term blood glucose level in diabetic and non pregnant subjects [13]. Thus by investigation of HbA_1C in each trimester, blood sugar control in each trimester can be done.

Thus, adequate screening, strict control of hyperglycaemia and careful planning for pregnant diabetic women ensure a happy outcome. We had undertaken this study to see the maternal fetal outcome in diabetic pregnancy in case of controlled and uncontrolled serum HbA_1C level.

Objectives of the Study

General Objective

To evaluate the usefulness of HbA_1C for good glycemic control for diabetes mellitus in pregnancy.

Specific Objective

To measure HbA_1C in the three trimester of pregnancy in women with diabetes.

To assess the pregnancy outcome in women with raised HbA_1C.

To assess the pregnancy outcome in women with normal HbA_1C.

Materials and Method

It was a prospective observational study carried out from September 2006 to August 2007 in and Gynaecology at Bangladesh Institute of Research and Rehabilitation in Diabetes, Department of Obstetrics Endocrine and Metabolic disorder (BIRDEM).Hundred pregnant women with diabetes who attended or admitted to BIRDEM Hospital during the study period were recruited. Pregnant women with preexisting diabetes and with gestational diabetes were included in this study. Multiple pregnancy, pregnancy with other metabolic disorders, heart disease, chronic hypertension were excluded from this study. The variables included in the proposed study were age, status of glycemic control, complications in 2nd and 3rd trimester of pregnancy, mode of delivery, intrapartum and postpartum complications and neonatal complications.

Data collection sheet has formed which include all the variables of interest.

Cases were collected from outdoor and inpatient department of Obstetric and Gynaecology, BIRDEM Hospital, Dhaka. Purpose and procedure of the study were discussed with the patients who fulfill the inclusion criteria. All the variables of interest were collected from history, clinical examination and biochemical investigation were recorded on the pre designed data collection sheet. Pregnancy was dated by early ultrasonography. Some patients were managed initially only by dietary advice and some needed injection Insulin also. From each patient 5c.c. blood was taken and HbA_1C was measured by laboratory method.HbA_1C level d" 6% was considered as normal. Data were processed by Computer and analyzed by using SPSS (Statistical Package for Social Science).

For statistical analysis *Student 't' test* was used. It was considered statistically significant if $p < 0.05$.

Results

Table-I

Age distribution of the study subject.

Age (in years)	Case (n=100)	Percentage (%)
20-25	12	(12.00%)
26-30	48	(48.00%)
31-35	26	(26.00%)
>35	14	(14.00%)

Mean age ±SD = 29.77±4.52

Table I shows the age distribution of the study objects. Age range was 20-38 years in study group. The highest incidence (48%) was found in age group 26 to 30 years.

Table-II

Status of glycemic control in 2nd & 3rd trimester of pregnancy in respect with HbA$_1$C level

Controlled HbA$_1$C		Uncontrolled HbA$_1$C	
(No.)	(%)	(No.)	(%)
17	(17.00)	83	(83.00)

Table II shows the status of glycemic control in 2nd & 3rd trimester in which 17% women have controlled HbA$_1$C level and 83% of women have uncontrolled level of HbA$_1$C.

Table-III

Maternal outcome in controlled and uncontrolled HbA$_1$C in 2nd & 3rd trimester of pregnancy

	Controlled HbA$_1$C (n=17)	(%)	Uncontrolled HbA$_1$C (n=83)	(%)	p value
Vulvovaginitis	1	(5.88)	18	(21.67)	0.02
UTI	2	(11.76)	15	(18.07)	0.24
Preterm delivery	3	(17.64)	20	(24.10)	0.04
Polyhydramnios	2	(11.76)	18	(21.69)	0.03

Unpaired 't' test, $p < 0.05$ was considered significant.

Table III shows maternal outcome in 2nd and 3rd trimester of pregnancy. Vulvovaginities (5.88% Vs 21.67%, p = 0.02), Preterm delivery (17.64% Vs 24.10%, p = 0.04) and Polyhydromnios (11.76% Vs 21.69%, p = 0.03) in controlled and uncontrolled HbA$_1$C level respectively. These differences are statistically significant whereas UTI (11.76% Vs 18.07%, p = 0.24) in controlled and uncontrolled HbA$_1$C level which is statistically not significant.

Table-IV

Mode of delivery in respect with status of HbA$_1$C in 2nd & 3rd trimester of pregnancy

	Controlle Controlled HbA$_1$C		Uncontrolled HbA$_1$C		p value
	(n=17)	(%)	(n=83)	(%)	
NVD	12	(70.59)	9	(10.84)	0.01
LUCS	5	(29.41)	74	(89.16)	0.23

Unpaired 't' test, $p < 0.05$ was considered significant.

Table IV shows statistically higher rate of Normal vaginal delivery (NVD) in women with controlled HbA$_1$C level than uncontrolled (70.59% Vs 10.84%, p = 0.01). Rate of LUCS was high in women with uncontrolled HbA$_1$C level (29.41% Vs 89.16%, p = 0.23) which is statistically not significant.

Table-V

Intrapartum complications in study group who delivered vaginally

	Controlled HbA$_1$C (n=12)	(%)	Uncontrolled HbA$_1$C (n=9)	(%)	P Value
Shoulder dystocia	0	(0.00)	3	(33.33)	0.01
Complete perineal tear	0	(0.00)	4	(44.44)	0.13
Cervical tear	3	(25.00)	6	(66.66)	0.23

Unpaired 't' test, $p < 0.05$ was considered significant.

Table V shows Shoulder dystocia in women with uncontrolled HbA$_1$C level was statistically higher than women with controlled HbA$_1$C level (0.00% Vs 33.33%, p = 0.01), whereas complete pereneal tear (0.00% Vs 44.44%, p=0.13) and cervical tear (25.00% Vs 66.66%, p = 0.23). These differences are not statistically significant.

Table-VI

Intrapartum complications in study group who delivered vaginally

	Controlled HbA$_1$C (n=12)	(%)	Uncontrolled HbA$_1$C (n=9)	(%)	P Value
Shoulder dystocia	0	(0.00)	3	(33.33)	0.01
Complete pereneal tear	0	(0.00)	4	(44.44)	0.13
Cervical tear	3	(25.00)	6	(66.66)	0.23

Unpaired 't' test, $p < 0.05$ was considered significant.

Table VI shows Shoulder dystocia in women with uncontrolled HbA$_1$C level was statistically higher than women with controlled HbA$_1$C level (0.00% Vs 33.33%, p = 0.01), whereas Complete pereneal tear

(0.00% Vs 44.44%, p=.13) and Cervical tear (25.00% Vs 66.66%, p = 0.23). These differences are not statistically significant.

Table-VII

Postpartum complications in study group who delivered vaginally

Complications	Controlled HbA_1C		Uncontrolled HbA_1C		p
	(n=12)	(%)	(n=9)	(%)	value
PPH	0	(0.00)	2	(22.20)	0.02
UTI	1	(8.30)	2	(22.20)	0.28
Endometritis	0	(0.00)	1	(11.10)	0.24

Unpaired 't' test, $p < 0.05$ was considered significant.

Table VII shows postpartum complications in women with uncontrolled HbA_1C level higher than controlled HbA_1C level. PPH (0.00% Vs 22.20%, p=0.02) which is statistically significant whereas UTI (8.30% Vs 22.20%, p= 0.28) and Endometritis (0.00% Vs 11.10%, p = 0.24) are statistically not significant.

Table-VIII

Postpartum complications in study group who delivered by caesarean section

Complications	Controlled HbA_1C		Uncontrolled HbA_1C		p
	(n=5)	(%)	(n=74)	(%)	value
PPH	0	(0.00)	12	(16.22)	0.01
UTI	1	(20.00)	10	(13.51)	0.24
Abd. Wound infection	0	(0.00)	4	(5.40)	0.03
Endometritis	0	(0.00)	4	(5.40)	0.08

Unpaired 't' test, $p < 0.05$ was considered significant

Table VIII shows PPH (0.00% Vs 16.22%, p = 0.01), Abdominal wound infection (0.00% Vs 5.40%, p = 0.03) are statistically higher in women with uncontrolled HbA_1C level than controlled HbA_1C level whereas UTI (20.00% Vs 13.51%, p=0.24) and Endometritis (0.00% Vs 5.40% p=0.08) are statistically not significant.

Table-IX

Fetal outcome of controlled and uncontrolled HbA_1C in 2nd & 3rd trimester of pregnancy.

	Controlled HbA_1C		Uncontrolled HbA_1C		p
	(n=17)	(%)	(n=83)	(%)	value
Hypoglycemia	1	(5.88)	32	(38.55)	0.02
Hyperbiliru-binemia	2	(11.76)	28	(33.73)	0.03
IGUR	1	(5.88)	3	(3.61)	0.13
RDS	0	(0.00)	10	(12.05)	0.02
Macrosomia	0	(0.00)	15	(18.07)	0.01
Septicemia	1	(5.88)	5	(6.02)	0.24
Birth asphyxia	1	(5.88)	10	(12.05)	0.04

Unpaired 't' test, $p < 0.05$ was considered significant.

Table IX shows neonatal Hypoglycemia (5.88% Vs 38.55%, p = 0.02), Hyperbilirubinemia (11.76% Vs 33.73%, p = 0.03), RDS(0.00% Vs12.05%, p = 0.02) Macrosomia (0.00% Vs 18.07%, p = 0.01) and birth asphyxia (5.88% Vs 12.05%, p= 0.04) are statistically more in women with uncontrolled HbA_1C level whereas IUGR (5.88% Vs 3.61%,p=0.13) and Septicemia (5.88% Vs 6.02%, p = 0.24) among controlled and uncontrolled HbA_1C group and the differences are statistically not significant.

Table-X

Perinatal mortality in Controlled and Uncontrolled HbA_1C level in 2nd & 3rd trimester of pregnancy.

	Controlled HbA_1C		Uncontrolled HbA_1C		p
	(n=17)	(%)	(n=83)	(%)	value
Unexplained Intra- uterine death (IUD)	0	(0.00)	9	(10.80)	0.02
Fresh Still Birth (FSB)	1	(5.88)	6	(7.20)	0.03

Unpaired 't' test, $p < 0.05$ was considered significant.

Table X shows unexplained IUD (0.00% Vs 10.80%, p = 0.02) and Fresh Still Birth (5.88% Vs 7.20%, p = 0.03) are statistically higher in women with uncontrolled HbA_1C level than controlled HbA_1C level.

Table-XI

Neonatal mortality in respect with HbA_1C level in 2nd & 3rd trimester of pregnancy.

	Controlled HbA_1C		Uncontrolled HbA_1C		P
	(n=17)	(%)	(n=83)	(%)	value
Survived	15	(88.23)	74	(89.15)	0.04
Expired	1	(5.88)	9	(10.80)	0.26

Unpaired 't' test, $p < 0.05$ was considered significant.

Table XI shows neonatal survival rate among two groups (88.23% Vs 89.15%, p= 0.04), these differences are statistically significant whereas Neonatal death among two groups (5.88% Vs 10.80%, p = 0.26) which is statistically not significant.

Discussion

Proper screening, diagnosis and management of diabetes in pregnancy can reduce both maternal and neonatal morbidity[8]. Diabetes and pregnancy may mutually affect each other over a range of interaction from conception to delivery, and possibly even later [14].

The highest incidence (48 %) was found in age group 26 to 30 years.HbA_1C level d" 6% was considered normal. In 2nd and 3rd trimester of pregnancy controlled and uncontrolled HbA_1C level was (17% Vs 83%).

The incidence of vulvovaginitis 21.67% in uncontrolled HbA_1C level similar to the finding in the study of Mangala R. et al[15] (19.8%). Incidence of UTI 18.07% in women with uncontrolled HbA_1C which is similar to the finding in the study of Khatun F[16] (17.8%). The incidence of Preterm delivery was 24.10% among uncontrolled HbA_1C group which higher than the study done by Kovilam O et al[8] (10%). The incidence of polyhydramnios was 21.69% among uncontrolled HbA_1C level which similar to the study of Eskandar M[17] (23%) but higher than the study done by Metal S et al[18] (3.7%). In this study rate of Caesarean section in uncontrolled HbA_1C group was 89.16% which is equivalent to the study done by Shikdar K et al[19] (87.33%), Ivy R[20] (88.32%), but higher than that reported by Metal S et al [18] (52%), Mangala R et al[15] (48.32%).

The incidence of Shoulder dystocia 33.33% in uncontrolled HbA_1C who delivered vaginally was similar to the study done by Kjos S.L. et al[21] (31.58%). In this study the incidence of PPH who delivered Caesarean section was 16.22% in uncontrolled HbA_1C group which is lower than the study done by Mangala et al[15] (29%). The incidence of Abdominal wound infection 5.40% and Endometritis 5.40% are equivalent to the study done by Mangala et al [15] (4.20% & 5.50%).

The higher incidence of Neonatal hypoglycemia 38.55% in uncontrolled group and found in agreement with that study done by Deorary AK et al[22] (40.02%). The incidence of Hyperbilirubinemia 33.73% among uncontrolled HbA_1C group, is higher than the study done by Deorary AK et al [22] (26 %).

The incidence of Macrosomia was significantly high in uncontrolled HbA_1C group (0.00% Vs 18.07%, p = 0.01) is equivalent to the study done by Beard R et al [23] (0.01% Vs 17.89%, p = 0.001). The incidence of Birth asphyxia in uncontrolled HbA_1C group was 12.05% which is similar to the study done by Deorary et al[22] (11.02%).

The incidence IUD in two groups (0.00% Vs 10.80%, p = 0.02) and Fresh still birth (5.88% Vs 7.20%, p = 0.03); these differences are statistically significant.

The incidence of Neonatal survival rate among two groups were (88.23% Vs 89.15%, p = 0.04) which is statistically significant whereas Neonatal death (5.88% Vs 10.80%, p=0.26) is statistically not significant.

Conclusion

Diabetes Mellitus in pregnancy is one of the leading cause of maternal and fetal morbidity and mortality.But it is preventable by controlling blood sugar level during pregnancy. There is increasing evidence that the raised level of maternal serum HbA_1C in antenatal period is associated with maternal and neonatal complication.There is a relative effect of HbA_1C level in three trimester of pregnancy on birth weight and other adverse fetal outcome. Birth asphyxia, perinatal death,congenital anomalies,preterm delivery showed singnificant reduction in tight control of HbA_1C level. HbA_1C is proved to be a useful indicator of average long term blood glucose level in diabetic subjects. By investigating HbA_1C level in each trimester blood sugar control can be done.Thus strict control of hyperglycemia in diabetic pregnant woman ensures a happy outcome.

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