

# HbA<sub>1c</sub> in Patients with Gestational Diabetes Mellitus

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## Abstract

**Introduction:** Approximately 7% of all pregnancies are complicated by Gestational Diabetes Mellitus. The study was designed to determine the relationship between HbA<sub>1c</sub> & Gestational Diabetes Mellitus to reduce complications & monitoring treatment. **Methods:** The present cross-sectional comparative study was carried out in departments of Biochemistry and Obstetrics & Gynecology, Chittagong Medical College, Chittagong, Bangladesh. The data were collected by a structured questionnaire including age, socioeconomic condition, gravida, para, blood pressure, BMI, FBS, PPBS & Family H/O diabetes mellitus. Patients suffering from shortened red blood cell life span, sickle cell disease or any other condition that could result in premature red blood cell death and longer red blood cell life span, such as vitamin B12 or folate deficiency were excluded. Total 110 pregnant women were included in this study. Among them 70 were considered as case (whose FBS & PPBS according to ADA criteria of FPG value of  $\geq 5.3$  mmol/l and the WHO criteria of a 2-h PPPG value of  $\geq 7.8$  mmol/l) and 40 were considered as control (whose FBS  $< 5.3$  mmol/L & PPBS  $< 7.8$  mmol/L). HbA<sub>1c</sub> were measured in all sample. **Results:** Study showed that HbA<sub>1c</sub> (6%) were more increased in GDM patients than that of the normal pregnancy (6.95 $\pm$ 1.38% Vs 5.05  $\pm$ 0.27 %,  $p < 0.001$ ). Result showed that percentage of raised plasma HbA<sub>1c</sub> is more in GDM patients than that of the normal pregnancy (57.1%,  $P < 0.001$ ). Pearson's correlation coefficient (r) showed that there are positive correlation between Blood Glucose Level & HbA<sub>1c</sub> (Fasting Blood Glucose & HbA<sub>1c</sub>,  $r = 0.869$ ,  $p < 0.001$  and Post Prandial Blood Sugar & HbA<sub>1c</sub>,  $r = 0.507$ ,  $p < 0.001$ ). **Conclusion:** Significantly raised level HbA<sub>1c</sub> in GDM help to formulate a management plan and thereby reduce the complications of this disease.

**Key words:** Gestational Diabetes Mellitus; Fasting blood sugar; Post-prandial blood sugar; Glycated hemoglobin.

## INTRODUCTION

Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy<sup>1-5</sup>. It does not exclude the possibility that unrecognized glucose intolerance may have antedated or begun concomitantly with pregnancy<sup>1</sup>. Approximately 7% of all pregnancies are complicated by GDM, though the prevalence range from 1% to 14% of total pregnancies, depending on the population studied & the diagnostic tests employed.<sup>3</sup> The prevalence of GDM in rural Bangladesh is comparable with any other population is higher<sup>6</sup>.

Pregnancy is characterized by a complex endocrine-metabolic process, including impaired insulin sensitivity, increased  $\beta$ -cell response, moderate increase in blood glucose level particularly following ingestion of meal and changes in the levels of circulating free fatty acids, triglycerides, cholesterol and phospholipids. All of these changes represent a necessary, possibly indispensable adaptation to ensure the energy demand of the fetus and to prepare the maternal organism for delivery and lactation<sup>7-9</sup>. Placental secretion of hormones, such as estrogen, progesterone, human chorionic somatotropin (hCS) or placental lactogen, prolactin and growth hormone is major contributors to the insulin resistant state seen in pregnancy. Insulin resistance develops in the second trimester and progresses throughout the remainder of pregnancy<sup>8-9</sup>. Insulin sensitivity is reduced by as much as 80%<sup>9</sup>. The impairment of insulin sensitivity however, makes pregnancy a diabetogenic condition<sup>7</sup>.

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HbA<sub>1c</sub> (glycated hemoglobin) is a form of hemoglobin which is measured primarily to identify average plasma glucose concentration over a period of time (12 weeks)<sup>7</sup>. HbA<sub>1c</sub> is formed in a non-enzymatic pathway by addition of glucose to the N-terminal of the hemoglobin beta chain. As average amount of plasma glucose increases, the fraction of glycated Hb also increases<sup>9</sup>. For every increase of A1c of 1%, mean plasma glucose increases by 35 mg/dl<sup>10</sup>.

In the fetus or neonate, GDM is associated with higher rate of perinatal mortality, macrosomia, birth trauma, hyperbilirubinemia, polycythemia, hypocalcaemia, shoulder's dystosia and neonatal hypoglycemia<sup>6-7</sup>. In the later life, the children born to mother with GDM have shown to have a higher incidence of obesity, IGT and DM in late adolescence and young adulthood<sup>3,6</sup>. In the setting of extremely poor control of diabetes, still birth is an important complication<sup>6</sup>. So GDM remain among the leading problems that threatened for fetus.

As HbA<sub>1c</sub> levels closely correlates to blood sugar level in GDM it is therefore a reliable indicator of overall glycemic control among the patients of diabetes in pregnancy<sup>11</sup>. The study showed that HbA<sub>1c</sub> levels were increased in GDM patients than that of the normal pregnancy, so increased HbA<sub>1c</sub> indicates poor glucose control. Therefore HbA<sub>1c</sub> is a useful indicator of blood glucose controlled in the recent past & may be used to monitor the effect of drug therapy on blood glucose level and thus reduce the complications due to GDM both in mother & fetus.

## MATERIALS AND METHODS

The cross sectional comparative study was carried out in the department of Biochemistry and department of Gynecology and Obstetrics, Chittagong Medical College Hospital from January 2010 to December 2010. Proper permission was taken from the Ethical Committee of Chittagong Medical College. Total 110 pregnant women were included in this study. Among them 70 were Case (Group A) GDM patients (whose FBG $\geq$ 5.3mmol/l & PPBG $\geq$ 7.8mmol/l) and 40 were Control (Group B) normal pregnant women (whose FBG $<$ 5.3mmol/l & PPBG $<$ 7.8mmol/l). The study group was subdivided into three groups on the basis of level of FPG & PPPG. **In Group-I**, FPG is  $\geq$ 5.3mmol/l and PPPG is  $<$ 7.8mmol/l. **In Group-II**, PPPG is  $\geq$ 7.8mmol/l and FPG is  $<$ 5.3mmol/l. **In Group-III**, FPG is  $\geq$ 5.3mmol/l and PPPG is  $\geq$ 7.8mmol/l. Women with shortened red blood cell life span, sickle cell disease or any other condition that could result in premature red blood cell death, longer red blood cell life span, such as vitamin B12 or folate deficiency were excluded from the study. Data were collected by interview of the study population by using research instruments.

The blood sample was analyzed for FBS, PPBS & HbA<sub>1c</sub>. Fasting blood glucose & post prandial blood glucose were determined by Glucose Oxidase Method & plasma HbA<sub>1c</sub> level by High Performance Liquid Chromatography (HPLC21). FBS & PPBS were analyzed in the semi autoanalyzer SPECTROPHOTOMETER-5010.

Normal level of blood glucose according to ADA criteria of FPG value is  $<$ 5.3mmol/l and the WHO criteria of a 2-h PPPG value is  $<$  7.8mmol/l. & HbA<sub>1c</sub>  $<$  6%<sup>12</sup>. Above which marked as raised level.

## Gestational Diabetes Mellitus

GDM is defined in this study on the basis of fasting and 2-h post prandial serum glucose values equal to or greater than 5.3 m mol/l and 7.8 m mol/l respectively. If any one or both of the criteria were fulfilled, the diagnosis of GDM was made.

## Data Analysis

Statistical processing of data is done by Appropriate Statistical Package for Social Science (SPSS). Data were expressed as mean  $\pm$ SD. Confidence was fixed at 95% level and "p" value of 0.05 or less considered significant. Student's 't' test for quantitative variable and Chi-square test for categorical variable were done where applicable.

## RESULTS

Total 110 pregnant patients were included in this study. Among them 70 (63.6%) were cases who were GDM patients, 40 (36.4%) were control, as normal pregnant women. 23% cases both FBG & PPBG both were increased (g III). FBG increased in 13.6% cases (g-I), PPBG increased in 27.3% cases (g-II). (Table I).

72.7% residing in urban area, 69.1% were house wife, 13% are service holder. 49% of the participants are below SSC, 27% under Graduate, 18% Graduates, 3.6% post graduates, 1.8% illiterates. 47.3% of the participants are from average socio-economic status, 29.1% from poor socio-economic status, 23.6% from affluent status. (Table II).

FBG is increased ( $\geq$ 5.3mmol/l) in 57.1% cases, in group I & III it is 100% increased. PPBG is increased in ( $\geq$ 7.8mmol/l) in 78.6%, in group II & III it is 100% increased. FBG & PPBG both are highly significant ( $P < 0.001$ ). (Table III)

HbA<sub>1c</sub> in GDM patients are more than that of normal pregnancy ( $6.95 \pm 1.38\%$  Vs  $5.05 \pm 0.27\%$ ) which is statistically highly significant ( $p < 0.001$ ). (Table IV)

FBG & HbA<sub>1c</sub> both are increased in Group I & III. PPBS & HbA<sub>1c</sub> both are increased in group III. (Table V).

There is appositive correlation between FBG & PPBG with HbA<sub>1c</sub>. As FBG & HbA<sub>1c</sub> ( $r = 0.869$ ). PPBG & HbA<sub>1c</sub> ( $r = 0.507$ ) and in both  $P < 0.001$ . (Table VI)

**Table I :** Distribution of study groups (n = 110)

Study Groups	Frequency	Percentage (%)
<b>Group-A (Group – I, II, III)-case.</b>		
Group I [FBS $\geq$ 5.3; PPBS $<$ 7.8]	15	13.6
Group II [FBS $<$ 5.3; PPBS $\geq$ 7.8]	30	27.3
Group III [FBS $\geq$ 5.3; PPBS $\geq$ 7.8]	25	22.7
<b>Group –B (Group IV) Control.</b>		
[FBS $<$ 5.3; PPBS $<$ 7.8]	40	36.4
Group-A(case)-GDM patients	70	63.6
Group –B(Control)-Normal	40	36.4
<b>Total</b>	<b>110</b>	<b>100.0</b>

**Table 2 :** Distribution of socio-demographic variables (n = 110)

Socio-demographic Variables		Frequency	Percentage (%)
Inhabitation	Urban	80	72.7
	Rural	30	27.3
Occupation	House Wife	76	69.1
	Student	20	18.2
	Service Holder	14	12.7
Educational Status	Illiterate	02	1.8
	Below SSC	54	49.1
	Under Graduate	30	27.3
	Graduate	20	18.2
	Post Graduate	04	3.6
Socio-economic Status	Poor	32	29.1
	Average	52	47.3
	Affluent	26	23.6
<b>Total</b>		<b>110</b>	<b>100.0</b>

**Table 3:** Distribution of blood sugar status among the study groups (with X<sup>2</sup> test significance)

Blood Sugar Status	Study Groups						X <sup>2</sup> Test Significance	
	Group-A		Group-B		Total			
	N	%	N	%	n	%		
<b>FBS Status</b>	Increased (≥ 5.3 mmol/L)	40	57.1	00	0.0	40	36.4	P = 0.000 <sup>HS</sup>
	Normal (< 5.3 mmol/L)	30	42.9	40	100.0	70	63.6	
<b>PPBS Status</b>	Increased (≥ 7.8 mmol/L)	55	78.6	00	0.0	55	50.0	P = 0.000 <sup>HS</sup>
	Normal (< 7.8 mmol/L)	15	21.4	40	100.0	55	50.0	

HS = Highly Significant (P &lt; 0.001)

Blood Sugar Status	Study Groups								X <sup>2</sup> Test Significance	
	Group I		Group II		Group III		Group IV			
	N	%	n	%	N	%	N	%		
<b>FBS</b>	Increased	15	100.0	00	0.0	25	100.0	00	0.0	P = 0.000 <sup>HS</sup>
	Normal	00	0.0	30	100.0	00	0.0	40	100.0	
<b>PPBS</b>	Increased	00	0.0	30	100.0	25	100.0	00	0.0	P = 0.000 <sup>HS</sup>
	Normal	15	100.0	00	0.0	00	0.0	40	100.0	

HS = Highly Significant (P &lt; 0.001)

**Table 4 :** Statistics of HbA<sub>1c</sub> among the study groups (n = 110)

	Study Groups	N	Mean	± SD	Median	Range	Sign.
<b>HbA<sub>1c</sub> (%)</b>	Group I	15	7.87	0.67	8.00	7.0 – 9.0	*P = 0.000
	Group II	30	5.51	0.21	5.55	5.2 – 5.8	Highly
	Group III	25	8.12	0.80	8.00	7.0 – 9.0	Significant
	Group IV	40	5.05	0.27	5.00	4.5 – 5.6	
	Group-A	70	6.95	1.38	7.00	5.2 – 9.0	**P = 0.000
	Group-B	40	5.05	0.27	5.00	4.5 – 5.6	Highly
	TOTAL	110	6.26	1.44	5.60	4.5 – 9.0	Significant

Significance; \*\*

**Table 5 :** Distribution of blood sugar status according to HbA1c status among the study groups (n = 110)

Study Groups	Fasting Blood Sugar Status	HbA1c Status		Total
		Increased	Normal	
Group I	Increased	15	0	15
	Normal	0	0	0
Group II	Increased	0	0	0
	Normal	0	30	30
Group III	Increased	25	0	25
	Normal	0	0	0
Group IV	Increased	0	0	0
	Normal	0	40	40
	Total	40	70	110

It was evident that increased FBS & HbA<sub>1c</sub> observed in group-I&III

Study Groups	Post Prandial Post prandial Blood Sugar Status	HbA1c Status		Total
		Increased	Normal	
Group I	Increased	0	0	0
	Normal	15	0	15
Group II	Increased	0	30	30
	Normal	0	0	0
Group III	Increased	25	0	25
	Normal	0	0	0
Group IV	Increased	0	0	0
	Normal	0	40	40
	Total	40	70	110

It was evident that increased PPBS & increased HbA<sub>1c</sub> observed in group-III

**Table 6:** Correlations between blood sugar levels & HbA<sub>1c</sub> (n = 110)

Correlations between	Pearson's Correlation Coefficient (r)	Significance (P Value)
FBS & HbA <sub>1c</sub>	0.869	P = 0.000
PPBS & HbA <sub>1c</sub>	0.507	P = 0.000

Highly Significant

## DISCUSSION

The present study provide the data on the relationship of Glycated Haemoglobin with Gestational Diabetes Mellitus and normal pregnancy .

Among the study group 73% live in urban area, 27% live in the rural areas.69% of the participants are housewife,18% are students,

13% are service holder. 49%of the participants are below SSC,27% under Graduate,18% Graduates, 3.6% post graduates,1.8% illiterates. 47.3% of the participants are from average socio-economic status,29.1% from poor socio-economic status,23.6% from affluent status.

In present study it is observed that HbA<sub>1c</sub> in GDM patients are more than that of normal pregnancy (6.95±1.38% Vs 5.05±0.27%) which is statistically highly significant(p<0.001). The finding is similar to the another study<sup>13</sup>.

In the study FBS level is increased (≥5.3mmol/L) in 57.1% cases(group I &III) but in control 100% normal. which is highly significant(P=<0.001). PPBS is increased (≥7.8 mmol/L.) in 78.6% cases(group II & III) but in control 100% normal, which is highly significant (P=<0.001)<sup>11</sup>.

In the obtained result of the study we observe that FBS & HbA<sub>1c</sub> both are increased in increased in Group I & III. PPBS & HbA<sub>1c</sub> both are increased in group III.. Again PPBS & HbA<sub>1c</sub> both are increased in 62.5% (group III) cases, which is highly significant (p=<0.001).

In the present study, Pearson's Correlation Coefficient (r) showed that there was a positive correlation between Fasting Blood Sugar and HbA<sub>1c</sub> (r=0.869, P=<0.001),Post Prandial Blood Sugar and HbA<sub>1c</sub> (r=0.507 ,P=<0.001) is significant. This study was consistent with that of other studies<sup>11,14</sup>.

Higher amounts of glycated hemoglobin ,indicating poorer control of blood glucose levels, have been associated with cardiovascular disease, nephropathy and retinopathy. The HbA<sub>1c</sub> strongly associated with the risk of development & progression of microvascular and nerve complications. High HbA<sub>1c</sub> (>9.0-9.5%) is associated with very rapid progression of microvascular complications<sup>9</sup>.

As HbA<sub>1c</sub> levels are closely correlate to blood sugar level in GDM. It is therefore a reliable indicator of overall glycaemic control among the patients of diabetes in pregnancy<sup>11</sup>. Levels of HA<sub>1c</sub> are not influenced by daily fluctuations in the blood glucose concentration, reflect the average glucose level over the prior 6 to 8 weeks. Therefore HbA<sub>1c</sub> is a useful indicator of blood glucose controlled in the recent past & may be use to monitor the effect of drug therapy on blood glucose level<sup>11</sup>.

HbA<sub>1c</sub> on other hand, is a spot test with no requirement for prior preparation, no risk of misinterpretation owing to recent meal or drug<sup>14</sup>. So by monitoring HbA<sub>1c</sub> we can reduce the complications both in mother & foetus due to GDM.

## CONCLUSION

GDM causes serious complications both in mother & baby. So early & easy diagnosis is necessary. HbA1C level is increased in GDM. This can be used as a measure of glycemic control in patient with GDM & design dosage regimen for GDM.

Levels of HA1c are indicator of blood glucose controlled in the recent past. Increased HbA1C level in early pregnancy indicates the patient is pre Diabetic. Early initiation of treatment may prevent complication.

## DISCLOSURE

All the authors declared competing interest.

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