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Glycosylated haemoglobin (HbA1c) in pregnancy

Diabetes is a major cause of perinatal and maternal morbidity and mortality. By the year 2030, the number of persons with diabetes is estimated to be about 79.4 million.[1] Diabetes mellitus is a medical complication of pregnancy associated with high morbidity. Gestational diabetes mellitus (GDM) has been defined as "any degree of glucose intolerance with onset or first recognition during pregnancy regardless of whether insulin or only diet modification is used for treatment or whether the condition persists after pregnancy. It represents nearly 90% of all pregnancies complicated by diabetes.[2] GDM affects approximately 7% of all pregnancies accounting for more than 2,00,000 cases every year.[3] Studies have shown that pregnant women with diabetes have undesirable pregnancy outcomes including increased rates of obstetric complications, still births, perinatal mortality, congenital malformations, macrosomia and increased risk for pre-term delivery compared to mothers without diabetes mellitus.[4,5] These complications can be minimized by early detection of diabetes and achieving strict glycaemic control.6 Glycosylated haemoglobin (HbA1c) is a reliable marker for the assessment of glycaemic control and according to the American Diabetes Association (ADA), HbA1c levels should be within 1% above the upper limit of the normal range in order to have a rate of complications no greater than those in pregnancies in women without diabetes mellitus.4 Inspite of following these guidelines and achieving good glycaemic control, such levels of control are still not good enough for preventing the occurrence of perinatal complications.[6,7] Studies on HbA1c in normal pregnancy have shown mixed results, with some showing an increase[8] and others a decrease.[9,10] Also, there is paucity of literature regarding the levels of HbA1c in pregnancy in Indian population. Hence this pilot study was undertaken to evaluate the levels of HbA1c in pregnancy and to compare these levels to the levels in the non-pregnant state.

Twenty pregnant women in the age-group of 18-35 years in the second trimester of pregnancy with no risk factors for GDM and 20 non-pregnant age-matched healthy women, not known to have diabetes mellitus were included in the study. Institutional Ethical committee approval was obtained. Informed consent was obtained from all the subjects included in the study. All of them underwent oral glucose challenge test (OGCT). Plasma glucose levels 1-hour after 50 g glucose load and HbA1c levels were measured in all participants.

Glucose was estimated by hexokinase/glucose-6-phosphate dehydrogenase method on a Siemens Dade Dimension RxL Max chemistry analyzer (Siemens Corporation, Munich, Germany). HbA1c

Table 1: Comaprision of HbA1c and OGCT values between pregnant women and non-pregnant control subjects

Parameter	Pregnant women (n = 20)	Non-pregnant women (n = 20)	Significance
HbA1c (%)	5.04±0.47	5.35±0.42	p = 0.033
Plasma glucose concentration 1-hour after a 50 g oral glucose load (OGCT) (mg/dL)	105.35±16.97	89.95±15.21	p = 0.004

HbA1c = Glycosylated haemoglobin; OGCT = Oral glucose challenge test
Data expressed as mean ± standard deviation; all values corrected to first decimal

was estimated by an ion-exchange high performance liquid chromatography (HPLC) method on a Bio-Rad D-10 (Bio-Rad, Hercules, CA, USA) analyzer.

HbA1c levels were significantly lower (p = 0.033) in pregnant women as compared to non-pregnant women (Table-1). The findings of this study are in good agreement with other reports across the world.[9-11] However, non-pregnant women were not included and hence the difference in the HbA1c levels between pregnant and non-pregnant women were not compared in these studies.[10,11] The reduction of HbA1c found during normal pregnancy is of significant clinical importance when defining the HbA1c goal for defining glycaemic control during pregnancy in women with diabetes. There was no correlation between HbA1c and OGCT values (r = 0.024; p = 0.883).

The changes in HbA1c can be attributed to changes in the carbohydrate metabolism or erythrocyte dynamics or a combination of both factors. HbA1c has a decreased reactivity to 2,3-bisphosphoglycerate and an increased affinity for oxygen. Hence, lower concentration of HbA1c facilitates oxygen delivery to the foetus.[12] During normal pregnancy, a decrease in fasting blood glucose occurs early in pregnancy, mainly between the sixth and tenth weeks, and is sustained during the remaining part of pregnancy.[13] New erythrocytes formed in pregnancy will therefore be exposed to a lower time-averaged glucose concentration than those of non-pregnant women. This leads to a lesser degree of glycosylation and therefore lower levels of HbA1c. In addition, the erythrocyte lifespan is likely to be decreased in pregnancy and the increase in young erythrocytes diminishes the HbA1c level.[14]

Thus in pregnant women with diabetes mellitus, HbA1c may not accurately reflect the glycaemic control. In conclusion, these results indicate that the targets for glycaemic control during pregnancy by HbA1c measurement need to be revised.

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