Glycated hemoglobin in early pregnancy as a predictor of gestational diabetes mellitus

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Abstract

Introduction: The prevalence of Gestational diabetes mellitus (GDM) is high in Asian subcontinent. As per current guidelines, the routine screening for GDM is at 24 to 28 weeks of gestation.30 to 50% of GDM cases may remain undiagnosed until such period of screening. This study aims to investigate HbA1C levels at as early as 12 weeks of pregnancy as a predictor of GDM. **Materials and Methods:** This prospective study included 100 patients enrolled at their first antenatal visit, or before 12 weeks of gestational age, who attended OPD. At the time of enrolment for HbA1c and routine antenatal investigations were done. A 75 gm GTT was done at 22 to 26 weeks of gestation. HbA1c cutoff was taken as $\geq 5.7 \& \leq 6.4$ and patients having value ≥ 5.7 were taken as abnormal. Subjects with HbA1c ≥ 6.5 , overt diabetes, hemoglobinopathies, anaemia, chronic renal diseases and multiple pregnancies were excluded from the study.

Results: It is found that women >28 years had higher levels of hbA1C in comparison to patients <28 years of age. There was a good statistical agreement between HbA1c & GTT with a p value of 0.581. Sensitivity of HbA1c was 70.4% and specificity 93.2%. **Conclusion:** The study concludes that women with higher HbA1c (\geq 5.7) were more likely to develop GDM than those women with lower HbA1C (\leq 5.7). HbA1c can be done routinely in early pregnancy (1st trimester). Women with higher HbA1c (\geq 5.7) can benefit from early interventions early in pregnancy thereby prevent GDM and adverse perinatal and pregnancy outcomes.

Keywords: Early pregnancy, Glycated hemoglobin, GDM, Maternal age.

Introduction

Diabetes mellitus is a major metabolic disorder affecting millions worldwide. The prevalence of Gestational diabetes mellitus (GDM) is high in Asian subcontinent.¹ The incidence of GDM in India, Chennai was $<1\%^1$ and $3.8\%^2$ in Kashmir. The mothers with GDM and their neonates may suffer adverse effects such as preeclampsia and macrosomia respectively and also associated with high rates of caesarean sections.³ As per current guidelines, the routine screening for GDM is at 24 to 28 weeks of gestation which may be unfortunate, for 30 to 50% of GDM cases may remain undiagnosed until such period of screening, the time by which the adverse effects might already have taken course.⁴ Early detection of GDM and treatment can reduce the risks of complication in both the mothers and their babies.⁵⁻⁸ HbA1c, is recently included as a diagnostic tool for diabetes in non-pregnant general population, but not vet recommended for the diagnosis of GDM by any current guidelines. This study aims to investigate HbA1C levels at as early as 12 weeks of pregnancy as a predictor of GDM.

Materials and Methods

The work embodied in this prospective study included 100 patients enrolled at their first antenatal visit, or before 12 weeks of gestational age, who attended OPD. Patients with overt diabetes, hemoglobinopathies, anaemia (hb <10%), chronic renal diseases, and multiple pregnancies were excluded from the study. Blood was collected at the time of enrolment for HbA1c and routine antenatal investigations. Subjects with HbA1c ≥ 6.5 were excluded from the study. Gestational age was confirmed with 1st trimester ultrasound and singleton pregnancies were included in the study. NT scan was done at 11-13 weeks, and anomaly scan before 20 weeks of gestation. All included in the study were then subjected to a 75 gm GTT at 22 to 26 weeks of gestation and values were interpreted using IADPSG 2010/ WHO2013 criteria. HbA1c cut-off was taken as ≥ 5.7 & ≤ 6.4 and patients having value ≥ 5.7 were taken as abnormal.⁷ The study duration was 2 years (September 2014 to August 2016). HbA1c was measured using HPLC method.

Results

The average gestational age in this study was 7 \pm 0.85 weeks.

Mean age of patients was 27.6 ± 4.67 , mean weight gain was 14.12 ± 2.99 .



Graph 1: Frequency distribution of HbA1C and GTT

Graph 2: Association of maternal age with HbA1C



Table 1: Frequency distribution of HbA1C in GDM and non GDM group

	GDM				
HbA1C	Yes		No		P Value
	n = 27	%	n = 73	%	
Abnormal (\geq 5.7)	19	70.3	5	6.8	0.581
Normal (≤ 5.7)	8	29.7	68	93.2	

Table 2: HbA1C in GDM

Sensitivity	70.4%
Specificity	93.2%
Predictive value positive	79.2%
Predictive value negative	89.5%
Accuracy	87%



Graph 3: Comparison of HbA1C in GDM and normal population

In all 100 patients there was no abortions or abnormalities observed. Other factors like mode of delivery, parity and maternal weight gain showed no comparable association.

Discussion

It is well documented in various studies that, in a normal, early pregnancy (between 6 to 10 weeks) there is a fall in fasting blood glucose.^{5,6,9} This remains so for the remaining part of pregnancy. Hence, the newly formed erythrocytes during this phase are exposed to lower glucose concentration in comparison to those of non-pregnant women. Consecutively the glycosylation is also less.

In all the 100 antenatal patients HbA1c was taken before 12 weeks of gestation and the diagnosis of GDM was done using GTT (modified IADPSG 2010) at 22–26 weeks. The objective of this study was to find out if early pregnancy HbA1c (between $\geq 5.7 \& \leq 6.4$) can be a predictor for GDM. The standard cut-off for HbA1c was taken as ≥ 5.7 in reference to earlier studies.¹⁰⁻¹² The sensitivity and specificity in various studies with respect to HbA1C cut off for diagnosis of GDM¹⁰⁻¹² shows, the lesser the HbA1C value, the better the specificity but sensitivity will decrease.

In this study the average maternal age taken was 28 years. It is found that women >28 years had higher levels of hbA1C in comparison to patients <28 years of age. Therefore increasing maternal age is found to be a risk factor for high HbA1C levels and development of GDM.

In this study, there is a good statistical agreement between HbA1c & GTT with a p value of 0.581. Sensitivity of HbA1c is 70.4% and Specificity being 93.2%. These results imply that women with higher HbA1c (\geq 5.7) were more likely to develop GDM than those women with lower HbA1C (\leq 5.7).

In all 100 patients there was no abortions or abnormalities observed. Other factors like mode of delivery, parity and maternal weight gain showed no comparable association which could be due to smaller sample size.

This study concludes that increasing maternal age is associated with increased levels of HbA1C in pregnancy (\geq 5.7) and development of GDM. Also HbA1C can be used as a reliable tool for predicting GDM in as early as 12 weeks of gestation.

Conclusion

HbA1c can be done routinely in early pregnancy (1st trimester). Women with higher HbA1c (\geq 5.7) can benefit from early interventions like appropriate diet and lifestyle modification early in pregnancy thereby prevent GDM and adverse perinatal and pregnancy outcomes.

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