

Glycosylated haemoglobin (HbA_{1c}) – Is it a useful screening test for gestational diabetes mellitus?

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Abstract

The objective of this study was to assess whether a single assay of glycosylated haemoglobin in pregnant women could be used as a screening test for detection of gestational diabetes mellitus in comparison to the formal 75g glucose tolerance test. A cross-sectional descriptive study was performed on 118 high risk and 126 low risk pregnant women attending the university antenatal clinics at Colombo South Teaching Hospital, using a systematic sampling technique. A 75g oral glucose tolerance test and glycosylated haemoglobin assay were performed. The reliability of the tests were assessed by calculating the sensitivity and specificity. In comparison to the 75g glucose tolerance test single assay of glycosylated haemoglobin (HbA_{1c}) gave a sensitivity of 88% and a specificity of 78% with regard to detection of gestational diabetes mellitus. Therefore a single assay of HbA_{1c} is shown to be a useful test for screening for gestational diabetes mellitus.

Keywords: Glycosylated haemoglobin, glucose tolerance test, gestational diabetes.

Introduction

Formation of glycosylated haemoglobin (HbA_{1c}) occurs irreversibly and progressively by the addition of glucose to the N-terminal valine of the haemoglobin beta-chain. This occurs throughout the normal life span of the erythrocytes which is approximately 120 days. Therefore HbA_{1c} concentration reflects the average glycaemic status of the past 4 - 6 weeks. The measurement of HbA_{1c} is a useful test for assessing the metabolic control of diabetic patients.

In pregnancy, insulin resistance and hyperinsulinaemia lead to a diabetogenic state (1). Most women in the normal population have sufficient pancreatic beta cell reserves to tolerate this insulin resistance but some have limited pancreatic beta cell reserves and develop diabetes during pregnancy (2). Early diagnosis of gestational diabetes mellitus is very important in reducing fetal and neonatal complications which are well documented (3).

The conventional way of diagnosing gestational diabetes is by a formal glucose tolerance test. This test is time consuming and inconvenient for the patients since they need to be fasting and necessitates taking several blood samples over a period of two to three hours. Therefore the usefulness of oral glucose tolerance test (OGTT) as a screening test has its own limitations. This study was performed to assess whether a single assay of glycosylated haemoglobin in pregnant women can be used as a screening test for detection of gestational diabetes mellitus, in comparison to the formal OGTT.

Materials and Methods

Two hundred and forty four women attending the antenatal clinics at Colombo South Teaching hospital (CSTH) were studied. The selected study population included all patients at 28 (±2) weeks of gestation attending university antenatal clinics at GSTH with following risk factors during the period of one year from July 1997.

- The presence of established history of diabetes mellitus among first degree relatives of the pregnant mothers

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- b. Women with previous unexplained stillbirths.
- c. Women with previous history of delivering babies over 4 kg.
- d. Women with a history of previous gestational diabetes mellitus.
- e. Women with polyhydramnios in the present pregnancy.

A low-risk sample as the control group was selected in patients with none of the above risk factors using a systematic sampling technique as described below. Patients who were known to have diabetes were excluded from this study.

Sampling

The study population consisted of pregnant women attending university antenatal clinic for the first occasion which averaged to about 30 mothers per week.

The test group consisted of all the above mentioned at risk mothers (n=118). For the controls (n=126) a systematic sampling technique with every sixth mother being selected after having identified the first mother by use of a lottery system was used.

Venous blood samples were taken on all 244 pregnant women after over night fasting and this was followed by oral intake of 75g of glucose and a second venous blood sample two hours later. Blood was collected into two sets of tubes using

aseptic techniques. One set contained sodium fluoride/potassium oxalate and the other set contained EDTA. Blood collected into tubes containing sodium fluoride/potassium oxalate was centrifuged immediately at 2000 rpm for 10 min. and the plasma was separated and assayed for glucose by standard colorimetric glucose oxidase method. The whole blood collected with EDTA was immediately subjected to glycohaemoglobin assay using a commercial assay kit (Human – Germany) which employs a weak binding cation-exchange resin for rapid separation of glycohaemoglobin from non glycohaemoglobin.

The sensitivity and specificity were calculated to assess the reliability of HbA_{1c} test. The cut off point with regard to glycosylated haemoglobin for diagnosis of gestational diabetes was regarded as a value greater than 7% (4) and the two hour plasma glucose level after 75g OGTT was regarded as greater than 144 mg/dl (5).

Results

The HbA_{1c} and plasma glucose levels of glucose tolerance test positive and normal subjects are given in Table 1.

The oral glucose tolerance test was positive in 100 pregnant women of whom 88 tested positive for HbA_{1c}. Therefore the sensitivity of this test is 88%. Of the 144 pregnant women tested negative by the oral glucose tolerance test, 112 were correctly identified by the HbA_{1c} test giving a specificity value of 78% (Table 2).

Table 1

The HbA_{1c} and plasma glucose concentrations of glucose tolerance test of normal and positive pregnant women

	Glucose Tolerance Positive		Glucose Tolerance Normal	
	High risk (n=61)	Low risk (n=39)	High risk (n=57)	Low risk (n=87)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Glucose (mg/dL)				
Fasting	122±8	116±8	91 ±7	79±7
2 hours	178±11	156±11	94 ±5	88±5
HbA _{1c} (%)	9.1±0.7	7.9±0.7	5.4 ±0.4	4.8±0.4

Table 2

Comparison HbA_{1c} with gold standard glucose tolerance test

	Number of mothers with glucose tolerance test			
	Positive		Negative	
	High risk	Low risk	High risk	Low risk
HbA _{1c}				
Positive	56	32	11	21
Negative	5	7	46	66
Total	100		144	

Discussion and Conclusions

In Sri Lanka the reported incidence of gestational diabetes is around 8% (6). Undiagnosed gestational diabetes mellitus (GDM) can result in significantly higher maternal and perinatal mortality and morbidity (3). The current practice in Sri Lanka is to screen only high risk mothers for GDM in antenatal clinics. But it has been suggested that screening should not be restricted to high risk subjects. Screening of all pregnant women should be performed at 24 to 28 weeks of pregnancy (7). The conventional way of screening for GDM with 75g OGTT is time consuming and inconvenient from the patient point of view since this involves the patient to be fasting and necessitates taking several blood samples over a period of two to three hours. Therefore this test has limitations for use as a screening test for GDM.

Present study shows that estimation of glycosylated haemoglobin with a cut-off point of more than 7% has a sensitivity of 88% and a specificity of 78%. In previous studies, HbA_{1c} is shown to be specific but the sensitivity for routine screening has been questionable (8,9,10). In our study, timing of the test at 28 weeks and criteria used for diagnosis of GDM would have resulted in the sen-

sitivity of 88%. The selection of a screening test depends on its simplicity to perform and ability to detect disease. Hence it should have a high sensitivity. Glucose challenge test which consists of taking a blood sample one hour after the ingestion of a 50g glucose load has been reported as having a sensitivity of 85.1% and specificity of 72.5% when used as a screening test (7). Although the cost analysis of HbA_{1c} revealed that it was expensive than the glucose challenge test (Rs. 207 *vs* Rs. 40), it has the advantage of not having the inconvenience of measuring and drinking glucose and the patient need not be kept waiting for an additional hour to take the second blood sample. Furthermore in the U. K. despite attempts to introduce the glucose challenge test over the last 15 years only 6% of maternity units are currently using it (11).

Hyperglycaemia of gestational diabetes usually develops only after the first trimester (12). Since the timing for screening was done at 28 weeks, the sensitivity reported in the present study is more meaningful. The sensitivity of 88% of the present study was greater than the value obtained for glucose challenge test in a different study which has been done around the same gestation (7). Furthermore, when evaluating the effi-

ciency of a screening test in identifying a high risk group, there should be a valid "gold standard" diagnostic test which identifies the disease process. In this study 75g oral glucose tolerance test (OGTT) was used as the gold standard diagnostic test. Using these criteria HbA_{1c} is shown to be a useful test for screening for gestational diabetes mellitus. A positive screen needs to be confirmed by an OGTT. In current obstetric practice, a simple, reliable screening test is extremely important as the incidence of gestational diabetes mellitus is showing a rising trend over the past years (13). Early diagnosis and proper control of hyperglycaemia in these patients has led to a remarkable improvement in perinatal outcome (14).

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