



Research Article

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Determination of Relationship between Hba1c Levels and Early Diagnosis of Gestational Diabetes

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ABSTRACT

Gestational diabetes mellitus (GDM) is associated with undesirable complications on the mother and newborn. Screening test for GDM is currently performed between 24-28 weeks of pregnancy. However, 30-50% of cases with type 2 diabetes remain undiagnosed during pregnancy. International Association of Diabetes and Pregnancy Study Groups, America Diabetes Association and World Health Organization recommend diabetes screening in pregnancy at the first visit for the pregnant women. However, the most appropriate test and its threshold are not yet clear. The HbA1c level seems an appropriate criterion for this screening test. Therefore, this study aimed to determine HbA1c levels in the first trimester of pregnancy for the diagnosis of GDM in high risk women referred to Ahvaz Imam Hospital. Total of 158 singleton pregnant women, in their gestational age less than 20 weeks, who were not the diagnosed cases of diabetes and referred for prenatal care participated in the study. A questionnaire consisting of clinical and demographic information such as maternal age, gestational age at the time of blood sample receipt, BMI, gestational diabetes history, and the number of previous pregnancy was filled for each patient. Blood sample of these women was taken once in gestational age less than 20 weeks after 12 hours of fasting, fasting blood sample, one-hour and two hours after ingestion of 75 g glucose, and HbA1c level was determined. Participants with HbA1c ≥ 6.5 or FBS ≥ 126 or sugar random sample ≥ 200 were diagnosed as diabetes before pregnancy and were excluded from the study. The test was repeated for those who entered the study in gestational ages 24-28 weeks. The results showed that average HbA1c level in pregnant mothers whose GDM has been diagnosed before 20th week of pregnancy is more than their counterparts whose GDM had not been diagnosed before 20th week of pregnancy ($P=0.02$). HbA1c cut point for the diagnosis of GDM before 20th week of pregnancy was obtained 5.550. Also HbA1c level average in pregnant mothers whose GDM was diagnosed in 24-28 weeks is higher than HbA1c levels in pregnant mothers whose glucose tolerance test was negative in 24-28 weeks ($P=0.005$). The specificity of the GTT 75 g glucose for GDM diagnosis before 20 weeks of pregnancy was relatively poor. The results also showed sensitivity, specificity, positive predictive value, and negative predictive value of 100%, 86.6%, 75.4%, and 100%, respectively. The findings showed that BMI variable is significantly effective on HbA1c changes in the diagnosis of GDM before 20 weeks of pregnancy ($P<0.0001$).

Keywords: Gestational diabetes mellitus, HbA1c, Body mass index, screening test, pregnancy

INTRODUCTION

Several studies have demonstrated that gestational diabetes mellitus (GDM) is associated with undesirable complications on the mother and newborn. Studies have shown racial differences affect prevalence of GDM and outcomes of pregnancy with GDM. For example, Indian immigrant women and European women show higher prevalence of GDM (1, 2). Now screening test for GDM is performed between 24-28 weeks of pregnancy. However,

reports indicate that there is 40-60% early diagnosis of GDM. Diagnosis of GDM until the third trimester of pregnancy results in a significant increase in the number of birth of big newborns, despite good glucose control, while early identification of impaired glucose tolerance will reduce complications related to hyperglycemia (3, 4).

Unfortunately, 30-50% of cases with type 2 diabetes remains undiagnosed and may delay during the period of pregnancy to screening time for GDM (24- 28 weeks)

Women with positive test for impaired glucose intolerance in the first trimester of pregnancy, more likely type 2 diabetes has not been diagnosed in them before pregnancy or they have GDM. These two clinical situations suggest that women with pre-pregnancy diabetes are at risk of disease and more risk during pregnancy and require more care (5). Reduction of mortality, perinatal and preeclampsia has been seen in women whose GDM has been diagnosed early (6). International Association of Diabetes and Pregnancy Study Groups (IADPSG), America Diabetes Association (ADA) and World Health Organization (WHO) have recommended diabetes screening in pregnancy at the first visit for the pregnant women. Although the most appropriate test and its threshold is not yet clear, in this regard, HbA1C measurement seems a proper test.

This is because it can be measured from blood samples examined in routine prenatal tests measurement and laboratory can measure it easily. In addition, this test compared to other blood sugar tests has the advantage that is stable and repeatable. HbA1C level of higher than or equal to 6.5% (48 mmol/mol) is Diagnostic Point Cut recommended for diabetes. These data are related to non-pregnant. Pregnant women have lower Point Cut level in the first trimester of pregnancy at rate of 6% at zero to 14 weeks of pregnancy (1, 3, 7, 8). Mukesh et al. (2005) tested 442 pregnant women as GDM screening test to evaluate HbA1C. They used two HbA1C thresholds to confirm or deny GDM. These two extents were confirmed by OGTTg-75 gold standard method (WHO criteria). The results showed that 19% of them had GDM and 81% of them were without GDM. HbA1C histogram diagram was totally coincided in these two populations.

Their results showed 0.54 (0.48-0.61 CI: 0.95%), area under the ROC Curve to diagnose HbA1C. They stated threshold less than 5.50 to reject GDM. They stated each threshold chosen for acceptable sensitivity requires a large number of healthy women to confirm OGTT (7). Lowe et al. (2012) examined the relationship between mother's blood sugar and HbA1C with undesirable pregnancy complications. They examined 23316 eligible pregnant women. Eligible women underwent 75 g OGTT between 24-32 weeks. Neonatal anthropometric dimensions and c-peptide in cord serum were measured. Their results showed that among participants that their blood sugar level was blinded for care providers, 21064 women had variable HbA1C results. Mean and standard deviation were $4.79 \pm 0.4\%$, respectively. A stronger significant relationship was observed between glucose and birth weight, sum of skinfolds, body fat percentage above 90 percentile, as well as 1-hour and fasting glucose with serum c-peptide compared to HbA1C (all $P < 0.01$).

They stated in a fully adjusted model, the odds ratio of birth weight higher than 90 percentile per 1 more standard deviation was observed 1.39, 1.45, and 1.38 for fasting, 1 and 2 hours glucose, and 1.15 for HbA1C, respectively. The odds ratio for cord C- peptide above 90 percentile was 1.56, 1.45, and 1.35 for glucose, and 1.32 for HbA1C, respectively. Also similar risk ratio was observed for glucose and HbA1C for primary cesarean delivery, preeclampsia, and preterm delivery. They concluded in this study that HbA1C measurement is not a good alternative for OGTT in pregnant women (9). Berggren et al. (2015) stated that a unit increase in the amount of HbA1c causes 13-fold increased risk of diagnosis of GDM (68.0, 2.6 CI, 13.959% OR). Their results showed that HbA1C level in first trimester of pregnancy in GDM group was significantly higher than normal group (5.4 ± 0.4 vs. 5.2 ± 0.3 , $P = 0.002$). The aim of this study is to determine HbA1C level in the first trimester of pregnancy for the diagnosis of GDM in high risk (8).

MATERIALS AND METHODS

In a prospective analytic study, 158 singleton pregnant women who are not the diagnosed case of diabetes, and had gestational age less than 20 weeks and referred for prenatal care were participated in the study. A questionnaire was recorded, which was indicative of clinical and demographic characteristics such as maternal age, gestational age at the time of blood sample receipt, BMI, GDM history, and the number of previous pregnancy. In addition, written consent was taken from them to participate in the scheme. Blood sample of these women was taken once in gestational age less than 20 weeks after 12 hours of fasting, fasting blood sample, one-hour and two hours after ingestion of 75 g glucose, and HbA1c level was determined. People with $HbA1c \geq 6.5$ or $FBS \geq 126$ or sugar random sample ≥ 200 were diagnosed as diabetes before pregnancy and were not entered the study. The above mentioned test was repeated for those who entered the study in gestational age 24-28 weeks. Therefore, the results were

classified based on HbA1c level, and patients with GDM were identified, and their relationship with HbA1c was measured.

According to the criteria (American Diabetes Association) ADA, in the case of the presence of any of cases: fasting blood sugar above 92 mg/dl (1.5 mmol/l), 1-hour blood sugar above 180 mg/dl (10 mmol/l), and 2-hour blood sugar above 153 mg/dl (5.8 mmol/l), diagnosis of GDM is definitive.

RESULTS AND DISCUSSION

Among the 158 examined cases, GDM in 46 women was diagnosed before 20 weeks and in 15 women was diagnosed in 24-28 weeks, and the rest were followed up until the end of pregnancy, and no new GDM was found. The relationship between HbA1C and GDM before 20 weeks of pregnancy has been shown in Table 1.

Table 1. Relationship of HbA1C level and diagnose of GDM before 20 weeks

GDM before 20 weeks	HbA1C Average	Standard deviation	Standard Error Rate
No	5.037	0.6252	0.0591
Yes	5.274	0.5483	0.0808

Results showed that HbA1C level average in pregnant mothers that their GDM had been diagnosed before 20 weeks is 5.27 ± 0.54 and HbA1C level average in pregnant mothers that their GDM had not been diagnosed until 20 weeks is 5.03 ± 0.62 . HbA1C level average in mothers that their GDM has been diagnosed before 20 weeks is more than HbA1C level average in pregnant mothers that their GDM has not been diagnosed until 20 weeks. This is a significant difference (P -value = 0.02).

Determination of HbA1C cut point for the diagnosis of GDM before 20 weeks of pregnancy

Figure 1 shows GDM diagnostic level before 20 weeks of pregnancy with HbA1C and Table 2 shows the changes in the area under the diagram.

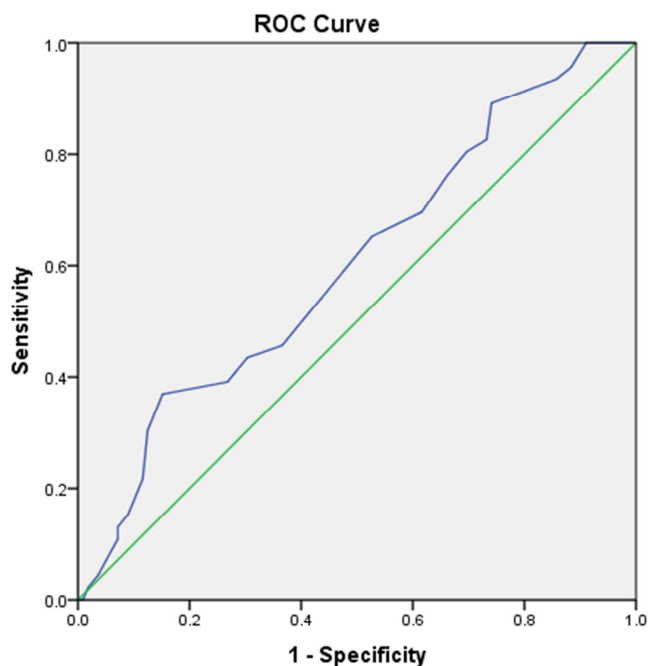


Figure 1. GDM diagnostic level before 20 weeks of pregnancy with HbA1C

Table 2: Changes in the area under the diagram of Roc curve, HbA1C

Area Under the Curve				
Test Result Variable(s): HbA1c				
Area	Std. Error ^a	Asymptotic Sig. ^b	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.602	0.049	0.044	0.506	0.699
<i>The test result variable(s): HbA1c has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.</i>				
<i>a. Under the nonparametric assumption</i>				
<i>b. Null hypothesis: true area = 0.5</i>				

The results presented in Table 2 show that the area under the curve Roc is equal to 0.602. This represents a relatively good prediction and above HbA1C for the diagnosis of GDM before 20 weeks of pregnancy. The generalized criteria value (sig.) was also calculated 0.04, which shows that this prediction is significant.

According to Figure 1, the nearest point of intersection to the left corner and the top curve is located in the range of sensitivity less than 0.4 and specificity less than 0.2. The range of this point in the HbA1C level is considered same cut point that the number of 5.550 was obtained. As a result, the number of cases of HbA1C that are at the top of this number have high odds risk for GDM and have more urgent need to examination and diabetes screening before 20 weeks.

Determination of the relationship between HbA1C level before 20 weeks and GDM in 24-28 weeks of pregnancy has been shown in Table 3.

Table 3. Relationship between HbA1C level before 20 weeks and diagnose of GDM in 24-28 weeks of pregnancy

GDM in 24-28 weeks	HbA1C Average	Standard deviation	Standard Error Rate
No	5.000	0.6232	0.0633
Yes	5.275	0.5570	0.0713

Results showed that HbA1C level average in pregnant mothers that their GDM was diagnosed before in 24-28 weeks is 5.27 ± 0.55 and HbA1C level average in pregnant mothers that their Glucose tolerance test was negative in 24-28 weeks is 5.00 ± 0.62 . HbA1C level average in mothers that their GDM was diagnosed before 24-28 weeks is more than HbA1C level average in pregnant mothers that their Glucose tolerance test in 24-28 weeks was negative. This is a significant difference ($P= 0.005$). As a result, people who have HbA1C higher in the first half of pregnancy are advised to take extra care in terms of incidence of GDM.

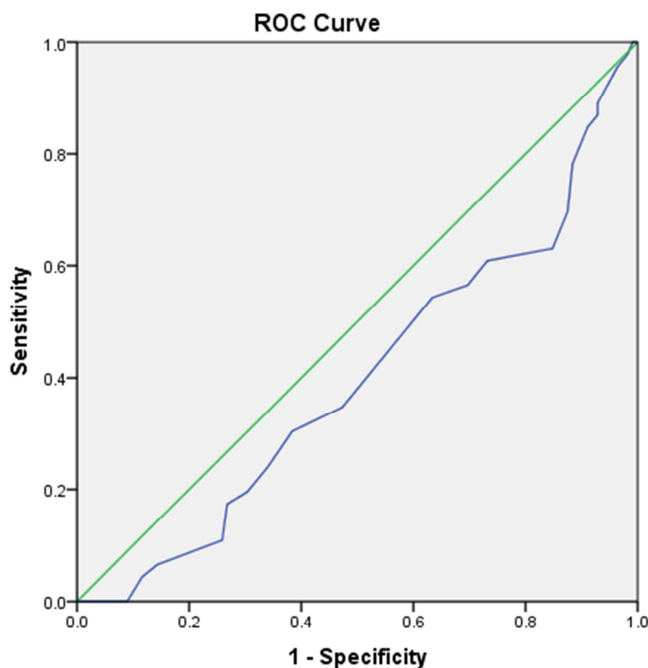


Figure 1. GDM diagnostic level before 20 weeks of pregnancy with 75 g GTT of glucose

Determination of sensitivity and specificity of 75 g OGTT for the diagnosis of GDM before 20 weeks of pregnancy

Figure 2 shows GDM diagnostic levels before 20 weeks of pregnancy with 75 g OGTT. According to drawn ROC curve diagram, GDM diagnostic levels before 20 weeks of pregnancy with 75 g OGTT is under normal curve. Therefore, the diagnosis of GDM with 75 g OGTT before 20 weeks has not appropriate specificity, and is not suggested as a screening test before 20 weeks of pregnancy.

Determination of sensitivity and specificity of GDM diagnostic test before 20 weeks of pregnancy compared to 24-28 weeks of pregnancy has been shown in table 3.

Table 3. Sensitivity and specificity of GDM diagnostic test before 20 weeks of pregnancy compared to 24-28 weeks of pregnancy

		75 g OGTT before 20 weeks		
		Negative	Positive	Total
75 g OGTT before 24-28 weeks	Negative	97	-	97
	Positive	15	46	61
	Total	46	112	158

The results presented in Table 3 show that 75 g OGTT for the diagnosis of GDM before 20 weeks compared to 24-28 weeks has 100% sensitivity, specificity 86.6% 75.4% positive predictive value, and 100% negative predictive value. According to the 75.4% positive predictive value, 75 g OGTT before 20 weeks cannot be suggested as an alternative screening test in 24-28 weeks.

BMI impact on HbA1C level in the diagnosis of GDM before 20 weeks of pregnancy

Table 4 shows average of BMI and HbA1C in patients who were diagnosed with GDM before 20 weeks of pregnancy.

Table 4. Average of BMI and HbA1C in patients diagnosed with GDM before 20 weeks of pregnancy

GDM before 20 weeks of pregnancy		
Variable	Positive	Negative
BMI	27.19±3.54	24.68±3.89
HbA ₁ C	5.27±0.54	5.03±0.62

The results presented in Table 4 show that BMI average of women who had GDM before 20 weeks of pregnancy was 27.19±3.54 and women who did not have GDM before 20 weeks of pregnancy was 24.68±3.89. Both BMI and HbA1C variables are alone significantly different toward diagnose of GDM before 20 weeks of pregnancy (P<

0.0001, P= 0.02). In addition, according to statistical calculation by Regression logistic method, BMI Variable is significantly effective in HbA1C changes in the diagnosis of GDM before 20 weeks of pregnancy (P< 0.0001).

Therefore, BMI as the independent variable has linear and direct impact on HbA1C in the diagnosis of GDM. It is anticipated that the increase in BMI increased the risk of HbA1C and the risk of GDM before 20 weeks of pregnancy.

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