Is HbA1c Predictive for Screening and Diagnosis of Gestational Diabetes Mellitus?

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**OBJECTIVE:** Evaluation of HbA1c value in diagnosis of gestational diabetes mellitus.

**STUDY DESIGN:** This retrospective cohort study included 131 women with gestational diabetes mellitus (GDM) that were screened and diagnosed between the 24-28 weeks of gestation by two-step testing regimen in Etlik Zübeyde Hanım Women’s Health Research and Educational Hospital. Venous blood samples of these women were collected for HbA1c. One sample test was performed to test the difference between our HbA1c results and the value in the literature.

**RESULTS:** The mean HbA1c result in our study was 5.6% (min:4.4%, max:8.0%), standard deviation was 0.5. We compared our results with the cut off value of 5.5 % that was notified for second trimester for non-diabetic pregnancies by different authors. Our HbA1c value that was 5.6% was significantly higher than the cut off values (5.5%) that was reported (p=0.008).

**CONCLUSION:** There is an ambiguity for the threshold values of HbA1c in GDM. Further studies are needed to evaluate true cut-off values for using HbA1c for screening and diagnosing GDM.

**Keywords:** Gestational diabetes mellitus, HbA1c, OGTT

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**Introduction**

Diabetes mellitus is a major cause of perinatal morbidity and mortality and maternal morbidity. Diabetes mellitus complicates about 3%-14% of all pregnancies. It has been estimated that 90% of the cases are gestational diabetes mellitus (GDM). GDM is defined as carbohydrate intolerance of varying degrees of severity with onset or first recognition during pregnancy. GDM has a significant risk for developing glucose intolerance later in life. Clinical recognition of GDM is important because therapy can reduce pregnancy complications.

Oral glucose tolerance test (OGTT) is the standard test for diagnosing GDM. Different criteria use different values for OGTT for diagnosing GDM. OGTT requires the participant to be in fasting state, requires at least 2 h for sample collections and minimum two blood samples are taken. Using 100-OGTT for the diagnosis of GDM has some problems. It was defined to yield a group of women in the top 98th percentile of glucose response but the definition of “abnormal” did not consider correlation with neonatal or fetal outcome. But the most significant morbidity associated with GDM is about neonatal or fetal outcome. Also after a large glucose load the problem of emesis invalidated the test. As a result of these, two-step diagnostic system causes delay in diagnosis of GDM and has a relatively high false-negative rate (10% to 20%).

WHO in 2011 accepted glycated hemoglobin A1c (HbA1c) for diagnosing diabetes mellitus but its use for diabetes screening in pregnancy or in the postpartum period is still unclear. The American Diabetes Association recommendations state that HbA1c concentrations 1% above the upper limit of the reference interval should be achieved before and during pregnancy to assure a good glycemic state.

Because of the ease of estimation of HbA1c in comparison to the OGTT, it is being utilized increasingly for screening and diagnosis of diabetes and prediabetes states in the recent years.
In this background we conducted a study to explore the utility of HbA1c in the 24-28 gestational weeks screening of women with gestational diabetes instead of OGTT at Etlik Zubeyde Hanım Women’s Health Research and Educational Hospital, a tertiary referral hospital, in Turkey. Aim of the present study was to determine HbA1c levels in a series of GDM patients, in order to verify the possible contribution of HbA1c to GDM management.

**Material and Method**

The study was approved by the study review group of Etlik Zubeyde Hanım Women’s Health Research and Educational Hospital. It was conducted retrospectively and included 131 GDM women that were screened and diagnosed between the 24-28 week of gestation by two-step testing regimen in Etlik Zubeyde Hanım Women’s Health Research and Educational Hospital. We used two-step testing regimen which involves a 50-g “challenge” pre-test followed by the 100-g OGTT only if the initial result is abnormal. Women with a history of type 1 and type 2 diabetes mellitus were excluded from this study. 50-g GCT was performed any time of the day. Each participant was given a glucose drink (50 g of D-dextrose powder dissolved in 200 mL of water). Samples for 1-h PPBG (post prandial blood glucose) were obtained by taking 2 mL of venous blood in tubes containing sodium fluoride. If the results were ≥ 200 mg/dL (11.1 mmol/L), 3 mL each of venous blood samples were collected in tubes containing EDTA for HbA1c and the patients were hospitalized for treatment. If the results were between 140-199 mg/dL, 100-g OGTT was performed. The positive test was considered according to National Diabetes Data Group (NDDG). Samples for fasting blood glucose (FBG) were obtained by starving at least 8 h. Before all else samples for FBG were obtained, if the result was <105 mg/dL (5.8 mmol/L), the patients were given 100 g glucose drink, after that, 1-h, 2-h and 3-h blood glucose were obtained by taking 2 mL of venous blood in tubes containing sodium fluoride. NDDG recommended using plasma glucose levels of 105 mg/dL (5.8 mmol/L), 190 mg/dL (10.5 mmol/L), 165 mg/dL (9.1 mmol/L) and 145 mg/dL (8.0 mmol/L) for fasting, 1-hour, 2-hour, and 3-hour post glucose load as the diagnostic thresholds for GDM, defined as having two or more plasma glucose values higher than these cutoffs during the oral glucose tolerance test.\textsuperscript{13} If the results defined that the patients were GDM, 3 mL each of venous blood samples were collected in tubes containing EDTA for HbA1c and the patients were hospitalized for treatment. HbA1c was measured using high performance spectrophotometry analyzer.

All women who were diagnosed with GDM, managed by diet/lifestyle modifications and/or medical treatment. When the patients were diagnosed as GDM, diet and exercise were the first-line treatment. They were defined as GDM A1 when the glucose levels were within normal levels by diet therapy and GDM A2 when the insulin therapy was required for glucose regulation. HbA1c values were noted to control of glycemic state of women.

**Results**

In our study group mean age was 32.6 (min:21-max:45), gravidity was min:1, max:11, parity was min:0, max:8, mean BMI was: 29.2 (min:19.1-max:50.5). 92 (70.2%) women were at the age of between 18-35 years-old. 2(1.5%) women were <18 years-old, 9 (6.9%) women were >40 years-old.

All the pregnant women had 50-g GCT between 24-28 gestational weeks and 85 (64.9%) women’s results were between 140-199 mg/dL, 46 (35.1%) women’s results were ≥ 200 mg/dL. The women results were ≥200 mg/dL were identified as GDM.

100 g OGTT was performed for 85 (64.9%) patients whose 50 g GCT results’ were between 140 mg -199 mg. 100 g OGTT results were: 5 (3.8%) patients had high FBG, 61 (46.6%) patients had high two blood glucose levels, 19 (14.5%) patients had three high glucose levels. All the patients diagnosed Gestational Diabetes Mellitus were hospitalized. 103 (78.6%) patients had only diabetic diet and exercise for therapy, 3 (2.3%) patients had diabetic diet, exercise and single dose insulin therapy at night, 25 (19.1%) patients had diabetic diet, exercise and four times insulin therapy all day.

The mean HbA1c result was 5.6% (min:4.4%, max:8.0%), standard deviation was 0.5 in our study. We calculated our results with the cut off value of 5.5% that was notified by Versantvoort et al. in 2013 for second trimester for nondiabetic pregnancies.\textsuperscript{14} Also Mosca et al. reported the HbA1c reference intervals 4.0%-5.5% for pregnant nondiabetic women in 2006.\textsuperscript{15} Our HbA1c value that was 5.6%, was significantly higher than the cut off values that was reported (p=0.008).

According to the objectives of the study, the collected data was compiled, tabulated and analyzed, using appropriate statistical tests. One sample test was performed to test the difference between our results and the value in the literature. All statistical analyses were performed using SPSS Statistics version 21.0 software (Table 1,2,3).

**Table 1: The age distribution of the study population (n= 131)**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>18-35</td>
<td>92 (70.2)</td>
</tr>
<tr>
<td>36-40</td>
<td>28 (21.4)</td>
</tr>
<tr>
<td>&gt;40</td>
<td>9 (6.9)</td>
</tr>
</tbody>
</table>
Table 2: The body mass index (BMI) distribution of the study population (n= 131)

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Number (%):</th>
</tr>
</thead>
<tbody>
<tr>
<td>18.5-24.99</td>
<td>28 (21.4)</td>
</tr>
<tr>
<td>25-29.99</td>
<td>51 (38.9)</td>
</tr>
<tr>
<td>30-34.99</td>
<td>38 (29)</td>
</tr>
<tr>
<td>35-39.99</td>
<td>11 (8.4)</td>
</tr>
<tr>
<td>≥40</td>
<td>3 (2.3)</td>
</tr>
</tbody>
</table>

Table 3: The parity distribution of the study population (n= 131)

<table>
<thead>
<tr>
<th>Parity</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>33 (29.8)</td>
</tr>
<tr>
<td>1</td>
<td>39 (25.2)</td>
</tr>
<tr>
<td>2</td>
<td>45 (34.4)</td>
</tr>
<tr>
<td>≥3</td>
<td>14 (10.6)</td>
</tr>
</tbody>
</table>

Discussion

In our study, two-step testing regimen which involves a 50-g “challenge” pre-test followed by the 100-g OGTT only if the initial result is abnormal were applied for screenings and diagnosing GDM according to NDDG values.

This study has shown that the mean HbA1c values of GDM women were significantly higher than non GDM pregnant women. The cut off value for HbA1c that were mentioned from Versantvoort et al. and Mosca et al. for the second trimester pregnancies. The mean HbA1c result was 5.6% (min:4.4%, max:8.0%), standard deviation was 0.5. The difference in the HbA1c values was found to be statistically significant (p=0.008). HbA1c levels are lower in pregnancy compared to nonpregnant state.15,16 This will be the result of a decrease in fasting plasma glucose occurs early in pregnancy due to diversion of glucose towards developing fetus. As a result, in GDM HbA1c, that reflects the last three months glucose levels, values are lower than diabetic levels.

In 2010 ADA recommended HbA1c for diagnosing diabetes mellitus but there are no such guidelines for use of HbA1c during pregnancy and for diagnosing GDM.17 Also using of HbA1c has been recommended as a test to diagnose diabetes by various international organizations.1,18,19 Advantage of blood sampling in the non-fasting state makes HbA1c check as a promising tool for diabetes screening. But the ambiguity of cut off value of HbA1c is a problem for routine use in GDM as a screening test.

Although HbA1c has advantage of good intra-individual reliability, we have to remember that measurement of HbA1c is affected by hemoglobinopathies and anemia. These are associated with accelerated red cell turn over.20

In a review in 2013, it was mentioned that glycated hemoglobin level had poorer test characteristics than fasting plasma glucose level or the OGTT. But using HbA1c level in pregnant women had advantages of a quick and simple screening test for the presence of overt diabetes. There was no suggestion using HbA1c for GDM.21

In conclusion, our results confirm the results of previous studies indicating that the targets for HbA1c during pregnancy should be lower than those currently used. But there is an ambiguity for the threshold values. Further studies are needed to evaluate true cut-off values for using HbA1c for screening and diagnosing GDM.

HBA1C Gestasyonel Diabetes Mellitus Tarama ve Tanısında Değerli midir?

AMAÇ: HbA1c sonucunun gestasyonel diabetes mellitus tanısındaki yerini araştırmak.


BULGULAR: Çalışmamızdaki ortalama HbA1c sonucu %5,6 (min:4,4-max:8), std.sapma 0,5 idi. Sonuçlarımızı farklı çalışmalarla verilen ikinci trimester sağlıklı gebelerin HbA1c değerleri ile karşılaştırdık. Çalışmamızın sonucu olan ortalamada değer (%5,6) diğer çalışmalar tarafından bildirilen cut-off değerinden (%5,5) anlamlı olarak yüksekti (p<0,008).

SONUÇ: GDM tanısında HbA1c eşik değeri için netlik bulunmamaktadır. GDM tarama ve tanısı için HbA1c eşik değerinin saptanması için daha fazla çalışma ihtiyaç vardır.

Anahtar Kelimeler: Gestasyonel diabet, HbA1c, OGTT

References

rural women residing in the Central Region of Limpopo Province, South Africa. Diabet Med 2007;24:233-239 [PMID:1726376]


