

# The effects of age, parity and body mass index on 50 g oral glucose tolerance test results and its predictive value in gestational diabetes mellitus

Yaş, parite ve vücut kitle indeksinin 50 gr glukoz tarama testi üzerine etkileri ve gestasyonel diabetes mellitus ile ilişkisi

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Ethics Committee Approval: The study protocol  
was approved by the Clinical Research Ethics  
Committee of Alanya Alaaddin Keykubat  
University, Faculty of Medicine (Date:05/06/2020  
No:19-21). All procedures in this study involving  
human participants were performed in accordance  
with the 1964 Helsinki Declaration and its later  
amendments.

Etik Kurul Onayı: Çalışma protokolü Alanya  
Alaaddin Keykubat Üniversitesi Tıp Fakültesi  
Klinik Araştırmalar Etik Kurulu tarafından  
onaylandı (Tarih: 05/06/2020 No: 19-21). İnsan  
katılımcıların katıldığı çalışmalardaki tüm  
prosedürler, 1964 Helsinki Deklarasyonu ve daha  
sonra yapılan değişiklikler uyarınca  
gerçekleştirilmiştir.

Conflict of Interest: No conflict of interest was  
declared by the authors.

Çıkar Çatışması: Yazarlar çıkar çatışması  
bildirmemişlerdir.

Financial Disclosure: The authors declared that  
this study has received no financial support.  
Finansal Destek: Yazarlar bu çalışma için finansal  
destek almadıklarını beyan etmişlerdir.

Published: 9/27/2020

Yayın Tarihi: 27.09.2020

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Published by JOSAM

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## Abstract

**Aim:** The aim of this study was to investigate the effects of age, parity, body mass index (BMI) and maternal risk factors on 50 g oral glucose tolerance test (OGTT) positivity and to evaluate the predictive value of 50 g OGTT in the diagnosis of gestational diabetes mellitus (GDM).

**Methods:** Medical data of pregnant women who were followed in a private obstetrics and gynecology clinic between June 2012 and April 2020 were analyzed in this retrospective cohort study. All patients underwent 50 g OGTT between 24 and 28 weeks of gestation. A 1-h postprandial venous plasma glucose cut-off of  $\geq 140$  mg/dL was considered positive for OGTT and the diagnosis was confirmed by 2-h 75 g OGTT. The relationship between the GDM and OGTT results, BMI, parity, age, and other maternal risk factors was analyzed in the regression analysis.

**Results:** A total of 323 pregnant women were included in the study. The mean age was 29.35 (5.29) years and the mean BMI was 27.23 (6.07) kg/m<sup>2</sup>. Among them, 35.9% had  $\geq 1$  risk factors. The sensitivity, specificity, positive predictive value, and negative predictive value of 50 g OGTT for GDM were 100%, 80.7%, 27.5%, and 100%, respectively. Regression analysis revealed that family history of diabetes, history of GDM, and macrosomic birth increased the GDM risk by 5.73, 4.95, and 1.43 folds, respectively.

**Conclusion:** Evaluation of advanced maternal age, pre-pregnancy BMI, and maternal risk factors is useful to predict GDM. In addition, 50 g OGTT is helpful in diagnosing GDM for both maternal and fetal health.

**Keywords:** Oral glucose tolerance test, Diabetes, Obesity, Advanced maternal age

## Öz

**Amaç:** Bu çalışmada yaş, parite, vücut kitle indeksi (VKİ) ile gebenin öyküsünde saptanan risk faktörlerinin 50 g glikoz tarama testi (OGTT) pozitifliği üzerine etkileri ve 50g OGTT'nin gestasyonel diabetes mellitus (GDM) tanısında etkinliği araştırıldı.

**Yöntemler:** Haziran 2012-Nisan 2020 tarihleri arasında özel bir kadın doğum kliniğinde takip edilen gebelerin tıbbi verileri bu retrospektif kohort çalışmasında incelendi. Gebeliğin 24 ila 28. haftaları arasında tüm gebelere 50 g OGTT uygulandı. 1 saatlik venöz kan şekeri düzeyi 140 mg/dL üzerinde ise test pozitif kabul edildi ve tanı için 75 g 2 saatlik glikoz tolerans testi yapıldı. Gebelerin OGTT sonuçları, VKİ, parite, yaş ve diğer risk faktörlerinin GDM ile ilişkisi regresyon analizi ile incelendi.

**Bulgular:** Çalışmaya toplam 323 gebe dahil edildi. Ortalama yaş 29,35 (5,29) yıl ve ortalama vücut kitle indeksi 27,23 (6,07) kg/m<sup>2</sup> idi. Grubun %35,9'unda en az bir risk faktörü mevcuttu. 50g OGTT'nin GDM tanısında duyarlılığı, özgüllüğü, pozitif prediktif değeri ve negatif prediktif değeri sırayla %100, %80,7, %27,5 ve %100 olarak bulundu. Regresyon analizinde ailede diyabet öyküsü GDM riskini 5,73 kat, GDM öyküsü 4,95 kat ve iri bebek öyküsü 1,43 kat artırdı.

**Sonuç:** İleri gebelik yaşı, gebelik öncesi VKİ ve öyküdeki risk faktörlerinin değerlendirilmesi GDM'nin öngörülmesi açısından faydalıdır. Ayrıca 50 g OGTT, anne ve bebeğin sağlığı için GDM tanısında yararlıdır.

**Anahtar kelimeler:** Oral glikoz tolerans testi, Diyabet, Obezite, İleri yaş gebelik

## Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance with onset or first recognition during pregnancy, and it usually resolves after delivery [1]. With varying degrees, it accounts for 1 to 14% (average 4 to 5%) of all pregnancies [2]. In Turkey, its prevalence ranges from 1.9 to 27.9% with a mean prevalence of 7.7% [3]. The variation in the prevalence of GDM depends on maternal anthropometric measurements such as the height and body mass index (BMI), as well as diagnostic instruments and criteria used. In previous studies, advanced maternal age and increased body weight were associated with a higher prevalence of GDM [4].

It has been well established that GDM is associated with adverse maternal outcomes including gestational hypertension, preeclampsia, polyhydramnios, vasculopathy and even type 2 diabetes mellitus (DM) in the long-term and adverse fetal outcomes including macrosomia, congenital malformation, and intrauterine fetal demise [5]. In addition, GDM increases the risk of neonatal birth trauma, hypoglycemia, respiratory distress syndrome, hyperbilirubinemia, hypocalcemia, polycythemia, and even mortality [6].

The oral glucose tolerance test (OGTT) is the gold standard for the diagnosis of GDM [7]. It is recommended for all pregnant women between 24 and 28 weeks of gestation. The test can be done as a one-step or two-step method [8]. The treatment of GDM decreases the maternal, fetal, and neonatal risks [9]. In the literature, the risk of GDM as assessed by the 50 g OGTT was higher in women aged >30 years, having a BMI of  $\geq 25$  kg/m<sup>2</sup>, and those who had given multiple births ( $\geq 4$ ) [10].

The aim of the present study was to investigate the effects of age, parity, BMI, and maternal risk factors on 50 g OGTT results and to evaluate the predictive value of 50 g OGTT in the diagnosis of GDM.

## Materials and methods

This single-center, retrospective study was conducted at a private obstetrics and gynecology clinic between June 2012 and April 2020. A written informed consent was obtained from each participant. The study protocol was approved by the Clinical Research Ethics Committee of Alanya Alaaddin Keykubat University, Faculty of Medicine (Date:05/06/2020-No:19-21). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Of all pregnant women, those having a healthy singleton pregnancy, who were non-diabetic, visited the clinic within the first six weeks of gestation and are still under regular follow-up were included. Data regarding the first examination within six weeks of gestation were collected and maternal age, gestational week at the time of screening, parity, and BMI were recorded. Considering no weight gain at the time of first examination within six weeks of gestation, pre-pregnancy BMI was defined as the value calculated at the time of first examination. Maternal and fetal risk factors including history of intrauterine fetal demise of unknown origin, macrosomic birth (birth weight >4,000 g), recurrent pregnancy loss, polyhydramnios, and family history of DM were evaluated.

All patients who were at low risk for GDM underwent fasting blood glucose (FBG) measurement between six and eight weeks of gestation. If the FBG level was >100 mg/dL, 2-h (postprandial) 75 g OGTT was performed to diagnose latent pre-gestational DM (PGDM). Irrespective of the GDM risk, all the remaining patients underwent 50 g OGTT between 24<sup>th</sup> and 28<sup>th</sup> weeks of gestation. A 1-h (postprandial) venous plasma glucose cut-off of  $\geq 140$  mg/dL was considered positive for OGTT and the diagnosis was confirmed by 2-h (postprandial) 75 g OGTT. Women who were at high risk for GDM and having unknown diabetic status (i.e., those having a history of macrosomic birth, recurrent pregnancy loss, unexplained intrauterine fetal demise, congenital fetal malformations, previous GDM and a family history of DM) underwent 2-h (postprandial) 75 g OGTT following the first examination. If the test result indicated a cut-off value or higher (FBG: 92 mg/dL; 1-h: 180 mg/dL; 2-h 153 mg/dL), the diagnosis of PGDM was established and excluded from the study. Women with DM were treated with dietary modifications alone or combined with insulin.

### Statistical analysis

Statistical analysis was performed using the SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean (Standard Deviation, SD), median (min-max) or number and frequency. Visual histogram and likelihood graphics and analytic methods such as Kolmogorov-Smirnov or Shapiro-Wilk tests were used to check the normal distribution of the variables. The chi-square and Fisher exact tests were performed for inter-group comparison. The Bonferroni-corrected Z multiple comparisons were used to compare multiple groups. A logistic regression analysis was performed using the backward elimination method to predict GDM based on clinical data. A *P*-value of <0.05 was considered statistically significant.

## Results

A total of 323 pregnant women were included in the study. The mean age was 29.35 (5.29) years and the mean BMI was 27.23 (6.07) kg/m<sup>2</sup>. Of the patients, 35.9% had  $\geq 1$  risk factors. Baseline sociodemographic and clinical characteristics of the patients are shown in Table 1.

Among all, 24.8% (n=80) had positive 50 g OGTT results and 6.8% (n=22) were diagnosed with GDM. The sensitivity, specificity, positive predictive value, and negative predictive value of 50 g OGTT for GDM were 100%, 80.7%, 27.5%, and 100%, respectively (Table 2).

According to the age groups, 50 g OGTT yielded the highest positive results in the 30-35 age group, while most women aged >35 years were diagnosed with GDM. The rates of OGTT positivity and GDM diagnosis according to the age groups are summarized in Table 3.

According to the BMI values, women with >35 kg/m<sup>2</sup> had the highest rate of 50 g OGTT positivity, indicating a statistically significant difference (*P*=0.001). However, there was no statistically significant difference in the rate of GDM diagnosis among the BMI groups (Table 4).

According to the number of parities, there was no statistically significant difference in the rate of GDM diagnosis, based on 50 g OGTT (Table 5).

Table 1: Baseline sociodemographic and clinical characteristics of patients

n=323	Mean (SD)	Median (min-max)
Age, years	29.35 (5.29)	29.00 (18-41)
BMI, kg/m <sup>2</sup>	27.23(6.07)	27.00 (18-39)
Parity	1.02(0.82)	1.00 (0-4)
Having risk factors	35.9%	n=116
Family history of DM	27.2%	n=88
History of GDM	4.6%	n=15
History of macrosomic birth	4.6%	n=15
History of recurrent pregnancy loss	4.6%	n=15
History of unexplained intrauterine fetal demise	0.3%	n=1

BMI: body mass index; DM: diabetes mellitus; GDM: gestational diabetes mellitus.

Table 2: Correlation between GDM and 50 g OGTT

	GDM+	GDM-
50g OGTT+	22 (22.5%)	58 (72.5%)
50g OGTT-	0 (0.0%)	243 (100.0%)

Sensitivity: 100.0%; specificity: 80.7%; PPV:27.5%; NPV:100.0%. GDM: gestational diabetes mellitus; OGTT: oral glucose tolerance test; PPV: positive predictive value; NPV: negative predictive value.

Table 3: Rates of OGTT positivity and GDM diagnosis according to the age groups

Age group	n (%)	50g OGTT+ n (%)	$\chi^2$	P-value	GDM n (%)	$\chi^2$	P-value
<25 years	72 (22.3)	11 (15.3)	11.302	0.010	1 (1.4)	8.391	0.039
25-30 years	123 (38.1)	25 (20.3)			7 (5.7)		
30-35 years	61 (18.9)	22 (36.1)			5 (8.2)		
>35 years	67 (20.7)	22 (32.8)			9 (13.4)		

GDM: gestational diabetes mellitus; OGTT: oral glucose tolerance test;  $\chi^2$ : chi-square.

Table 4: Rates of OGTT positivity according to the BMI values

BMI group	n (%)	50g OGTT+ n (%)	$\chi^2$	P-value	GDM n (%)	$\chi^2$	P-value
<20 kg/m <sup>2</sup>	58 (18.0)	9 (15.5)	25.417	0.001	2 (3.4)	8.588	0.072
20-25 kg/m <sup>2</sup>	77 (23.8)	8 (10.4)			2 (2.6)		
25-30 kg/m <sup>2</sup>	84 (26.0)	26 (31.0)			5 (6.0)		
30-35 kg/m <sup>2</sup>	40 (12.4)	9 (22.5)			5 (12.5)		
>35 kg/m <sup>2</sup>	64 (19.8)	28 (42.8)			8 (12.5)		

BMI: body mass index; GDM: gestational diabetes mellitus; OGTT: oral glucose tolerance test;  $\chi^2$ : Chi-square.

Table 5: Rates of OGTT positivity according to the number of parity

Parity	n (%)	50g OGTT+ n (%)	$\chi^2$	P-value	GDM n (%)	$\chi^2$	P-value
0	90 (27.9)	16 (17.8)	5.196	0.268	3 (3.3)	8.721	0.068
1	150 (46.4)	38 (25.3)			13 (8.7)		
2	71(22.0)	21 (29.6)			4 (5.6)		
3	10 (3.1)	4 (40.0)			1 (10.0)		
≥4	2 (0.6)	1 (50.0)			1 (50.0)		

GDM: gestational diabetes mellitus; OGTT: oral glucose tolerance test;  $\chi^2$ : chi-square.

Risk factor analysis showed no significant difference in the OGTT results between the groups. However, family history of DM ( $P=0.001$ ) and a history of GDM ( $P=0.013$ ) were significant risk factors for GDM (Table 6).

Table 6: Risk factor analysis results

Risk factor	n (%)	50g OGTT+ n (%)	$\chi^2$	P-value	GDM n (%)	$\chi^2$	P-value
Family history of DM	88 (27.2)	58 (24.7)	0.023	0.538	14 (15.9)	15.721	0.001
History of GDM	15 (4.6)	6 (40.0)	1.959	0.138	4 (26.7)	9.771	0.013
History of macrosomic birth	15 (4.6)	5 (33.3)	0.619	0.303	2(13.3)	1.053	0.272
History of recurrent pregnancy loss	15 (4.6)	3 (20.0)	0.192	0.467	1 (6.7)	0.012	0.728
History of unexplained intrauterine fetal demise	1 (0.3)	1 (100.0)	0.248	3.047	1 (100.0)	13.724	0.068

DM: diabetes mellitus; GDM: gestational diabetes mellitus; OGTT: oral glucose tolerance test;  $\chi^2$ : chi-square.

A logistic regression analysis was performed using the backward elimination method to predict GDM based on the family history of DM, history of GDM, macrosomic birth, recurrent pregnancy loss, and unexplained intrauterine fetal demise. The analysis yielded statistically significant results ( $\chi^2$ :

48.402,  $P=0.001$ ). The model explained 15.9% of variance in heart disease (Nagelkerke $R^2$ ) and classified 93.2% of the patients accurately. Family history of DM, history of GDM, history of macrosomic birth increased the GDM risk by 5.73, 4.95, and 1.43 folds, respectively (Table 7).

Table 7: Logistic regression analysis results

Model	$\chi^2$	R <sup>2</sup>	P-value	OR	95%CI
Family history of DM	48.402	0.159	0.001	5.73	1.72-94.37
History of GDM			0.002	4.95	1.30-56.45
History of macrosomic birth			0.048	1.43	0.94-2.21

DM: diabetes mellitus; GDM: gestational diabetes mellitus; OR: odds ratio; CI: confidence interval;  $\chi^2$ : chi-square.

## Discussion

In the present study, the primary objective was to examine the effects of age, parity, BMI, and maternal risk factors on 50 g OGTT results and to evaluate the predictive value of 50 g OGTT in the diagnosis of GDM. The study results showed that a total of 323 pregnant women were included, the mean age was 29.35 (5.29) years and the mean BMI was 27.23 (6.07) kg/m<sup>2</sup>. Among all patients, 35.9% had  $\geq 1$  risk factor and 6.8% were diagnosed with GDM based on 2-h 75 g OGTT. These results are consistent with the literature [3].

The 50 g OGTT is a simple and cost-effective test, as it requires blood collection at a single session without a prerequisite of fasting state [11]. In the current study, a 1-h postprandial venous plasma glucose cut-off of  $\geq 140$  mg/dL was considered positive for OGTT and sensitivity, specificity, positive predictive value, and negative predictive value of 50 g OGTT for GDM were 100%, 80.7%, 27.5%, and 100%, respectively. In a previous study, De Sereday et al. [12] examined an alternative cut-off point to increase the predictive value in pregnancies at elevated risk for GDM. A total of 473 healthy pregnant women underwent a screening test with 1-h 50 g OGTT and the sensitivity was 66.7%, when the cut-off value was established at 137 mg/dL. In another study conducted in Turkey, the sensitivity, specificity, positive predictive value, and negative predictive value were 96.30%, 80.34%, 24.07%, and 99.70%, respectively, using a cut-off value of 145 mg/dL [13]. Although some authors have advocated that a cut-off value of 140 mg/dL is more accurate, the results of the present study are consistent with previous findings. In the current study, the American Diabetes Association (ADA) classification was used for the diagnosis of GDM. According to this classification, the positive predictive value of 50 g OGTT was 17.6% in previous studies [14], consistent with the findings of the current study.

According to the age groups, 50 g OGTT yielded the highest positive results in the 30-35 years age group, while most women aged  $>35$  years were diagnosed with GDM. In previous studies, there was a significant correlation between the maternal age and GDM diagnosis based on the 50 g OGTT. In a recent study including 307 healthy pregnant women, the incidences of a positive OGTT and GDM increased significantly with advanced maternal age from 20% and 2.2%, respectively in women aged  $\leq 25$  years to 37.8% and 14.7%, respectively in women aged  $>35$  years [15]. These results indicate that women aged  $>35$  years are at a higher risk for GDM, consistent with the findings of the current study. In another study conducted in Turkey, the GDM risk increased by 7.84-fold in women aged  $>40$  years [16].

Similarly, the rate of GDM was higher among women aged 31-35 years compared to the other age groups in another study [13].

According to the BMI values, the majority of women with  $>35 \text{ kg/m}^2$  had the highest rate of 50 g OGTT positivity, indicating a statistically significant difference. However, there was no statistically significant difference in the rate of GDM diagnosis among the BMI groups. In a study, there was a significant correlation between a BMI value of  $>25 \text{ kg/m}^2$  and GDM diagnosis based on the 50 g OGTT [15]. In another study, a BMI value of  $\geq 25 \text{ kg/m}^2$  increased the risk of GDM by 1.74-fold [16]. According to the current guidelines, a BMI value of  $\geq 30 \text{ kg/m}^2$  before pregnancy indicates an elevated risk for GDM and routine screening test between 24 and 28 weeks of gestation should be performed, even if the first-trimester screening test results are normal [8].

According to the number of parities, there was no statistically significant difference in the rate of GDM diagnosis based on 50 g OGTT. Although there are studies showing a correlation between the number of parities and GDM in the literature [17], a growing number of studies showed no statistically significant correlation, despite a constant increase in the GDM incidence based on the 50 g OGTT results [10,15].

In the current study, 35.9% of the women had  $\geq 1$  risk factors. According to the risk factor analysis, there was no significant difference in the OGTT results between the groups. However, family history of DM and history of GDM were significant risk factors for GDM. In addition, family history of DM, history of GDM, history of macrosomic birth increased the GDM risk by 5.73, 4.95, and 1.43 folds, respectively. In previous studies, family history of DM in the first-degree relatives (3.2-fold), history of GDM in previous pregnancies (23-fold), history of recurrent pregnancy loss, intrauterine fetal demise, and macrosomic birth (3.3-fold) were shown to be primary risk factors of GDM [8,18]. Furthermore, a correlation was found between the history of GDM in previous pregnancies based on 50 g OGTT and increased GDM risk [19]. Review of the literature revealed that history of GDM is the most significant predictor of GDM in the current pregnancy [20]. Similarly, some authors demonstrated that both history of GDM and family history of DM were the major predictors of GDM and 50 g OGTT positivity [15]. In a study investigating the relationship between the GDM risk factors and 50 g OGTT efficacy, a total of 426 pregnant women were divided into two groups according to the presence of risk factors and all underwent 50 g OGTT [21]. The positive predictive value of 50 g OGTT was 40.9% in the women having risk factors, while it was 22.2% in those having no risk factors, indicating a statistically significant difference between the groups. The authors concluded that 50 g OGTT should be applied to only pregnant women having risk factors in the screening of GDM.

### Conclusion

The results of the present study suggest that evaluation of advanced maternal age, pre-pregnancy BMI, and maternal risk factors is useful to predict GDM. In addition, 50 g OGTT is helpful to diagnose GDM for both maternal and fetal health.

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