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Could different cut-off values be used for 50-gram glucose tolerance test in low and high risk groups?

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ABSTRACT

Objectives: There are controversies about screening strategy and cut-off levels for gestational diabetes mellitus (GDM). Here, we aimed to identify optimal cut-off values for 50-gram oral glucose tolerance testing (OGTT) in high and low risk pregnant women.

Methods: A total of 500 patients who underwent two step OGTT were divided into two groups as GDM (n=31) and controls (n=469). Moreover, patients were grouped as high (n=114) and low risk (n=386) for GDM. Having≥2 risk factors such as family history of type-2 diabetes, obesity, glucosuria, previous history of GDM, macrosomia and diabetic complications were accepted as high risk. Demographic data, OGTT results, birth characteristics were recorded and compared between groups. A cut-off value for 50-gram OGTT was evaluated in low and high risk groups.

Results: The 50-gram OGTT value above 140 mg/dL discriminated GDM with 100% sensitivity and 92.11% specificity in all patients (AUC=0.969, P<0.001). The prevalence of GDM was 19.3% in high and 2.3% in low risk group. The 50-gram OGTT value above 140 mg/dL discriminated GDM with 100% sensitivity and 94.57% specificity in high risk patients (AUC=0.992, P<0.001). Furthermore, 50-gram OGTT value above 149 mg/dL discriminated GDM with 100% sensitivity and 93.63% specificity in low risk patients (AUC=0.976, P<0.001). Conclusions: Although screening in low risk population is a debating issue worldwide, our local guidelines still recommend screening all pregnant women. We suggest that performing 100-gram OGTT only in patients who have higher values than 149 mg/dL in 50-gram OGTT can be an alternative screening strategy in low risk group. Keywords: Cut-off, gestational diabetes mellitus, oral glucose tolerance test, threshold

estational diabetes mellitus (GDM) is one of the most common endocrine disorders of pregnancy. It is defined as any degree of glucose intolerance with first recognition during pregnancy [1]. Gestational diabetes mellitus have catastrophic effects for both mother and fetus during pregnancy. Moreover, it has long-term consequences. For this reason, accurate diagnosis and treatment has crucial role in maternal and fetal well-being [2, 3].

Screening programmes have been recommended by The American College of Obstetricians and Gynecologists (ACOG) and the American Diabetes Association (ADA) [4, 5]. Although 50-gram oral glucose tolerance testing (OGTT) followed by 100-gram OGTT is commonly performed all around the world for screening, there are still controversies about the

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optimal screening strategy [6, 7]. Another debating issue about GDM screening is the threshold values of OGTT [8]. Previous studies have suggested different cut-off points due to the nutrition and ethnicity [6, 7, 9, 10]. Generally, a glucose value \geq 140 mg/dL is accepted worldwide which can identify 80% of women with GDM. Besides this, ADA and ACOG claimed that a cut-off value of 130 mg/dL could be acceptable and identify 90% of GDM cases. Also, it has been suggested that GDM screening is not mandatory in low risk pregnant women for GDM. Having two or more risk factors including being above 45 years old, obesity, physical inactivity, high-risk ethnicity, family history of diabetes, previous GDM, macrosomia, pregestational diabetes, history of coronary artery disease, hypertension and medications leading to hyperglycemia is defined as high-risk population whereas patients who have no risk factor are defined as low risk [11]. Significant prevalance has been reported in low risk pregnant women all around the world and countries are still going on screening for this groups [4, 5, 9]. Unfortunately, there is no consensus in the literature about cut-off values in low risk pregnant women for GDM.

Considering that higher cut-off values leads to undiagnosed cases and lower threshold values cause performing more diagnostic tests, we grouped pregnant women to high and low risk groups and then aimed to identify optimal cut-off values for risk groups in Turkish pregnant women in the present study.

METHODS

This is a retrospective study performed at a high-volume university affiliated research and training hospital between January 2022 and December 2023. Local ethics committee approved this study with a decision number of 2024-TBEK 2024/06-11. Also, the present study complies with the declaration of Helsinki. Written informed consent was taken from all study participants for using data from medical records.

Study Population

During two year study period, OGTT screening for GDM was applied to 632 patients and these patients were obtained from medical records. Then, patients with unavailable perinatal data and who underwent 75-gram OGTT were excluded. Also, patients who have any contraindications and intolerance to OGTT, a history of pregestational diabetes, chronic diseases, and drugs affecting glucose metabolism such as corticosteroids noted in the medical reports of our hospital were excluded.

After selected according to the exclusion criteria, a total of 500 consecutive patients who were admitted to our obstetrics and gynecology outpatient clinic for prenatal visits, screened with two step OGTT for GDM and who had given birth in our hospital were enrolled in the study. The participants were divided into two groups based on 100-gram OGTT results as GDM (n=31) and controls (n=469). Moreover, patients were grouped as high-risk (n=114) and low-risk (n=386) groups for GDM.

In our clinic, pregnant women were routinely screened for GDM by one step protocol of 75-gram OGTT or a two-step protocol of 50-gram OGTT followed by 100-gram OGTT. Since 75-gram OGTT is both a diagnostic and screening test and our aim in the study is to determine the cut-off for the screening test, only patients screened with a two-step protocol were included. In two step protocol, accordance with recommendations by ADA and ACOG, 1 hour 50-gram OGTT was performed followed by 3 hours 100-gram OGTT if plasma blood glucose levels at first hour exceeds 140 mg/dL. According to the Carpenter and Coustan criteria, GDM was established with two abnormal values of 95 mg/dL for fasting, 180 mg/dl for first hour, 155 mg/dL for second hour and 140 mg/dL for third hours in 100-gram OGTT. Also plasma glu $cose \ge 200 \text{ mg/dL}$ after OGTT was accepted as GDM [4, 12].

High risk patients for GDM was diagnosed according to these criteria: (a) Family history of type-2 diabetes, (b) obesity (prepregnancy body mass index [BMI) \geq 30 kg/m²), (c) previous history of GDM, (d) previous history of macrosomia (fetal weight \geq 4500 gram), (e) history of diabetic complications, and (f) Glucosuria. Patients who had two or more risk factors accepted as high risk for GDM. In high risk group, 50gram OGTT was done in initial antenatal visit and if it was negative then the test repeated between 24-28 gestational week.

Demographic data such as age, BMI, gravida, par-

ity, OGTT results, birth characteristics such as birth weight, delivery week, delivery mode, baby gender, and Apgar scores were recorded for each patient for further analysis and compared between groups. A cutoff value for a 50-gram OGTT screening test was detected by ROC analysis both in low and high-risk groups.

Statistical Analysis

Shapiro Wilk test was used to determine whether the variables were distributed normally or not. All continuous variables were distributed non-normally and the Mann Whitney-U test was used for comparisons between two groups. Categorical variables were compared with the Chi-square test. Variables were presented as median (minimum-maximum) values for continuous variables and frequency (percentages) for categorical variables. The ROC analysis was used to evaluate the discriminative role of 50-gram OGTT values for GDM and Youden index was used to determine the cut-off values. Analyzes were carried out by using SPSS version 22.0 and MedCalc 18 programs, and P value ≤ 0.05 was considered as statistically significant.

RESULTS

The prevalance of GDM was found to be 6.2%. The sociodemographic, laboratory and birth characteristics of GDM and control groups were presented in Table 1. There was no statistically significant difference between two groups in terms of age, gravida, parity, gestational week, cesarean section rate, birth weight, baby gender, Apgar scores of first and fifth minutes, and 100-gram OGTT values at third hour. Gestational diabetes mellitus patients have significantly higher BMI and lower birth week. Moreover, GDM group had higher fasting blood glucose, 50-gram OGTT and 100-

	GDM	Control	P value	
	(n=31)	(n=469)		
Age (years)	29 (18-43)	26 (18-43)	0.090	
BMI (kg/m ²)	32 (24-42)	29 (20-41)	<0.001	
Gravida (n)	3 (1-6)	3 (1-9)	0.474	
Parity (n)	1 (0-5)	1 (0-4)	0.079	
Gestational week (week)	26 (24-28)	27 (24-29)	0.077	
Delivery week (week)	37 (31-41)	38 (32-41)	0.017	
Cesarean section, n (%)	22 (71)	297 (63.3)	0.391	
Birth weight (gram)	3300 (1760-4690)	3185 (1720-4250)	0.463	
Baby gender, n (%)			0.990	
Female	19 (61.3)	288 (61.4)		
Male	12 (38.7)	181 (38.6)		
Apgar scores of first minutes	9 (8-10)	9 (8-9)	0.725	
Apgar score of fifth minutes	10 (9-10)	10 (9-10)	0.117	
Blood glucose (mg/dL)	90 (61-125)	84 (61-121)	0.001	
50-gram OGTT values (mg/dL)	158 (141-218)	119 (61-171)	<0.001	
100-gram OGTT values (mg/dL)				
1st hour	185 (161-235)	171 (153-178)	<0.001	
2nd hour	160 (131-205)	145 (109-154)	<0.001	
3th hour	123 (81-164)	110 (89-140)	0.088	

Table 1. The sociodemographic, laboratory and birth characteristics of GDM and control patients

BMI=body mass index, OGTT=oral glucose tolerance testing



Fig. 1. A 50 gram OGTT for GDM for all patients.

Fig. 2. A 50 gram OGTT for GDM for high risk patients.

	High risk for GDM (n=114)	Low risk for GDM (n=386)	P value
Age (years)	28 (18-43)	26 (18-43)	0.170
BMI (kg/m ²)	32 (30-41)	28 (20-42)	<0.001
Gravida (n)	3 (1-9)	2 (1-9)	0.199
Parity (n)	1 (0-4)	1 (0-5)	0.118
Gestational week (week)	26 (24-28)	27 (24-29)	0.611
Delivery week (week)	38 (31-41)	38 (32-41)	0.926
Delivery mode, n (%)	73 (64)	246 (63.7)	0.953
Birth weight (gram)	3245 (1720-4500)	3185 (1720-4690)	0.222
Baby gender, n (%)			0.511
Female	73 (64)	234 (60.6)	
Male	41 (36)	152 (39.4)	
Apgar scores of first minutes	9 (8-10)	9 (8-9)	0.607
Apgar score of fifth minutes	10 (9-10)	10 (9-10)	0.240
Fasting blood glucose (mg/dL)	81 (64-112)	81 (61-125)	0.735
50-gram OGTT values (mg/dL)	113 (61-210)	122 (85-218)	0.273
100-gram OGTT values (mg/dL)			
1st hour	182 (171-235)	171 (153-214)	<0.001
2nd hour	155 (131-205)	145 (109-205)	0.004
3th hour	110 (81-145)	110 (81-164)	0.877
GDM diagnosis, n (%)	22 (19.3)	9 (2.3)	<0.001

Table 2. The sociodemographic,	laboratory and birth	characteristics of hi	igh and low risk	for
GDM				

BMI=body mass index, GDM=gestational diabetes mellitus, OGTT=oral glucose tolerance testing

gram OGTT values at first and second hours.

A ROC analysis was performed to determine the cut-off value for GDM for all patients. The 50-gram OGTT value >140 mg/dL discriminated GDM with 100% sensitivity and 92.11% specificity in all patients (AUC=0.969, P<0.001) (Fig. 1).

The sociodemographic, laboratory and birth characteristics of high and low risk patients for GDM were shown in Table 2. No significant difference was found between high and low risk groups according to age, gravida, parity, gestational week, delivery week, delivery mode, birth weight, baby gender, Apgar scores of first and fifth minutes, fasting blood glucose, 50gram OGTT values and 100-gram OGTT values at third hours. GDM was diagnosed at 19.3% of high risk patients whereas the ratio of GDM was 2.3% in low risk group (P<0.001). BMI, 100-gram OGTT values at second and third hours were significantly higher in high risk group as compared to low risk group.

The ROC curve analysis revealed that 50-gram OGTT value >140 mg/dL discriminated GDM with 100% sensitivity and 94.57% specificity in high risk patients (AUC=0.992, P<0.001) (Fig. 2). Furthermore, 50-gram OGTT value >149 mg/dL discriminated GDM with 100% sensitivity and 93.63% specificity in low risk patients (AUC=0.976, P<0.001) (Fig. 3).

DISCUSSION

The prevalence of GDM is gradually increasing worldwide and reaching 10-20% in high-risk populations [13]. The prevalence of GDM tightly depends on ethnicity, obesity, and medical and family history. Asians are known to have higher GDM rates as compared to other ethnicities [14]. In a study from Turkey, the prevalence of GDM was reported as 8.1% using Carpenter and Coustan criteria [15]. Similarly, in a systematic review and meta-analysis, the prevalence of GDM was reported as 7.7% which varies from 1.9 and 27.9% in different forty-one Turkish articles [16]. Consistent with the literature, we found GDM prevalence as 6.2% in our study.

Another factor affecting the prevalence of GDM is the threshold values for OGTT [17]. In a study of Juntarat *et al.* [18], the prevalence of GDM was reported as 4.14% when the 50-gram OGTT cut-off



Fig. 2. A 50 gram OGTT for GDM for low risk patients.

level was accepted as 130 mg/dL and 4.08% when it was accepted as 140 mg/dL. Kösüs *et al.* [15] revealed the prevalences as 8.1% and 7.1% for the same cut-off levels in a study performed in Turkey [15]. Tan *et al.* [19] found the prevalence 11.4% for 130 mg/dL and 9.5% for 140 mg/dL threshold levels. These higher rates can be related to the different risk statuses in study populations. Having risk factors is too important for GDM prevalence. Basnet *et al.* [20] reported a 7.07% prevalence in high-risk pregnancies for GDM while Juntarat *et al.* [18] reported this prevalence as 20.16%. Consistent with the literature, we found the GDM prevalence as 19.3% in the high-risk group in our study.

There is not enough data searching the prevalence of GDM in low-risk patients. Jimenez Meleon *et al*. [21] reported the prevalence as 0.6% in low-risk pregnant women. In another study using the cut-off levels of 130 mg/dL, the prevalence was 2.1% among lowrisk patients [22]. When 75-gram OGTT was performed, the incidence was detected as 3.4% in low-risk pregnant women [23]. In our study, we performed 50-gram OGTT, accepted the cut-off level as 140 mg/dL, and found the prevalence as 2.3%.

Considering these data, higher cut-off values lead to undiagnosed cases, and lower threshold values cause more diagnostic tests. Thus, defining an appropriate cut-off level for both high and low-risk groups would be logical. In the literature, there is little data about this issue. Basnet et al. [20] suggested that 130 mg/dL could identify extra cases of GDM in high-risk women [20]. Similarly, many studies have shown that 10% of GDM cases may be missed by using a 140 mg/dL cut-off level for all risk groups [15, 19]. Juntarat et al. [18] concluded not adopting lower cut-off values for low-risk groups. To the best of our knowledge, there are not many studies evaluating a new cutoff value for GDM screening. In a study of Vitoratos [24], a cut-off value of 126 mg/dL was offered while Mahasukontachat et al. [25] suggested the threshold of 176 mg/dl with 58.5% sensitivity and 88.2% specificity for 50-gram OGTT. However, they recommended this value for screening during the first antenatal visit [24,25]. Punthumapol et al. [26] searched cut-off values for each trimester and recommended 177 mg/dL with 60.78% sensitivity and 75% specificity in high-risk populations. In the study of Eslamian and Remazani [27], a cut-off value of 135 mg/dl was suggested with a sensitivity of 91.7% and 83.6% specificity. In a study by Kösüs et al. [15], 808 pregnant women were searched and the optimal cutoff level was reported as 132 mg/dL for 50-gram OGTT. They reported no GDM for patients who have glucose levels below 130 mg/dL [15]. Different from our study, patients who have a previous history of GDM, family history, macrosomia, hypertension, glucosuria, polyhydramnios, multiple pregnancies, previous unexplained fetal loss, and delivery before the 24th gestational week were excluded. So, we could not make any conclusion about cut-off levels in high-risk group. Miyakoshi et al. [28] identified the cut-off value as 140 mg/dL with 96% sensitivity and 76% specificity. Similar to this study, we suggested a cutoff value of 140 mg/dL with 100% sensitivity and 92.11% specificity in all patients. Also, we found that a 50-gram OGTT value >140 mg/dL discriminated GDM with 100% sensitivity and 94.57% specificity in high-risk patients. This value could be higher but we only performed 100-gram OGTT for patients who have a 50-gram result above 140 mg/dL. For low-risk patients, a study from Turkey suggested that 50-gram OGTT can be omitted up to a threshold value of 147.5 mg/dL [29]. Similarly, we propose that a cut-off value of 149 mg/dl could be used for 50-gram OGTT screening in low-risk pregnant women. Due to the sensitivity of 100% and specificity of 93.63%, performing 100gram OGTT only in patients who have higher values than 149 in 50-gram OGTT can be an alternative option to the present screening strategy.

Limitations

The present study has some limitations. It has a retrospective design and the datas obtained from single center and prone to selection bias. More importantly, cut-off level was accepted as 140 mg/dL for 50-gram OGTT for all groups but it could be more appropriate to accept it as 130 mg/dL because the cut-off level for high risk group can be below 140 mg/dL. The main reason of this limitation is due to the screening recommendations of our Ministry of Health. Thus we do not have any suggestions about patients who have 50-gram OGTT values between 130 mg/dL and 140 mg/dL. Lastly, the present study was lack of showing the relationship between adverse neonatal outcomes and 50-gram OGTT cut-off values.

CONCLUSION

Gestational diabetes mellitus screening with OGTT is an appropriate approach for our population. Although screening in low risk population is a debating issue worldwide, our local guidelines still recommend screening all pregnant women for GDM. Accordingly, we suggest using higher cut-off points in low risk group would be more appropriate than not screening in Turkish population.

Authors' Contribution

Study Conception: BD, GÖ, LÖ; Study Design: BD, GÖ; Supervision: LÖ, GÖ; Funding: N/A; Materials: N/A; Data Collection and/or Processing: GÖ; Statistical Analysis and/or Data Interpretation: BD; Literature Review: LÖ, BD; Manuscript Preparation: BD and Critical Review: GÖ, BD.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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