

Using an initial fasting plasma glucose to decrease the need for the Oral Glucose Tolerance Test during pregnancy

Gebelik sırasında Oral Glukoz Tolerans Testi ihtiyacını azaltmak için açlık kan şekeri kullanımı

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Abstract

Purpose: To evaluate the utility of initial fasting plasma glucose (FPG) to limit the number of oral glucose tolerance test (OGTT)s needed for the diagnosis of gestational diabetes mellitus (GDM).

Materials and methods: 390 pregnant women (estimated gestational ages 24–28 weeks) were evaluated for GDM using OGTT based on International Association of Diabetes and Pregnancy Study Group (IADPSG) criteria. Two FPG thresholds (of the OGTT) were used to rule in and to rule out GDM.

Results: Using IADPSG criteria, 61 (15.6%) of the participants had GDM. The area the under ROC curve of FPG used to detect GDM was 0.933. An FPG cut-off value of ≥ 5.1 mmol/l had sensitivity of 70.49% and specificity of 100.00% in diagnosing GDM. An FPG cut-off value of ≤ 4.5 mmol/l had sensitivity of 93.44% and specificity of 67.6% in diagnosing GDM. Undergoing an initial FPG could have saved 67.7% of these women from taking the OGTT and only 1.5% (4 of the 264) would have been misclassified.

Conclusion: Screening using an initial FPG rule-in and rule-out algorithm reduces the number of OGTTs needed for the diagnosis of GDM. Almost all GDM pregnancies can be diagnosed.

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Key words: GDM, diagnosis, fasting plasma glucose, OGTT

Özet

Amaç: Gestasyonel diabetes mellitus (GDM) tanısı için gerekli Oral glukoz tolerans testi (OGTT) sayısını sınırlamak için açlık plazma glikozun (APG) kullanımı değerlendirmektir.

Gereç ve yöntem: Tahmini gebelik yaşları 24-28 hafta arasında 390 gebe GDM açısından değerlendirildi. Tanı için OGTT'e dayalı International Association of Diabetes and Pregnancy Study Group (IADPSG) kriterleri kullanıldı. İki APG eşik değeri GDM'nin ekarte edilmesi ve dahil edilmesi için kullanıldı.

Bulgular: Katılımcıların 61 (%15.6)'i GDM tanısı aldı. GDM tespit etmek için kullanılan APG'nin ROC eğrisi altında kalan alan 0.933 oldu. GDM tanısı için APG'nin ≥ 5.1 mmol/l eşik değer kullanıldığında sensitivite %70.49 ve spesifite %100.00 oldu. APG'nin ≤ 4.5 mmol/l eşik değer kullanıldığında sensitivite %93.44 ve spesifite %67.60 oldu. Başlangıç APG'nin kullanılması OGTT ihtiyacını %67,7 oranında azalmaktadır ve sadece %1,5'i yanlış sınıflandırılmaktadır.

Sonuç: GDM tanısı için AFP'nin alt ve üst eşik değerlerinin kullanılması OGTT ihtiyacını azaltmaktadır. Bu yöntemle GDM hastalarının hemen hemen tümü tanınabilmektedir.

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Anahtar sözcükler: GDM tanısı, açlık plazma glukoz, OGTT

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Introduction

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance that begins or is first recognized in pregnancy [1]. GDM is one of the most common medical complications of pregnancy, with an overall prevalence of 3–5%, but as high as 18% depending on the population and diagnostic criteria. The oral glucose tolerance test (OGTT), although the gold standard test for diagnosing GDM [2-4], is inconvenient, unpleasant, poorly reproducible, expensive, time consuming, and unsuitable for large-scale screening. In addition, it requires at least 2 h for sample collections and a minimum two blood samples are needed.

On the other hand, fasting plasma glucose (FPG) is inexpensive, reproducible, and easy to perform. Because of the varied results in different populations, however, the efficacy of FPG as a screening test in pregnancy remains unclear [5]. For example, in the HAPO study using the International Association of Diabetes and Pregnancy Study Group (IADPSG) diagnostic criteria, 51% of GDM was diagnosed by an FPG > 5.1 mmol/L (92 mg/dl) [6]. This prospective study evaluates the utility of initial FPG with the goal of limiting the number of OGTTs needed for the diagnosis of GDM.

Materials and Methods

This study was a prospective observational study conducted from May 2011 to November 2012 at the Department of Obstetrics and Gynecology, Bezmialem Vakif University, Istanbul, Turkey. We excluded women who had multiple pregnancies, those with pregestational diabetes mellitus, those with fetal anomalies diagnosed prenatally, those who delivered prior to the 28-week gestation, and those who did not follow the protocol. The study protocol was approved by the Research and Ethics Committee of Bezmialem Vakif Hospital.

During the study period, all pregnant women between 24 and 28 weeks of gestation who had been referred for GDM screening were informed about the study by their obstetricians. Women who agreed to participate in the study signed an informed consent and were asked to come to the hospital in a fasting state. Venous blood samples were then collected three times: after 8 to 12 hours of overnight fasting, 1 hour after ingesting 75 g of glucose, and 2 hours after

ingesting 75 g of glucose. The patients received the diagnosis of GDM if their 2h OGTT results met one of the following thresholds of the IADPSG criteria: a fasting glucose \geq 5.1 mmol/L (92 mg/dl), a 1 hour plasma glucose \geq 10 mmol/L (180 mg/dl), or a 2 hour plasma glucose \geq 8,5 mmol/L (153 mg/dl) [4]. Women classified as GDM were then referred to an endocrinologist, received a glucose monitoring device, and were assigned a special diet (treatment) and, if needed, medication. Plasma glucose was estimated by the glucose oxidase method.

A rule-in and rule-out algorithm was used to evaluate the utility of initial FPG to limit the number of OGTTs needed for the diagnosis of GDM [7]. Briefly, this approach involves considering two FPG threshold values. The higher threshold, with an inherently increased specificity, rules in GDM; the lower threshold, with its innate increased sensitivity, rules out GDM. Women who have FPG values in between these two thresholds are indeterminate and would need the diagnostic OGTT.

Statistical analyses

T-tests were performed to test the difference between two means. The ROC curve was drawn to determine sensitivity and specificity. All statistical analyses were performed using SPSS Statistics version 17.0 software.

Results

The mean maternal age, parity, BMI, and gestational week of the 390 pregnant women were 27.8 ± 4.8 years, 0.9 ± 0.9 , 25.4 ± 4.0 kg/m², and 25.7 ± 1.0 , respectively.

Using the IADPSG criteria, 61 (15.6%) of the participants had GDM.

High FPG was seen in the 28 participants, high 1-h plasma glucose levels was revealed in 11 of the participants, high 2-h plasma glucose occurred in 4 of the participants, high FPG and 1-h plasma glucose levels were found in the 10 participants, high FPG and 2-h plasma glucose levels elicited in the 2 participants, high 1-h plasma glucose and 2-h plasma glucose levels were manifested in 4 of the participants, and 2 of the participants presented with high FPG and 1-h plasma glucose and 2-h plasma glucose levels.

Using the IADPSG criteria, 61 (15.6%) of the participants had GDM. The mean \pm SD FPG value in women with GDM was 96.13 ± 18.21 and 78.38 ± 6.65 in women without GDM, a statistically significant difference ($p=0.00$). The ROC curve (Fig. 1) was drawn to determine the sensitivity and specificity of FPG in detecting GDM. The area under the ROC curve of FPG to detect GDM was 0.933 (95% CI 0.903-0.956). The higher threshold (5.1mmol/l (92 mg/dl)), and the lower threshold (4.5 mmol/l (81 mg/dl)) was chosen based on data from our ROC curve and data from the HAPO study. An FPG cut-off value of ≥ 5.1 mmol/l (92 mg/dl), had sensitivity of 70.49% and specificity of 100.00% in diagnosing GDM. An FPG cut-off value of ≤ 4.5 mmol/l (81 mg/dl) had sensitivity of 93.44% and specificity of 66.77% in diagnosing GDM.

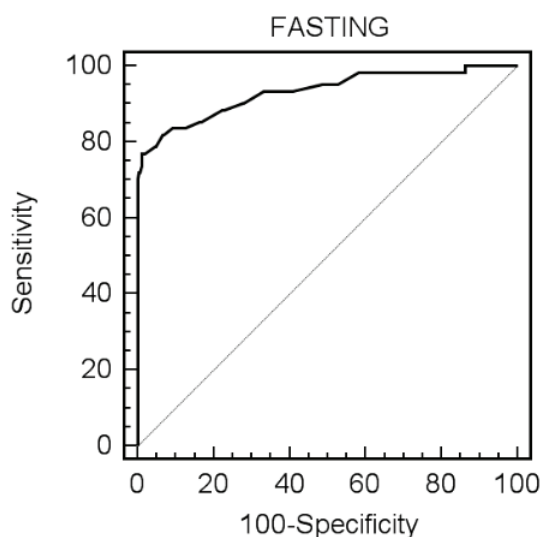


Figure 1. ROC curve showing the sensitivity and specificity of FPG in detecting GDM using IADPSG criteria.

Discussion

In March 2010, the International Association of Diabetes and Pregnancy Study Group (IADPSG) issued consensus guidelines with the goal of potentially attaining a single approach for GDM diagnosis worldwide [4], recommending that every pregnant woman should undergo the OGTT, a costly and cumbersome test for both the patient and the health provider. To decrease the need of the extremely demanding OGTT, as an alternative approach we here evaluate the use of initial FPG. A two threshold rule-in and rule-out algorithm was used for this purpose.

In our study using the IADPSG diagnostic criteria, 70.4% (11.02% of the total population) of GDM was diagnosed by an FPG ≥ 5.1 mmol/L (92 mg/dl), whereas 51% and 40% of GDM was diagnosed by an FPG > 5.1 mmol/L (92 mg/dl), in the HAPO study and that of Mahdavian et al., respectively [6,8]. In our view, FPG ≥ 5.1 mmol/L (92 mg/dl), may be sufficient to diagnose the majority of women with GDM.

The number of OGTTs avoided is dependent on the criteria used for GDM diagnosis (Table 1) [9-14]. In this study, using the new IADPSG criteria, the FPG ≥ 5.1 mmol/L (92 mg/dl) value, the higher threshold with an inherently increased specificity (100%) and FPG ≤ 4.5 mmol/L (81 mg/dl) value, the lower threshold with its innate increased sensitivity (93.44%), was used to limit the number of OGTTs needed for the diagnosis of GDM. Using FPG as the initial test, if the level of FPG ≥ 5.1 mmol/L (92 mg/dl), then the women can be labeled as having GDM. If the level of FPG ≤ 4.5 mmol/L (81 mg/dl), then the women can be labeled as normal. For women with FPG levels between 4.5 mmol/L (81 mg/dl), and 5.1 mmol/L (92 mg/dl), an OGTT should be performed to correctly identify those with GDM (Fig. 2). Using the two cut-off approach, a higher FPG threshold of ≥ 5.1 mmol/l (92 mg/dl), ruled in GDM in 44 women. A lower FPG threshold of ≤ 4.5 mmol/l (81 mg/dl), ruled out GDM in 220 women. Using this methodology, 93.5% of the GDM cases would have been detected, thereby obviating an OGTT for 67.7% the women in our study.

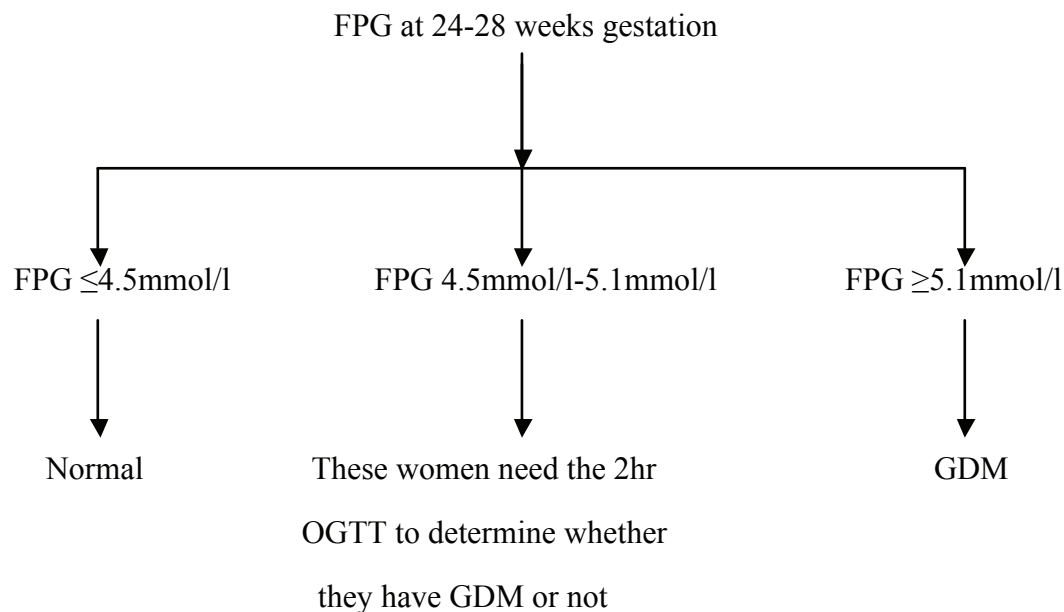
In the Agarwal et al. study, 4.6% of GDM cases would have been missed while 23% of women with GDM would have been misclassified as healthy in the study of Mahdavian et al. by not performing OGTT for women whose FPG < 4.4 mmol/l (80 mg/dl), [8,14]. In our study, the women those level of FPG ≤ 4.5 mmol/l (81 mg/dl), could be labeled as normal and only 1.5% of those with GDM were misclassified as healthy. Reasons for such discordant results probably were associated with ethnicity and higher baseline insulin resistance in Turkish women.

One limiting factor for this approach is laboratory turnaround time for the initial FPG result, i.e., the time the pregnant woman has to wait in a fasting state. Furthermore, generally all women have to await results of their FPGs in order to rule out overt diabetes mellitus.

Table 1. Reports the number avoided of OGTT dependent on the criteria used for GDM diagnosis.

Reference	No. of OGTTs circumvented, %	Thresholds (lower and higher) mmol/	OGTT	Diagnostic criteria	Comments
Agarwal et al. (2000) ⁹	50.9	4.4 and 5.3	100 g	ADA	Biased sampling: Preselected by clinical/GCT
Agarwal et al. (2005) ¹⁰	30.1	4.7 and none	75	WHO	FPG performance poor with WHO criteria
Agarwal et al. (2008) ¹¹	68.5	4.9 and 7.0	75	ADA	Glucometer used for FPG
Agarwal et al. (2006) ¹²	63.8	4.9	75	ADA	FPG screening criteria dependent
Agarwal et al. (2009) ¹³	50.1	4.7 and 7.0	75	ADA	Fasting capillary glucose used
Agarwal et al. (2010) ¹⁴	50.6	4.4 and 5.1	75	IADPSG	Data from four studies
Mahdavian et al. (2010) ⁸	40	4.4 and 5.1	75	IADPSG	FPG performance poor with IADPSG criteria
Results of our study	67.7	4.5 and 5.1	75	IADPSG	FPG performance good with IADPSG criteria

OGTT, oral glucose tolerance test; ADA, American Diabetes Association; GDM, gestational diabetes mellitus; IADPSG, International Association of Diabetes and Pregnancy Study Group; GCT, glucose challenge test; WHO, World Health Organization; FPG, fasting plasma glucose.

**Figure 2.** Flow diagram showing utility of initial FPG along with OGTT in order to diagnose GDM per IADPSG criteria

We have shown that the initial FPG identifies the majority of GDM pregnancies in our population. Using the initial FPG rule-in and rule-out algorithm for GDM diagnosis, almost all GDM pregnancies can be diagnosed, thereby decreasing the need of OGTT by 67.7%. Considering laboratory costs and workload [15], making use of an initial FPG is an advantageous approach, both effective and efficient, so that it will be proportionate to expected risk.

Conflict of Interest: The authors report no conflict of interest.

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