

## **Examining Diagnostic Value of the Fasting Plasma Glucose in Screening Gestational Diabetes**

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### **Abstract**

**Background:** Many different tests have been introduced for screening gestational diabetes mellitus (GDM). The Objectives of this study were to determine both the diagnostic value of fasting plasma glucose (FPG) and the suitable cut-off point of plasma glucose with the best sensitivity and specificity for diagnosing gestational diabetes mellitus (GDM).

**Methods:** This cross-sectional study was done on 242 women in Karaj-Iran who had at least one risk factor for GDM. Having conducted 50 gram glucose challenge test (GCT), the diagnostic values of FPG were determined by receiver operating characteristic curve (ROC). Then the level of plasma glucose, with the highest sensitivity and specificity rate, were determined for the diagnosis of GDM.

**Results:** Based on the results of ROC curve, FPG with cut-off point  $\geq 91$  mg/dl revealed 63.89% and 76.56% sensitivity and specificity for diagnosing GDM, respectively.

**Conclusion:** It is recommended to use FPG as a suitable screening test for GDM with acceptable specificity and sensitivity.

**Keywords:** Oral glucose tolerance test, FPG, ROC curve, GDM

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## Introduction

By definition, Gestational diabetes mellitus (GDM) is the various degree of carbohydrate intolerance that is first diagnosed with or during pregnancy (1). According to the population under survey, the prevalence of GDM is variable from 1-14% (2-4). GDM is the most common medical complication during pregnancy (1,5) that is accompanied by many maternal and fetal complications. Therefore, appropriate screening and diagnosis are necessary. Despite the clear importance of this issue for more than four decades of research, whether to use an universal method for the diagnosis of GDM is still highly debatable (6). Recently an international workshop of GDM in the USA has introduced the 50g oral glucose test as gold standard test for GDM screening. Hence, after prescribing 50g oral glucose, regardless of fasting time, if one-hour plasma glucose is equal to or above 140 mg/dl, the 100g oral glucose test and determining plasma glucose 1, 2 and 3 hour post prescription will be done. The 100g oral glucose test will be interpreted given to the criteria of the American College of Obstetrics and Gynecology and Carpenter and Coustan criteria (1, 2, 5).

Although 50g oral glucose test is the standard method for screening, it would present numerous problems; such as high costs and being time consuming, not considering the individual's body weight during the test, the possibility of different results in different races and the intolerance of patients in high consumption of glucose powder (7). Besides, the sensitivity and specificity of this test in one-hour plasma glucose for cut-off values of 130 mg/dl and 140 mg/dl has been under discussion by researchers (1,2,7). Due to these complexities, cheaper and easier methods as alternatives are recommended. In this case, different studies on FPG, as a screening test for GDM, have long been performed leading to different results (6,8).

Due to its simplicity and cost-effectiveness, FPG is recommended as the appropriate screening test in some studies. The cut-off values based on this test were specified with suitable sensitivity and specificity for the diagnosis of GDM (2, 6, 7). But the cut-off values were different and still debatable.

This study aims at determining the suitable cut-off point for fasting plasma glucose with suitable sensitivity and specificity of test for diagnosis of GDM.

## Methods

This cross-sectional study included pregnant women at 24-28 weeks of pregnancy who were referred from four health clinics and one endocrine clinic in Karaj-Iran, during 2005-2007.

Inclusion criteria were presence of at least one risk factor for GDM; including maternal age above 25 years, unexplained previous abortion, history of macrosomia (birth weight more than 4000 grams), history of diabetes in first degree relatives, previous stillbirths and body mass index above 27 kg/m<sup>2</sup> who referred to health clinics for routine prenatal care. Glucose screening test, regardless of fasting status, was done for patients with 50g hypertonic water soluble glucose. With 2ml venous blood sampling after the prescription of glucose, plasma glucose was measured one hour later. If one-hour glucose was equal to or above 130mg/dl, 100 g oral glucose test by taking 2 ml of venous blood was carried out according to the latest ADA Protocol. Then the glucose levels of fasting, 1, 2 and 3 hours were checked after prescription of glucose powder and evaluated according to the criteria of Carpenter and Coustan. Plasma glucose tests were done by method of glucose oxidase and using of Hitachi 911 autoanalyzer with Elitic French kite in Hakim's laboratory in the city of Karaj. According to the conducted four tests, if two test results were above the desired criteria, the participant was considered as GDM positive. All the participants signed informed consent forms, and confidentiality of personal information was considered. This survey was approved by ethics committee of Islamic Azad University-Karaj branch.

The sample size was determined based on the data from a pilot study calculating the area under ROC curve equal to 77% (SE= 0.05), and with a 95% confidence level, a total of 242 samples was computed to be recruited into the study.

Data were reported as mean ( $\pm$ SD), median ( $\pm$  inter quartile range), frequency and percent. To assess the diagnostic value of FPG for GDM, ROC analysis was used. In this analysis, the prediction power was tested by area under curve. Then, sensitivity, specificity and positive- negative predictive power of the mentioned test were calculated, based on the best prediction and selective cut-off point (9, 10). To compare the median number of parity in the two groups (GDM positive and negative) Mann-Whitney test, and to compare the

percentage of abortions between the two groups, Chi-Square test were used (12). The significant level for all tests was considered 0.05 and data were analyzed by SPSS software version 17.

## Results

The 50g oral glucose test was performed on 242 pregnant women who participated in this study. This test was positive in 100 patients (i.e., one-hour plasma glucose was equal to or greater than 130 mg/dl). Then the diagnostic test of 100g glucose was done on these 100 participants and identified 36 GDM positive cases. The mean age of total participants was  $29.4 \pm 4.6$  years (the mean age of participants with and without GDM were  $29.5 \pm 5$  and  $29.3 \pm 4.4$  years, respectively) which the difference wasn't significant between the two groups ( $p=0.80$ ). The number of parities of total participants in this study was (median  $\pm$  IQR)  $2 \pm 2$  of pregnancy (for those with GDM  $1 \pm 0.5$  and without GDM  $1 \pm 0$ ) which wasn't significantly different between two groups ( $p=0.693$ ). The frequency of abortion in all the participants was 43.38% (for those with GDM 17.7% and without GDM 15.3%), and there

was no significant difference between the two groups either ( $p=0.49$ ) (Table 1).

In assessing the value of FPG levels in the diagnosis of GDM, the area under ROC curve was 0.75 with confidence interval (CI) 0.65 to 0.83. FPG level of 91mg/dl showed the highest sensitivity and specificity equal to 63.89% and 76.56%, respectively. The positive predictive power (ppp) for this glucose level was 73.16% and negative predictive power was 32.05%. This cut-off value was considered as the criterion for the diagnosis of GDM. In the other words, pregnant women with glucose level greater than 91mg/dl were GDM positive and those with lower 91mg/dl were GDM negative (Table 2).

The area under ROC curve indicates that the sensitivity and specificity of plasma glucose were 0.87 (95% confidence interval: 0.79 to 0.93) and 0.95 (95% confidence interval: 0.65 to 0.83), respectively (Fig. 1).

In this study, given 100g glucose tolerance test, the best sensitivity and specificity was considered with two-hour plasma glucose at 153mg/dl level (with the sensitivity and specificity of 91.67% and 89.06%).

Table 1. Characteristics of study participants

Characteristics	GDM-positive	GDM-negative	P-value
Maternal age years (mean $\pm$ SD)	$29.58 \pm 5.08$	$29.34 \pm 4.43$	0.806
Parity (median $\pm$ IQR)	$1 \pm 0.5$	$1 \pm 0$	0.693
History of Abortion (percent)	22 (17.7)	83 (15.3)	0.493

Table 2. Results of diagnostic values of FPG for cut-off point (91 mg/dl)

Variable	Area under curve (95% CI)	Sensitivity	Specificity	PPP	NPP	LR+	LR-
FPG	0.75(0.65-0.83)	63.98% (47.6-77.5)	76.56% (64.9- 85.3)	60.5% (44.7-74.4)	79.00% (67.4-87.3)	2.73 (1.64- 4.52)	0.47 (.299-.744)

PPP: Positive predictive power

NPP: Negative predictive power

LR+: Likelihood ratio Positive

LR-: Likelihood Ratio Negative

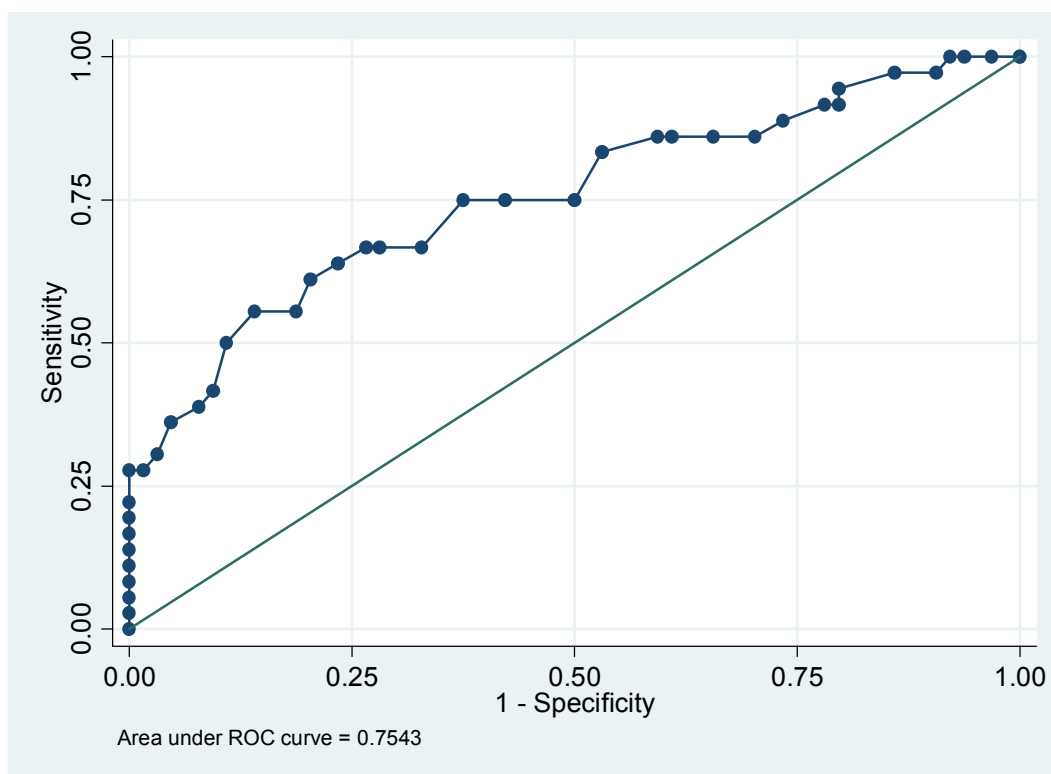


Figure 1. Area under curve for FPG

## Discussion

In the present study, the area under curve for FPG was 0.75 that was at an acceptable level. However, higher values were observed in other studies (in Kashi's and Rey's study, it was 0.85 and 81%, respectively (2, 8)). The study done by Agarwal and et al. established that appropriate capillary fasting glucose with Accu-Check is a suitable screening test for high risk populations and different communities (area under curve ROC was 0.83). The data indicate that cut-off point of FPG was 84 mg/dl with 86% sensitivity and 100% specificity for the diagnosis of GDM (13).

An appropriate test for screening should have a desirable threshold of sensitivity and specificity. A highly sensitive test is very helpful for clinicians when the test result is negative. A highly specific test is the most helpful when its result is positive. It is obviously desirable to use a test which be both highly sensitive and highly specific. Unfortunately, this is usually not possible (14).

In the present study, Cut-off point of FPG was 91mg/dl with 63.89% and 76.56% sensitivity and specificity, respectively. In addition, positive and negative predictive values were 73.16% and 32.05% respectively. In various studies such as Kashi's survey, cut-off point FPG was 91.5 mg/dl with 80% and 92%

sensitivity and specificity, respectively (2). In Aguir's study, cut-off point FPG was 88 mg/dl with 80% sensitivity and 40% specificity (7) and in the Sennayake's study, cut-off point FPG was 84 mg/dl with 82.7% sensitivity and 67% specificity (6). This difference seems to rise from different screening and diagnostic methods (75 and 100 grams) and different population ethnicities.

There is a trade-off between the sensitivity and specificity of a diagnostic test. This is true when clinical data take on a range of values. In those situations, determining the location of a cut-off point and the distinctive point on the normal-abnormal continuum is an arbitrary decision to make. Consequently, for any given test result represented on a continuous scale, one characteristic, such as sensitivity can only be increased at the expense of the other. (e.g., specificity)(14).

In this study, with 100g glucose tolerance test, the best sensitivity and specificity was seen in two-hour plasma glucose. It was 153mg/dl and the best sensitivity and specificity were 91.67% and 89.06%. According to this study, an FPG higher than 91mg/dl had suitable sensitivity and specificity for diagnosing GDM.

There are some limitations in carrying out this survey. In this study, 50 gram glucose challenge test was done on 242 pregnant women. The result was positive in 100 patients

(i.e. one-hour plasma glucose was equal to or greater than 130 mg/dl). In this respect, GCT might have some false negative results and some participants were accordingly omitted from the study (i.e. if gold standard had been done on participants at first, some results would have been positive). It follows that, some subjects in any study where participants are examined on screening test before standard test are found with a high probability of affliction (verification bias), and the false negative results of screening test are not detected. In this study, if the test had initially been conducted, the

sensitivity and specificity would have been more valid.

Based on this survey, it is recommended that FPG be used as a suitable screening test for GDM.

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