Can Fasting or Post-prandial Blood Glucose Monitoring be used as a Method in the Diagnosis of Gestational Diabetes and Predicting its Complications in Patients who Refuse OGTT?

Gulchin Babayeva,[1] Yunus Emre Purut[2]

[1]Private Hospital, İstanbul, Türkiye
[2]Van Training and Research Hospital, Van, Türkiye

ABSTRACT

Objective: Gestational diabetes mellitus (GDM) is one of the most common metabolic diseases in pregnancy. Negative news in the media has made the GDM test controversial among patients. We aimed to investigate the usability of fasting blood glucose (FG), HgA1c, and post-prandial 2nd-h blood glucose (PG) instead of an oral glucose tolerance test (OGTT) in the diagnosis of GDM and predict its possible complications.

Methods: This retrospective cohort study was conducted among patients admitted to a private hospital in Istanbul between December 2020 and July 2022. In our clinic, patients who refuse OGTT are routinely asked for FG and PG after a normal meal. We also evaluate the HgA1c value. Data of 374 patients were obtained and 150 patients were included in the study after exclusion criteria. Women aged 24–28 weeks who refused OGTT were considered the study group. Patients who accepted OGTT were diagnosed with diabetes before, and FG and PG results could not be reached and were excluded from the study. In addition, patients with a body mass index above 35 were not included in the study. Polyhydramnios and macrosomia, which are common diabetes complications, were evaluated during the follow-up of patients, and these conditions were associated with FG and PG.

Results: Due to our results, it was determined that FG was weak and PG was moderately successful in estimating the emergence of abnormal fetal characteristics in pregnant women. When the threshold value of FG was taken as 94 mg/dL, the sensitivity was 43%, and the specificity was 8.8%. When the threshold value of post-prandial blood glucose was taken as 143.5 mg/dL, the sensitivity was 64%, and the specificity was 14% (p<0.05). The HgA1c values of the patients did not show a significant difference between the patients who were diagnosed with polyhydramnios and macrosomia and those who did not.

Conclusion: The OGTT is still the most valuable test for the diagnosis of GDM. Women who refuse to do OGTT, especially PG, may be valuable in terms of GDM and its complications. For these patients, more study is needed.

INTRODUCTION

Diabetes is a complicated metabolic disorder that is increasing worldwide, linked with obesity, sedentary lifestyle, and aging.[1,2] Gestational diabetes mellitus (GDM) refers to diabetes that is first diagnosed during pregnancy. This affects approximately 3–9% of pregnancies.[3,4] Because most women do not receive screening for diabetes mellitus before pregnancy, it can be challenging to distinguish GDM from pre-existing diabetes.[5] Many researches show that GDM can increase perinatal morbidity and mortality; hence, screening and early diagnosis are important in this case. As we know GDM resolves and recovers after pregnancy. Women who develop GDM during pregnancy are at high risk of permanent Type 2 diabetes.[6] It is predicted that approximately 70% of women with GDM will develop diabetes within 22–28 years after pregnancy.[7]

Women with GDM have a higher risk of developing pre-eclampsia (9.8% in those with fasting glucose <115 mg/dL and 18% in those with fasting glucose higher or equal to

115 mg/dL) and undergoing a cesarean delivery (25% of women with GDM who require medication and 17% of women with diet-controlled GDM underwent cesarean delivery versus 9.5% of controls).[8]

GDM is a high-risk condition for the mother and fetus. The offspring of women with GDM are at elevated risk of macrosomia, neonatal hypoglycemia, hyperbilirubinemia, shoulder dystocia, and birth trauma. There is also an increased risk of stillbirth, although how relevant is this outcome to glycemic control is controversial.[9]

Criteria for the diagnosis of GDM based on the association of levels of glycemia during pregnancy with subsequent maternal diabetes were first published 55 years ago.[10] There are no significant changes during these years. If the results are not positive for an obvious DM and fasting plasma glucose (FPG) is higher than 92 mg/dL, diagnosis of GDM is doubtless. If fasting glucose is lower than 92 mg/dl at the first antenatal visit, it is suggested to apply a 2-h 75 g OGT test at 24 28 weeks.[11,12]

In general, the current screening for GDM is proposed between 24 and 28 weeks of pregnancy. This period was specified because the level of insulin resistance is increased in the second trimester, and glucose levels are rising because the insulin secretion is insufficient to balance this resistance.[13]

In Turkey since 2014, there is a bias about OGTT among pregnant women.[14,15] The rate of those who refuse OGTT with the negative impact of media sources (56.5%) among pregnant women is high-OGTT rates decreased, however, the prevalence of GDM in pregnant women has continued to elevate. In our study, we tried to associate fasting blood glucose (FG) and post-prandial 2nd h blood glucose values with polyhydramnios and macrosomia, which are the most common complications of diabetes in the outpatient clinic, and thus to find alternative ways for patients who refuse OGTT; with these easy and acceptable scans, we tried to determine a blood value that could be a threshold value for the diagnosis of GDM.

MATERIALS AND METHODS

We conducted our retrospective cohort study in Istanbul Private Hospital between December 2020 and July 2022 among 374 pregnant patients and collected data. In our clinic, we recommend the OGTT test to all pregnant women between 24 and 28 weeks. In patients who do not routinely accept OGTT, we check FG on the same day and blood glucose values in the 2nd h after a normal meal between 24 and 28 weeks. In this context, we obtained the data of 374 patients retrospectively. With most patients who accepted to do OGTT and whose birth information could not be reached; patients with a body mass index (BMI) above 35 and patients with a previous diagnosis of diabetes/gestational diabetes were excluded from the study. When patients whose fasting and post-prandial blood glucose values could not be reached were excluded from the study, 150 patients could be included in the study. Ethics Committee approval obtained from Van Training and Research Hospital (2022/19-02).

The study was carried out by collecting the laboratory data and birth results of 150 patients. It was examined whether these patients were diagnosed with polyhydramnios and macrosomia, which are frequently encountered in diabetes. The threshold value for the diagnosis of fetal macrosomia was accepted as 4000 g. Ultrasound measurements and estimated fetal weights at the measurement week of babies born macrosomic were also examined.

The data were collected by SPSS software version 26. The values were shown as mean±standard deviation, n (%), and median (min–max). The significance of FPG value for GDM was analyzed based on the receiver operating characteristic (ROC) curve. The sensitivity, specificity, positive and negative likelihood ratios, and positive and negative predictive values also were evaluated.

RESULTS

Macrosomia and polyhydramnios were detected in 14 of the 150 patients included in the study; these findings were not found in 136 patients (Table 1).

The age, gestational week, and glycated hemoglobin (HbA1C) values did not differ according to the fetal characteristics of the women examined (p>0.05). However, FG and post-prandial blood glucose (hour 2) values differed

Table 1. Comparison of descriptive statistics by fetal characteristics of examined pregnant patients

Characteristic	Fetal characteristic		p-value
	Normal (n:136)	Abnormal (n:14)	
	Mean±SD	Mean±SD	
Age	27.75±5.06	28.50±4.47	0.595
Gestational week	26.10±1.43	26.50±1.40	0.322
Fasting blood sugar	84.74±9.22	92.21±14.21	0.007**
Post-prandial blood sugar (hour 2)	125.15±20.26	150.14±29.17	0.000**
HbA1 C	5.72±0.55	5.88±0.43	0.452

*p<0.05, **p<0.01; Mean, SD: Standard deviation.

Table 2. Correlation between pregnant women showing signs of fetal abnormality and various parameters

Variable	Coefficient	Age	Gestational week	Fasting blood sugar	Post-prandial blood sugar (hour 2)	HbAI C
Showing abnormal	r	0.044	0.081	0.219**	0.326**	0.169
fetal characteristics	p	0.595	0.322	0.007	0.000	0.452
	N	150	150	150	150	22

*p<0.05, **p<0.01; r: Pearson correlation.

Table 3. Logistic regression estimating the probability of pregnant women to show abnormal fetal features

Variables	B (Coefficient)	S.E.	Sig.	Exp(B)/Odds ratio	Confidence intervals 95% CI for EXP(B)	
					Lower limit	Upper limit
Fasting blood sugar	0.011	0.031	0.712	1.011	0.952	1.074
Post-prandial blood sugar (hour 2)	0.047	0.017	0.005	1.049	1.015	1.084
Constant	−9.751	2.485	0.000	0.000		

$R^2=0.100$ (Cox and Snell R Square); $R^2=0.216$ (Nagelkerke) Model: $\chi2(2)=15.760$; p=00.00, p<0.01.

according to the fetal characteristics of the pregnant women (p<0.05). FG and post-prandial blood glucose values were lower in women with normal fetal characteristics than in women with abnormal fetal characteristics.

The correlation between pregnant women showing abnormal fetal characteristics (polyhydramnios and macrosomia) and various parameters is shown in Table 2.

No correlation was found between abnormal fetal characteristics and the pregnant women's age, gestational week, and HbA1C values (p>0.05). However, the presence of abnormal fetal characteristics in pregnant women showed a weak positive correlation with FG and a moderate positive correlation with post-prandial blood glucose (2-h) (p<0.05). These findings indicate that an increase in FG and post-prandial blood glucose (2 h) will increase abnormal fetal characteristics in pregnant women.

The effects of age, gestational week, FG, post-prandial blood glucose (2 h), oral glucose tolerance test (OGTT), and HbA1C values on abnormal fetal features of pregnant women were examined with logistic regression analysis and are shown in Table 3. Since no relationship could be found between showing signs of fetal abnormality and the pregnant women's age, gestational week, and HbA1C values, these values were excluded from the model. The logistic regression analysis model created with the independent variables of FG and post-prandial blood glucose (2 h) was found to be statistically significant ($\chi2(2)$ =15.760, p=00.00, p<0.01). This model showed that women with normal and abnormal fetal characteristics could be distinguished by their independent variable values. This model correctly predicted 90.7% of pregnant women with normal and abnormal fetal characteristics. Independent variables explain changes in showing abnormal fetal features 10%, according to Cox and Snell and 22%, according to

Nagelkerke.

As shown in the analysis of independent variables in Table 3, FG is not effective in predicting abnormal fetal characteristics in women, whereas post-prandial blood glucose is a significant variable in predicting fetal abnormalities in pregnant women. Exp(B) values in this model showed that a one-unit increase in post-prandial blood glucose would increase the probability of women having abnormal fetal characteristics 1.046-fold.

ROC analysis was performed to estimate the probability of women displaying abnormal fetal characteristics with the various parameters studied. The results of the ROC analysis performed to estimate the probability of women showing abnormal fetal features with age, gestational week, FG, and post-prandial blood glucose (2-h) parameters are shown in Figure 1.
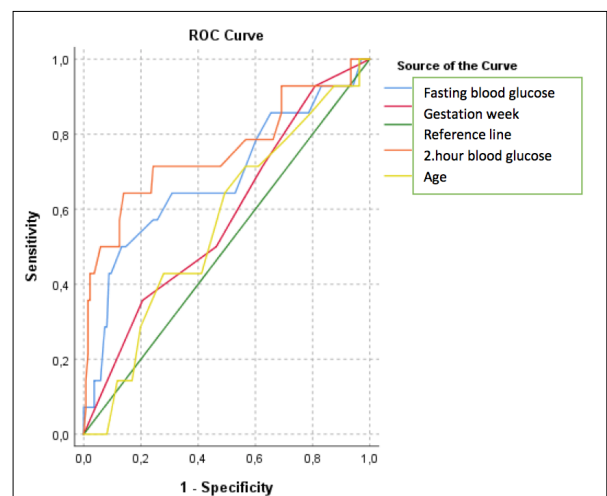

Figure 1. Estimating the probability of women to show abnormal fetal characteristics with various parameters.

Table 4. ROC Analysis results on predicting abnormal fetal characteristics of pregnant women with various parameters

Test variable	Area*	SE	p-value	Cutoff value	Sensitivity (Sensitivity) (%)	Specificity (%)	Confidence interval (95%)	
							Lower Limit	Upper Limit
Age	0.562	0.077	0.425	27.5	0.643	0.493	0.410	0.713
Gestational week	0.581	0.079	0.310	27.5	0.357	0.206	0.425	0.736
Fasting blood sugar	0.682	0.085	0.033	94	0.429	0.088	0.515	0.849
Post-prandial blood sugar (hour 2)	0.754	0.084	0.002	143.5	0.643	0.14	0.590	0.918

*AUC: Area under the curve.

Table 4 shows the area under the curve, sensitivity, and specificity results obtained from the ROC analysis which was performed to estimate the probability of women displaying abnormal fetal characteristics with age, gestational week, FG, and post-prandial blood glucose (2-h) parameters.

It was determined that fasting blood sugar was weak and post-prandial blood sugar was moderately successful in estimating the emergence of abnormal fetal characteristics in pregnant women. When the threshold value of FG was taken as 94, the sensitivity was 43%, and the specificity was 8.8% (p<0.05). When the threshold value of post-prandial blood glucose was taken as 143.5, the sensitivity was 64%, and the specificity was 14% (p<0.05).Parameters that can predict occurance of fetal abnormality are shown in Figure 2.

DISCUSSION

GDM is one of the most common complications of pregnancy. For diagnosing pregnancy can be used "1-step" technique with a 75-g OGTT or "2-step" method with a 50-g (non-fasting) screening followed by a 100-g OGTT for those who screen positive.[16] Therefore, in our country because of the toxicity prejudice of this test, women re-

fuse to perform glucose challenging test. In our study, we tried to find alternative ways and to review the studies of other authors in other countries.

Nowadays, most authors recommend early detection of diabetes mellitus in pregnancy. These trials seeking for alternative ways to diagnose GDM before the 24th weeks. [17] Sovio et al. tried to conduct whether the overgrowth of the fetus can predict GDM. They reported that excessive fetal growth can be seen between 20 and 28 weeks gestation, before the diagnosis of GDM, especially among women with higher BMI (kg/m2).[18] Likewise, Venkataraman and coauthors' study showed that a 'thin but fat' phenotype as an indicator of unequal increase in adiposity despite smaller or similar lean body mass was observed in the fetuses of mothers with GDM, even at 20 weeks, can predict GDM.[19] They suggest that anterior abdominal wall thickness can be used as an early marker in GDM.

Although there is no preferred test alone to predict GDM, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommends screening early GDM by courtesy of a fasting glucose of 5.1 mmol/L to 6.9 mmol/L (92–124 mg/dL).[20] FPG during early pregnancy can predict or at least eliminate high-risk pregnant women.[21] Riskin-Mashiah et al. in their cohort study checked above 6000 pregnant women's FGP at 9th week gestation
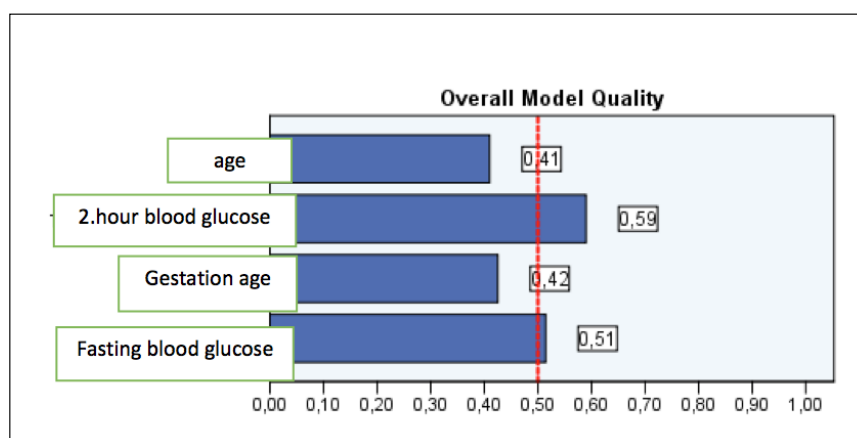

Figure 2. Estimating the probability of pregnant women having abnormal fetal characteristics with various parameters (variables above 0.5 are good at predicting, variables below 0.5 are poor at predicting).

and found a positive relationship between FGP ≥104 mg/dL and subsequent diagnosis of GDM, large for gestational age (LGA) fetus and cesarean section.

In Zhu et al. found early FPG rates between 110 and 124 mg/dL are strongly correlated with later GDM diagnosis, however, this data cannot be used as a predictor marker alone.[22] López et al. reported similar findings with our study in their article. They found a statistically significant correlation between FGP ≥92 mg/dL and higher macrosomia rates. However, FGP alone is not a reliable alternative for the diagnosis of GDM. Nevertheless, these pregnant women with FGP level ≥92 mg/dL are in the risk group for fetal macrosomia, even if they do not have a clear diagnosis of GDM, and may benefit from nutritional measures and physical exercise.[23] In our study, we found this rate to be 94 mg/dL (specificity 8.8, sensitivity 43%; p<0.05). In our study, macrosomia and polyhydramnios were found in the fetus in pregnant women with FGP ≥94 mg/dL.

Jamieson et al. suggested to interpret HbA1c to predict GDM in the early gestation week. In their study, HbA1c ≥5.6% (≥38 mmol/mol) was highly predictive (71.4%, 95% CI; 47.8–88.7%) for GDM and increased risk for LGA newborn (RR 2.04, 95% CI; 1.03–4.01, p=0.040).[24] In our study, we could not find a correlation between HbA1c rates and fetal macrosomia and polyhydramnios. Further investigations and more patient data are needed.

Peng et al. in their study tried to evaluate whether HbA1c, FPG, 1-h plasma glucose, or 2-h plasma glucose can serve as a predictor of GDM in early pregnancy (6–14th week). They found that each of these values are significant, however, 1-h plasma glucose was found to be a more significant value in the estimation of GDM in 1st trimester.[25] Contrary to this study we found that 2nd-h post-prandial glucose levels can be a stronger predictor for GDM diagnosis.

Rupala et al. provided a positive correlation between 1st trimester HbA1c >5.5%, 2nd trimester, and OGTT positive screening.[26] In our study, the HbA1c level threshold was not found because of the few number of patients. Further studies are needed.

As an early predictor in in-vitro fertilization pregnancies, Coussa et al. showed 12 weeks of weight gain (delta: 3.4 vs. 1.5 kg) as a significant predictor marker.[27] We did not include the weight gain data to our study. This can be considered the missing part of our study. It can be the subject of our subsequent research.

Very few studies have evaluated the correlation between GDM and 2nd-h post-prandial blood glucose levels. The great amount of researchers pay attention to the relationship of FPG on predicting GDM. Huikun Liu and friends in their cohort study involving 1263 GDM women at 1–5 years after delivery were followed up with these women. They have shown that for women with prior GDM, 2-h plasma glucose, and HbA1c during pregnancy are independent predictors of post-partum diabetes, but FPG during pregnancy is not.[28]

Conclusion

In our study, although patients who had a 75-g OGTT could only be diagnosed with FG; it is valuable in terms of emphasizing the incompatibility between isolated FG values and the diagnosis of gestational diabetes and the occurrence of its complications. Nevertheless, we think that lifestyle changes should be offered to pregnant women who refuse to have OGTT, especially with FGP ≥94 mg/dL, and insistence on OGTT should be applied to these patients. In any case, in patients who refused OGTT, data such as post-prandial 2nd-h blood glucose, which we found valuable in our study, can be investigated among larger patient groups. Again, FPG and post-prandial 2-h blood glucose testing can simplify the IADPSG diagnostic algorithm, as it is cost-effective. Educating patients that OGTT is not harmful may still make the use of this gold standard method popular in the diagnosis of GDM.

Ethics Committee Approval

This study approved by the Van Training and Research Hospital Clinical Research Ethics Committee (Date: 07.09.2022, Decision No: 2022/19-02).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: G.B., Y.E.P.; Design: G.B., Y.E.P.; Supervision: G.B., Y.E.P.; Materials: G.B., Y.E.P.; Data: G.B., Y.E.P.; Analysis: G.B., Y.E.P.; Literature search: G.B., Y.E.P.; Writing: G.B., Y.E.P.; Critical revision: G.B., Y.E.P.

Conflict of Interest

None declared.

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OGTT'yi Reddeden Hastalarda Açlık veya Tokluk Kan Şekeri Takibi Gestasyonel Diyabet Tanısında ve Komplikasyonlarını Öngörmede bir Yöntem Olarak Kullanılabilir mi?

Amaç: Gestasyonel diyabet, gebelikte en sık görülen metabolik hastalıklardan biridir. Medyada yer alan olumsuz haberler, gebelik diyabeti testini hastalar arasında tartışmalı hale getirdi. Çalışmamızda açlık kan şekeri ve tokluk ikinci saat kan şekerinin OGTT yerine gestasyonel diyabet tanısında ve olası komplikasyonlarını öngörmede kullanılabilirliğini araştırmayı amaçladık.

Gereç ve Yöntem: Bu retrospektif kohort çalışma, Aralık 2020-Temmuz 2022 tarihleri arasında İstanbulda özel bir hastaneye başvuran hastalar arasında yapıldı. Kliniğimizde OGTT'yi reddeden hastalarda rutin olarak açlık ve normal bir öğün sonrası tokluk ikinci saat kan şekeri istenilmektedir. Bu hastalarda HgA1c değerine de bakılır. 374 hastanın verilerine ulaşılmış; dışlama kriterleri sonrası 150 hasta çalışmaya dahil edildi. OGTT'yi reddeden 24-28 haftalık kadınlar çalışmaya alındı. OGTT yaptıran, daha önce diyabet tanısı alan ve OGTT yaptırmamış ancak açlık ve tokluk kan şekeri sonucuna ulaşılamayan hastalar çalışma dışı bırakıldı. Ayrıca vücut kitle indeksi 35'in üzerinde hesaplanan hastalar da çalışmaya dahil edilmedi. Kriterleri karşılayan hastaların takipleri sırasında sık görülen diyabet komplikasyonları olan polihidramnios ve makrozomi durumları değerlendirildi ve bu durumlar açlık kan şekeri ile tokluk kan şekeriyle ilişkilendirildi.

Bulgular: Çalışma için uygun 150 hasta tespit edildi. Sonuçlarımıza göre gebelerde anormal fetal özelliklerin ortaya çıkışını tahmin etmede açlık kan şekerinin zayıf olduğu ve tokluk ikinci saat kan şekerinin kısmi başarılı olduğu belirlendi. Açlık kan şekeri eşik değeri 94 mg/dL olarak alındığında duyarlılık %43, özgüllük %8.8'di. Tokluk kan şekeri eşik değeri 143.5 mg/dL olarak alındığında duyarlılık %64, özgüllük %14 (p<0.05) bulundu. HgA1c değeri ile makrozomi ve polihidramnios arasında ilişki yoktu.

Sonuç: OGTT hala gestasyonel diyabet taısı için en önemli testtir. OGTT yaptırmayı reddeden kadınlarda tokluk 2. saat kan şekeri; gestasyonel diyabet ve komplikasyonları açısından değerli olabilir. bu hastalar için daha fazla çalışmaya ihtiyaç vardır.

Anahtar Sözcükler: Açlık kan şekeri; gestasyonel diyabet; OGTT; postprandial kan şekeri.