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Evaluation of First Trimester Fasting Blood Glucose, HOMA-IR and HbA1c in Prediction of Gestational Diabetes Mellitus in Non-Obese Pregnant Women: A Retrospective Study

Mehmet Mete KIRLANGIÇ[1], Belfin Nur ARICI HALICI[2]

[1]Kartal Dr. Lutfi Kirdar City Hospital, Department of Obstetrics and Gynecology, Istanbul, Turkey
[2]Tuzla Government Hospital, Department of Obstetrics and Gynecology, Istanbul, Turkey

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ABSTRACT

Aim: Gestational Diabetes Mellitus (GDM) is the most common endocrine complication in pregnancy with fetomaternal comorbidities. It is aimed to evaluate fasting blood glucose (FBG), homeostasis model assessment of insulin resistance (HOMA-IR), and hemoglobin A1c (HbA1c) values in the first trimester in non-obese pregnant women for early detection of GDM.

Material and Methods: Pregnant women with first-trimester FBG, HOMA-IR, HbA1c values, and second-trimester OGTT results were scanned from the hospital database. First-trimester height, weight, age and gestational weeks were also recorded. The presence of Body Mass Index (BMI) over 30 kg/m2, chronic and systemic disease and history of G(DM) were not included in the study. ROC analysis was performed on FBG, HOMA-IR, and HbA1c.

Results: This retrospective study was conducted between 01/01/2021, and 01/01/2022 in Tuzla State Hospital Gynecology and Obstetrics Clinic. 131 pregnant women who met the inclusion criteria were reached. Twenty of pregnant women were evaluated as GDM positive(+). Age, height, weight, BMI, gestational week, and nulliparity were observed to be similar between the groups. FBG, insulin, HOMA-IR, and HbA1c values were higher in the group with GDM. As a result of ROC analysis, those with an FBG value of 88,5 mg/dl (sensitivity 68.2%, specificity 68.2%), a HOMA-IR value of 2.24 (sensitivity 63.6%, specificity 64.5%), and a HbA1c (sensitivity 68.2%, specificity 66.7%) value of over 5.25% were observed to be at risk for GDM.

Conclusion: It has shown that pregnant women with high first trimester FBG, HOMA-IR and HbA1c have a high risk for GDM and can be used as a predictor of GDM.

Keywords: *First trimester, FBG, GDM, HOMA-IR, HbA1c, Prediction*

Obez Olmayan Gebe Kadınlarda Gestasyonel Diabetes Mellitus Tahmininde Birinci Trimester Açlık Kan Şekeri, HOMA-IR ve HbA1c Analizi: Bir Retrospektif Çalışma

ÖZ

Amaç: Gestasyonel Diabetes Mellitus (GDM), fetomaternal komorbiditeleri olan gebelikte en sık görülen endokrin komplikasyondur. GDM'nin erken tanısı için obez olmayan gebelerde ilk trimesterde açlık kan şekeri (AKŞ), insülin direnci homeostaz modeli değerlendirmesi (HOMA-IR), Hemoglobin A1c (HbA1c) değerlerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Birinci trimester AKŞ, HOMA-IR, HbA1c değerleri ve ikinci trimester OGTT sonuçları olan gebeler hastane veri tabanından tarandı. İlk trimester boyu, kilosu, yaşı ve gebelik haftaları da kaydedildi. Vücut kütle indeksi (VKİ) 30 kg/m2'nin üzerindekiler, kronik ve sistemik hastalığı ve (GDM) öyküsü olanlar çalışmaya dahil edilmedi. ROC analizi AKŞ, HOMA-IR, HbA1c üzerinde yapıldı.

ORCID: Mehmet Mete Kırlangıç / 0000-0002-9750-1594, Belfin Nur Arıcı Halıcı / 0000-0002-8822-4740

Correspondence Address / Yazışma Adresi:
Mehmet Mete KIRLANGIÇ
Kartal Dr. Lutfi Kirdar City Hospital, Department of Obstetrics and Gynecology, Istanbul, Turkey
Phone: +90 506 464 18 19 • E-mail: metekirlangic@gmail.com

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Bulgular: Bu retrospektif çalışma 01/01/2021-01/01/2022 tarihleri arasında Tuzla Devlet Hastanesi Kadın Hastalıkları ve Doğum Kliniği'nde yapıldı. Dahil edilme kriterlerini karşılayan 131 hamile kadına ulaşıldı. Gebelerin yirmisi GDM pozitif (+) olarak değerlendirildi. Yaş, boy, kilo, VKİ, gebelik haftası, nulliparite gruplar arasında benzer olarak gözlendi. AKŞ, insülin, HOMA-IR, HbA1c değerleri GDM'li grupta daha yüksekti. ROC analizi sonucunda, AKŞ değeri 88,5 mg/dl (sensitivite %68.2, spesifite %68.2), HOMA-IR değeri 2.24 (sensitivite %63.6, spesifite %64.5) ve HbA1c değeri %5.25'in (sensitivite %68.2, spesifite %66.7) üzerinde olanların GDM için risk altında olduğu gözlenmiştir.

Sonuç: Birinci trimester yüksek AKŞ, HOMA-IR ve HbA1c olan gebelerin GDM için yüksek risk taşıdığını ve GDM'nin bir göstergesi olarak kullanılabileceğini göstermiştir.

Anahtar Sözcükler: *İlk trimester, GDM, AKŞ, HOMA-IR, HbA1c, Öngörü*

INTRODUCTION

Gestational diabetes mellitus (GDM) is the most common endocrinological disease observed during pregnancy, characterized by an increase in fetal and maternal complications (1). In studies, high body mass index (BMI), fasting blood glucose (FBG), maternal abdominal circumference, and the presence of polycystic ovary syndrome have all been identified as risk factors for GDM in studies (2). The American Diabetes Association evaluated haemoglobin A1C (HbA1c) ≥6.5 among the diagnostic criteria for diabetes in 2010 (3). Studies have also found that high HbA1c levels in GDM patients increase GDM presence and the medication needed for GDM (4). GDM-associated fetal risks include fetal death, macrosomia, shoulder dystocia, hypoglycemia, respiratory distress syndrome, and childhood obesity. Maternal risks include preeclampsia, caesarean (C/S) delivery, and more importantly, an increased risk of developing type 2 diabetes mellitus (T2DM) in later life (1,5,6). Therefore, it is critical to detect GDM early in pregnancy and take measures to reduce the risk.

Insulin resistance (IR) is an important pathogenic mechanism for GDM development. Maternal hyperinsulinemia and IR are the characteristic patterns during normal pregnancy to meet the needs of the fetus (7). However, more IR is formed in peripheral tissues in pregnant women with GDM (8). The homeostasis model assessment of insulin resistance (HOMA-IR) which is used to measure FBG and insulin, is an excellent parameter to detect IR. Being overweight before pregnancy and weight gain during pregnancy is associated with GDM development in pregnancy. Patients with a high BMI and IR have a greater risk of developing GDM (9). Increased BMI and the presence of a history of GDM are risk factors for GDM. However, normal BMIs and without risk factors for GDM can also develop GDM.

This study aims to evaluate the relationship between FBG, HOMA-IR and HbA1c results in the first trimester and GDM in non-obese pregnant women.

MATERIALS and METHODS

This study was planned between 01/01/2021 - 01/01/2022 as a retrospective study in which pregnant women whose fasting blood glucose and fasting insulin values in the first trimester were available and had oral glucose tolerance test (OGTT) at 24-28th gestational weeks in Tuzla State Hospital. Approval was obtained from the Marmara University Faculty of Medicine Ethics Committee for the study (decision no: 09.2022.48). The study was designed in accordance with the Helsinki Declaration.

Study Population

Pregnant women whose first-trimester FBG, fasting insulin, HbA1c, and second-trimester OGTT values data were available included in the study. Those with known chronic and systemic diseases, previous history of DM or GDM, multiple pregnancies, perinatal complications (preeclampsia, eclampsia, intrahepatic cholestasis of pregnancy, polyhydramnios, oligohydramnios, intrauterine growth retardation), a BMI level over 30 kg/m^2 or whose BMI values were unavailable were excluded from the study. A total of 212 pregnant women with FBG, fasting insulin, and HbA1c levels in the first trimester were reached. As a result, 131 pregnant women whose OGTT values in their 2nd trimester were available and met the inclusion criteria were evaluated (Figure 1) .

GDM Screening

HOMA-IR assessment was calculated with the formula FBG*fasting insulin/405 (10). Pregnant women whose HOMA-IR and OGTT results were available in the hospital database were evaluated. In addition, the pregnant women age and BMI were recorded via the system. In the second-trimester GDM screening of these patients, those with a 50-gram OGTT result >200 mg/dl, those whose 75-gram OGTT result is >92 mg/dl in fasting, >180 mg/dl in the 1st hour, >155 mg/dl in the second hour, and the cases in which at least 2 of the values of fasting >95 mg/dl, first hour >180 mg/dl, second hour >155mg/dl, third hour >140 mg/dl were positive were defined as GDM (11,12).

The Primary Outcome of the Study

FBG, fasting insulin values, HOMA-IR values, and HbA1c values are important parameters in terms of GDM. It aimed to evaluate the relationship between the value of these parameters in the first trimester and the OGTT results, which is the gold standard in diagnosis, and the relationship between GDM prediction and these parameters in patients diagnosed with GDM.

Statistical Analysis

Statistical analyses were performed using the IBM SPSS ver 23 (www.ibm.com/products/spss-statistics). The variables were investigated using visual and analytical methods (Kolmogorov-Smirnov/Shapiro–Wilk's test) to determine whether or not they are normally distributed. Descriptive analyses were presented using means and standard deviation for normally distributed variables and interquartile range (IQR) and medians for the non-normally distributed variables. Nonparametric comparisons were made using the Mann–Whitney U test and parametric comparisons were made using Student's t-test. A p-value of less than 0.05 was considered to show statistically significant results. Correlation tests and ROC analysis were also used to evaluate the relationship between GDM and first-trimester parameters. Comparison of ROC curves were calculated according to DeLong method. A p-value of less than 0.05 was considered to show statistically significant results.

RESULTS

Between the dates determined for the study, 212 pregnant women who met the inclusion criteria with their FBG, fasting insulin, HbA1c, height, and weight data in the first trimester of pregnancy were reached via the hospital data system. 131 pregnant women who underwent OGTT in the second trimester among these pregnant women were included in the study. While 111 of these pregnant did not have GDM, 20 (15.27%) of them had GDM.

When the pregnant women demographic characteristics were examined, the mean age was 31.50 ± 4.65 years in the GDM group and 27.40 ± 5.11 years in the healthy group,

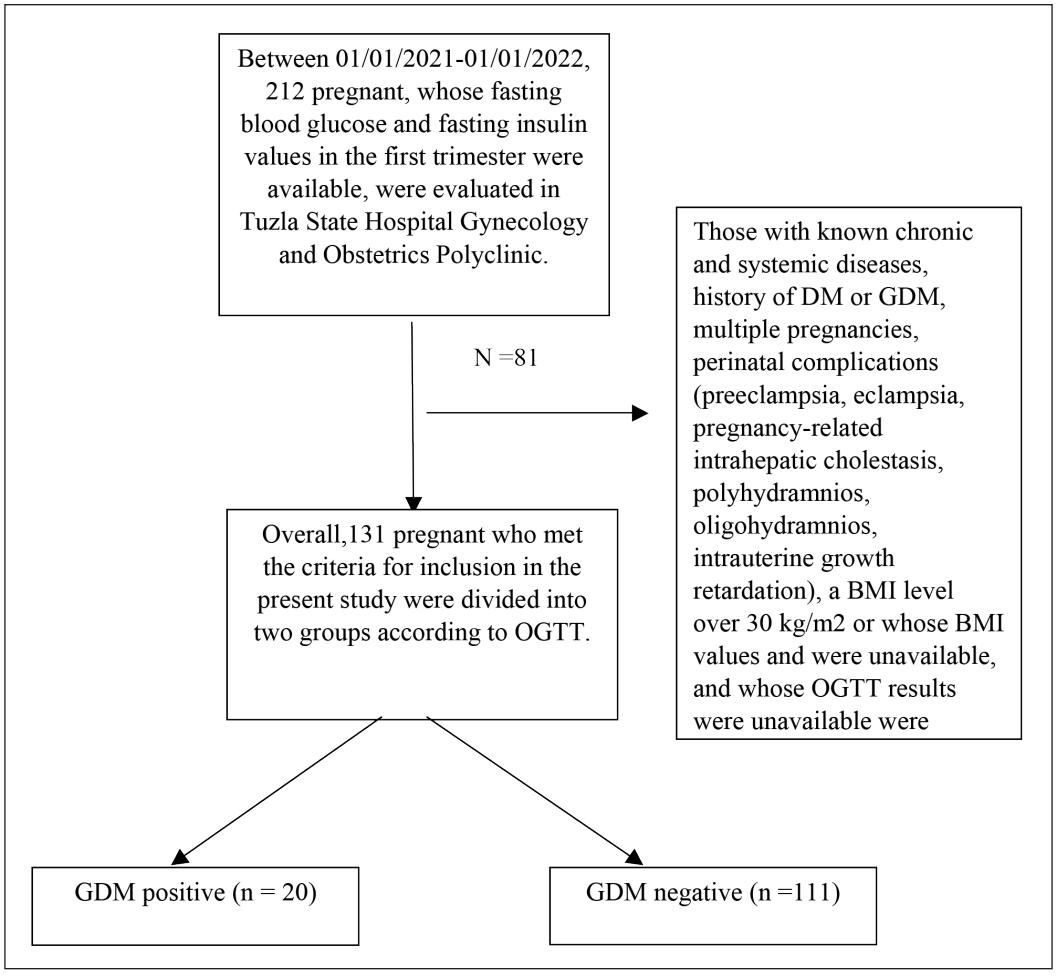

Figure 1. Flow chart for the study population

and there was a significant difference between the groups (p<0.001). Maternal weight (p=0.235), height (p=0.355), BMI (p=0.095), gestational week at sampling (p=0.107), and nulliparity rates (p=0.423) were similar in both groups (Table 1).

When the biochemical parameters were evaluated, a significant increase in FBG was observed in the group with GDM and in the healthy group at 91.81 ± 7.00 and 86.00 ± 9.13, respectively (p<0.001). Again, the insulin level was 12.38 ± 6.97 and 10.22 ± 7.61 in the group with GDM and the healthy group, respectively. The difference in the group with GDM was found to be significantly higher (p=0.032). In the evaluation of HOMA-IR, it was observed as 2.88 ± 1.83 and 2.24 ± 2.06 in the GDM group and healthy group, respectively (p=0.010). HbA1c was 5.30 ± 0.28 in the GDM group and 5.13 ± 0.27 in the healthy group. It was higher in the GDM group (p=0.016) (Table 2).

As a result of the ROC analysis, it was shown that the HOMA-IR value of 2.24, the HbA1c value of 5.25%, and the FBG value above 88.50 mg/dl caused GDM positivity(p=0.010, p=0.017, p=0.001, respectively) (Table 3). Sensitivity, specificity, negative predictive values and positive predictive values are shown in Table 3.

ROC curves were compared in pairs using DeLong method. The differences between the areas of FBG-HbA1c (p=0.422), FBG-HOMA-IR (p=0.271), and HbA1c-HOMA-IR (p= 0.922) were similar (Figure 2) (Table 3).

DISCUSSION

The most common metabolic abnormality in pregnancy is GDM, and it brings many maternal and fetal risks (9). Identification and treatment of even mild GDM can reduce adverse pregnancy outcomes, emphasizing the need to appropriately screen and diagnose this important comorbidity (5). Although the OGTT is widely regarded as the "gold standard" test for GDM diagnosis, its disadvantages include the requirement to fast for eight hours, the collection of at least two blood samples, vomiting, and high variability. Various researchers have proposed alternative screening tests such as fasting plasma glucose, HbA1c, fructosamine, and HOMA-IR to reduce the number of OGTTs for the diagnosis of GDM (13,14).

This study aims to evaluate the prediction of GDM in the first trimester of HbA1c and HOMA-IR levels in non-obese pregnant women by excluding GDM and DM history, which are the most important predisposing factors for GDM, and obesity.

Table 1: Evaluation of demographic characteristics between groups.

Characteristics	GDM (n=20)	Control (n=111)	p
Age (year)	31.50 ± 4.65	27.40 ± 5.11	<0.001
Weight (kg)	63.40 ± 9.83	62.61 ± 9.84	0.235
Height (m)	1.61 ± 0.85	1.62 ± 0.05	0.355
BMI (kg/m^2)	24.02 ± 3.44	23.81 ± 3.73	0.095
Gestational week	11.59 ± 1.73	10.50 ± 2.47	0.107
Nulliparity	8 (%40)	49 (%44.1)	0.423

Table 2: Evaluation of biochemical parameters between groups.

Parameters	GDM (n=20)	Control (n=111)	p
HOMA-IR	2.88 ± 1.83	2.24 ± 2.06	0.010
HbA1c (%)	5.30 ± 0.28	5.13 ± 0.27	0.016
FBG (mg/dl)	91.81 ± 7.00	86.0 ± 9.13	<0.001
Insulin(mIU/L)	12.38 ± 6.97	10.22 ± 7.61	0.032

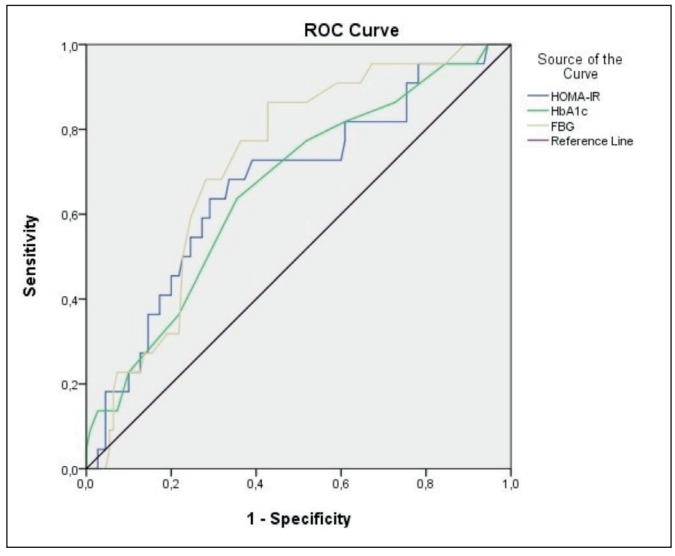

Figure 2. ROC curves for FBG, HOMA-IR, and HbA1c for the diagnosis GDM.

Table 3: Area under the receiver operating characteristic curve (AUROC), threshold value, and sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) for GDM.

	Threshold value	Sensitivity (%)	Specificity (%)	AUROC (CI 95%)	NPV	PPV
FBG (mg/dl)	88.50	68.2	68.2	0.722	91.5	30.8
HbA1c (%)	5.25	63.6	64.5	0.662	89.9	26.4
HOMA-IR	2.24	68.2	66.7	0.674	91.4	28.8

Our study has some important findings. 1) The mean first-trimester HOMA-IR values in non-obese pregnant women were significantly higher at 2.88±1.83 in pregnant with GDM and the same value was 2.24±2.06 in healthy pregnant women. 2)Nevertheless, the mean first-trimester HbA1c values were higher at 5.30±0.28 in pregnant women with GDM compared to healthy pregnant women, of which HbA1c values were 5.13±0.27 in the healthy pregnant women. 3) It was observed that even the first-trimester FBG, which can be measured with a simple method, can be observed as 91.81±7.00 mg/dl in the group with GDM and 86.0±9.13 mg/dl in the healthy control group, which can provide with a prediction in terms of GDM.

The International Association of Diabetes and Pregnancy Study Groups (IADPSG) and the American Diabetes Association (ADA) recommend that patients in certain high-risk populations (those with obesity, a history of GDM, and polycystic ovarian syndrome) be screened at the first prenatal visit and positive results diagnosed with overt DM (11). However, whether this practice should be used routinely is still a matter of debate (15).

In their study, Bartha et al. demonstrated that early screening for glucose intolerance and maintenance can prevent some diabetes-related complications in pregnant women with GDM (16).

In the study by Seshiah et al., 471 pregnant women with GDM (17.6%) were examined, with 121 (16.3%) at the 16th week, 166 (22.4%) between the 17th-23rd weeks, and 454 (61.3%) at 24 weeks or more. Therefore, in this study, 38.7% of those with GDM developed GDM even before the 24th gestational week (17). According to the study of Fong et al., among the outcomes of 526 pregnant women, more than 10% of the pregnant had early screening HbA1c values between 5.7-6.4%, and it was shown that the pregnant women in this group had a significantly higher risk of progression to GDM compared to the group with normal values. It was concluded that early screening with HbA1c values can help identify pregnant women with the highest risk of developing GDM (18).

As a result of the study performed by Valadan et al. on 700 pregnant womenand GDM was detected in 115 pregnant women(16.4%), it was concluded that the HbA1c values were measured in the first trimester in the GDM group and the healthy group were 5.45 ± 0.39 and 4.96 ± 0.30, respectively. The mean FBG was observed as 92.01 ± 7.79 mg/dl and 82.61 ± 6.46 mg/dl in the GDM group and the healthy group, respectively. Valadan et al. found that the mean first-trimester FPG and HbA1c values of pregnant women with GDM were significantly higher than those of normoglycemic pregnant women (19).

In the study of Benaiges et al. in Spain on 1195 pregnant women, they found that although first-trimester HbA1c was found to be higher in pregnantwith GDM, it did not have sufficient sensitivity or specificity to diagnose GDM. And they concluded that only using a higher or lower threshold can simplify the diagnostic process by reducing the number of OGTTs, associated costs, and patient discomfort (20). In their study conducted in Singapore, Poo et al. found that a first-trimester HbA1c of less than 5.2% may be useful to exclude low-risk Singaporean pregnant women, from further testing, while those with an HbA1c of 5.2% or higher would need OGTT (21).

In the study conducted by Song et al. on 700 pregnant women in which they evaluated HOMA-IR as a risk factor for GDM in early pregnancy, 145 (20.7%) pregnant women were found to have GDM. They showed that HOMA-IR was higher in the GDM group than in the healthy group and was an individual risk factor for GDM (22). The study by Benhalima et al. reported that high insulin resistance in pregnant women with GDM suggested a more unfavorable metabolic profile and pregnancy outcomes when compared to pregnant women with normal glucose tolerance (23). In the study by Alptekin et al., the mean HOMA-IR value in the non-GDM group was 2.2 ± 1.7, while it was 3.8 ± 1.6 in the group with GDM. The difference was found to be significant. They reported that they determined the GDM predictability in patients with a HOMA-IR score of >2.08 in the first trimester using ROC analysis with 90% sensitivity and 61% specificity (14). As a result of the study conducted by Özçimen et al., it was reported that GDM can be predicted in the first trimester if the HOMA-IR score is >2.60 (24).

Considering the studies conducted in different societies, it is concluded that GDM can be predicted by FBG, HOMA-IR and HbA1c, in this study conducted in the Turkish population, as in previous studies.

It was shown in this study that first-trimester values were higher in the group with GDM, who were not obese and had no history of DM.

Maternal insulin resistance is one of the characteristics of normal glycemic physiology during pregnancy, and excessive insulin resistance is GDM's main characteristic (25). There are also ambiguities about the effectiveness of the biochemical markers examined. In the "Hyperglycemia and Adverse Pregnancy Outcomes" study, FBG levels showed that the probability of GDM increased and there was a continuous gradual relationship between FBG and adverse pregnancy outcomes such as C/S delivery, macrosomia, and neonatal hypoglycemia (1).

In the current study, it was also found that the risk of developing GDM is higher in those with high FBGs. However, studies on first-trimester FBG values have not conclusively demonstrated a clinically useful breakpoint for the first-trimester fasting glucose that is sensitive enough to obviate the need for further testing or specific enough to start treatment early (26). In addition, physiological hydration, anemia, slower intestinal transit, increased erythrocyte life cycle and nutritional changes are the factors that can significantly affect the HbA1c value during pregnancy (27). Therefore, there is no guideline for the use of HbA1c in the diagnosis of GDM (19).

In a review by Li et al in which 127 million pregnant women were examined, it was observed that the risk of GDM increases with age. In this study, it was found that the age was higher in those with GDM (28).

First of all, for use in early GDM risk assessment, HOMA-IR and HbA1c have practical benefits since they require a single blood draw, are interpreted with a single value, and are better tolerated by pregnant women. It is possible to obtain information about GDM with HOMA-IR and HbA1c in patients who refuse OGTT. In addition, lifestyle changes such as diet and exercise can be recommended to patients with high values, and measures can be taken to prevent GDM formation from the very beginning.

Secondly, it has been shown in studies that it cannot replace OGTT, which is still the gold standard for GDM, even though different results were obtained and the application and evaluation of the parameters examined seemed to be simpler than OGTT.

Finally, larger clinical trials or cost-effectiveness analyses of screening and treatment approaches based on first-trimester biochemical GDM markers are required to transform observational study findings into clinical practice.

Our study has limitations. It was retrospective, so the results could be reached only via the data registered in the hospital database. HbA1c and fasting insulin are not routine tests in the first trimester. Therefore, the number of patients was lowand the small number does not reflect the entire society. It is not known how the current COVID-19 pandemic takes place on diseases and may affect GDM as it triggers a sedentary life. The fact that the COVID-19 histories of the evaluated patients is not known is also a limitation of the study.

It has been shown that pregnant women with higher HOMA-IR and HbA1c in the first trimester have a higher risk for GDM. As a result, a HOMAIR value of 2.24, an HbA1c value of 5.25%, and a FBG value of 88.5 mg/dl constitute a risk for GDM. These seem to be predictors of GDM. At least a lifestyle change can be recommended to patients with these high values. However, in line with all studies, it has been concluded that OGTT cannot replace OGTT due to both its sensitivity-specificity and cost-effectiveness.

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Author Contributions

All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Conflict of Interest

Authors have stated that there were no conflicts of interest associated with this study or its results.

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Ethical Approval

Approval was obtained from the Marmara University Faculty of Medicine Ethics Committee for the study (decision no: 09.2022.48). The study was designed in accordance with the Helsinki Declaration.

Peer Review Process

Extremely peer-reviewed and accepted.

REFERENCES

1. Lowe LP, Metzger BE, Dyer AR, Lowe J, McCance DR, Lappin TR, Trimble ER, Coustan DR, Hadden DR, Hod M, Oats JJ, Persson B; HAPO Study Cooperative Research Group. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study: associations of maternal A1C and glucose with pregnancy outcomes. Diabetes Care. 2012;35:574-580.
2. Popova PV, Grineva EN, Gerasimov AS, Kravchuk EN, Ryazantseva EM, Shelepova ES. The new combination of risk factors determining a high risk of gestational diabetes mellitus. Endocrine Abstracts. 2012; 29:511.
3. American Diabetes Association. Standards of medical care in diabetes--2010. Diabetes Care 2010;33 Suppl 1(Suppl 1):S11-61.
4. Clayton W Jr, Agarwal N, Wang L, Jagasia S. Clinical markers implying the need for treatment in women with gestational diabetes mellitus. Endocr Pract. 2012;18(1):62-65.
5. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS; Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med. 2005;352(24):2477-2486.

6. Yogev, Chen, Hod, Coustan, Oats, McIntyre, Metzger, Lowe, Dyer, Dooley, Trimble, McCance, Hadden, Persson, Rogers; Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study Cooperative Research Group. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study: Preeclampsia. Am J Obstet Gynecol. 2010;202(3):255.e1-7.
7. Colomiere M, Permezel M, Lappas M. Diabetes and obesity during pregnancy alter insulin signalling and glucose transporter expression in maternal skeletal muscle and subcutaneous adipose tissue. J Mol Endocrinol. 2010;44(4):213-223.
8. Hedderson MM, Gunderson EP, Ferrara A. Gestational weight gain and risk of gestational diabetes mellitus. Obstet Gynecol. 2010;115(3):597-604.
9. Yuen L, Saeedi P, Riaz M, Karuranga S, Divakar H, Levitt N, Yang X, Simmons D. Projections of the prevalence of hyperglycaemia in pregnancy in 2019 and beyond: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 2019;157:107841.
10. Kırlangıç MM, Eraslan Şahin M, Vural Yalman M, Akdemir E, Çöl Madendağ İ, Sade OS, Kütük S. Progesterone and progesterone-induced blocking factor (PIBF) levels in non-obese women with polycystic ovary syndrom. Cukurova Med J. 2022;47(3):114-1120.
11. Diabetes IAo, Panel PSGC. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010;33(3):676-682.
12. Kırlangıç MM, Eraslan Sahin M. Assessment of the roles of ABO blood types and Rh factors in gestational diabetes mellitus. Perinatal Journal (2022);30(1):38-42.
13. Agarwal MM, Hughes PF, Punnose J, Ezimokhai M, Thomas L. Gestational diabetes screening of a multiethnic, high-risk population using glycated proteins. Diabetes Res Clin Pract. 2001;51(1):67-73.
14. Alptekin H, Çizmecioğlu A, Işık H, Cengiz T, Yildiz M, Iyisoy MS. Predicting gestational diabetes mellitus during the first trimester using anthropometric measurements and HOMA-IR. J Endocrinol Invest. 2016;39(5):577-583.
15. Moyer VA; U.S. Preventive Services Task Force. Screening for gestational diabetes mellitus: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2014;160(6):414-420.
16. Bartha JL, Martinez-Del-Fresno P, Comino-Delgado R. Early diagnosis of gestational diabetes mellitus and prevention of diabetes-related complications. Eur J Obstet Gynecol Reprod Biol. 2003;109(1):41-44.
17. Seshiah V, Balaji V, Balaji MS, Paneerselvam A, Arthi T, Thamizharasi M, Datta M. Gestational diabetes mellitus manifests in all trimesters of pregnancy. Diabetes Res Clin Pract. 2007;77(3):482-484.
18. Fong A, Serra AE, Gabby L, Wing DA, Berkowitz KM. Use of hemoglobin A1c as an early predictor of gestational diabetes mellitus. Am J Obstet Gynecol. 2014;211(6):641.e1-7.
19. Valadan M, Bahramnezhad Z, Golshahi F, Feizabad E. The role of first-trimester HbA1c in the early detection of gestational diabetes. BMC Pregnancy Childbirth. 2022;22(1):71.
20. Benaiges D, Flores-Le Roux JA, Marcelo I, Mañé L, Rodríguez M, Navarro X, Chillarón JJ, Llauradó G, Gortazar L, Pedro-Botet J, Payà A. Is first-trimester HbA1c useful in the diagnosis of gestational diabetes? Diabetes Res Clin Pract. 2017;133:85-91.
21. Poo ZX, Wright A, Ruochen D, Singh R. Optimal first trimester HbA1c threshold to identify Singaporean women at risk of gestational diabetes mellitus and adverse pregnancy outcomes: A pilot study. Obstet Med. 2019;12(2):79-84.
22. Song S, Zhang Y, Qiao X, Duo Y, Xu J, Peng Z, Zhang J, Chen Y, Nie X, Sun Q, Yang X, Lu Z, Liu S, Zhao T, Yuan T, Fu Y, Dong Y, Zhao W, Sun W, Wang A. HOMA-IR as a risk factor of gestational diabetes mellitus and a novel simple surrogate index in early pregnancy. Int J Gynaecol Obstet. 2022;157(3):694-701.
23. Benhalima K, Van Crombrugge P, Moyson C, Verhaeghe J, Vandeginste S, Verlaenen H, Vercammen C, Maes T, Dufraimont E, De Block C, Jacquemyn Y, Mekahli F, De Clippel K, Van Den Bruel A, Loccufier A, Laenen A, Minschart C, Devlieger R, Mathieu C. Characteristics and pregnancy outcomes across gestational diabetes mellitus subtypes based on insulin resistance. Diabetologia. 2019;62(11):2118-2128.
24. Ozcimen EE, Uckuyu A, Ciftci FC, Yanik FF, Bakar C. Diagnosis of gestational diabetes mellitus by use of the homeostasis model assessment-insulin resistance index in the first trimester. Gynecol Endocrinol. 2008;24(4):224-229.
25. Temming LA, Tuuli MG, Stout MJ, Macones GA, Cahill AG. Maternal and Perinatal Outcomes in Women with Insulin Resistance. Am J Perinatol. 2016;33(8):776-780.
26. Powe CE. Early Pregnancy Biochemical Predictors of Gestational Diabetes Mellitus. Curr Diab Rep. 2017;17(2):12.
27. Lippi G, Targher G. Glycated hemoglobin (HbA1c): Old dogmas, a new perspective? Clin Chem Lab Med. 2010;48(5):609-614.
28. Li Y, Ren X, He L, Li J, Zhang S, Chen W. Maternal age and the risk of gestational diabetes mellitus: A systematic review and meta-analysis of over 120 million participants. Diabetes Res Clin Pract. 2020;162:108044.