Özgün Araştırma / Original Article

Jinekoloji - Obstetrik ve Neonatoloji Tıp Dergisi
The Journal of Gynecology - Obstetrics and Neonatology

DOI: 10.38136/jgon.1059937

Prediction of birth weight by HbA1c and glucose levels in diabetic pregnant women

Diyabetik gebelerde HbA1c ve glukoz düzeyleriyle doğum ağırlığının tahmin edilmesi

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ÖZ

Amaç: Pregestasyonel diabetes mellitus (PGDM) ve gestasyonel diabetes mellitus (GDM) tanılı gebelerde 28 ve 32. gebelik haftalarında açlık glukozu, tokluk 1. saat glukozu ve Hemoglobin A1c düzeyleri ile doğum ağırlığını tahmin etmek.

Gereç ve Yöntemler: Çalışmamıza 66 GDM, 39 PGDM (7 tip 1 DM ve 32 tip 2 DM) tanılı toplam 105 gebe dahil edildi. Tüm katılımcıların yaşı, obstetrik öyküleri, gebelik öncesi vücut kitle indeksi (VKİ), gebelikte kilo alımı (GKA), gebelik haftaları, açlık ve 1. saat tokluk glukozu, HbA1c, doğumda gebelik haftası, doğum ağırlığı ve persentili ve 1. ve 5. dakika Apgar skorları kaydedildi

Bulgular: 28. ve 32. gebelik haftalarında ölçülen açlık glukozu, tokluk 1. saat glukozu ve HbA1c değerleri PGDM grubunda GDM grubuna göre anlamlı derecede yüksekti, GKA ve gebelik öncesi VKİ değerleri benzerdi. GDM grubunda gebelik yaşına göre büyük doğum ağırlığı (LGA)'yı öngören açlık glukozu, 1. saat tokluk glukozu ve GKA'ya göre ROC analizi yapıldı (sırasıyla, EAA: 0,663, %95 CI [0,526, 0,800], EAA: 0,678, %95 CI [0,540, 0,816], AUC: 0,677, %95 CI[0,548, 0,805]). Ayrıca, PGDM grubunda LGA'yı öngören açlık glukozu, 1. saat tokluk glukozu ve HbA1c'ye göre ROC analizi yapıldı (sırasıyla, EAA: 0.889, %95 CI [0.782, 0.996], EAA: 0.893, %95 CI [0.737, 1.000], EAA: 0,931, %95 CI [0,807, 1,000]).

Sonuç: PGDM ve GDM'li gebelerde glisemik kontrol kritik öneme sahiptir. LGA riski, PGDM'de HbA1c ve tokluk glukozu ve GDM'de ve tokluk glukozu ve GKA'yı yakından izleyerek azaltılabilir. Fetal aşırı büyümeyi en aza indirerek çocukluk çağı obezitesi ve uzun vadede gelişebilecek metabolik sendrom riski azaltılabilir.

Anahtar Kelimeler: HbA1c, Açlık glukoz düzeyi, Tokluk glukoz düzeyi, Doğum ağırlığı, Gebelik yaşına göre büyük doğum ağırlığı, Diyabetik gebeler

ABSTRACT

Objective: To estimate the birth weight by examining the fasting glucose, 1st -hour postprandial glucose, and Hemoglobin A1c levels in pregnant women diagnosed with pregestational diabetes mellitus (PGDM) and gestational diabetes mellitus (GDM) at 28th and 32nd gestational weeks.

Materials and Methods: A total of 105 pregnant women diagnosed with 66 GDM, 39 PGDM (7 of type 1 DM and 32 of type 2 DM) were included in our study. All participants' age, obstetric histories, pre-pregnancy body mass index (BMI), gestational weight gain (GWG), gestational weeks, fasting and 1st-hour postprandial glucose, HbA1c, gestational week at delivery, newborn weight and percentile, and 1st and 5th minute Apgar score were noted.

Results: Fasting glucose, 1st-hour postprandial glucose, and HbA1c values measured at 28th and 32nd gestational weeks were significantly higher in the PGDM group compared to the GDM group, and the GWG and pre-pregnancy BMI values were similar. ROC curve analysis was used to assess for fasting glucose, 1st-hour postprandial glucose, and GWG predicting large for gestational age (LGA) in the GDM group (AUC: 0.663, %95 CI [0,526, 0,800], AUC: 0.678, %95 CI [0,540, 0,816], AUC: 0.677, %95 CI [0,548, 0,805], respectively). Also, determined to fasting glucose, 1st-hour postprandial glucose, and HbA1c predicting LGA in the PGDM group (AUC: 0.889, %95 CI [0,782, 0,996], AUC: 0.893, %95 CI [0,737, 1,000], AUC: 0.931, %95 CI [0,807, 1,000], respectively).

Conclusion: Glycemic control is critical in pregnant women with PGDM and GDM. The risk of LGA may be reduced by closely monitoring HbA1c and postprandial glucose in PGDM and postprandial glucose and GWG in GDM. By minimizing fetal overgrowth, the risk of childhood obesity and metabolic syndrome that may develop in the long term may be reduced.

Keywords: HbA1c, Fasting glucose level, Postprandial glucose level, Birth weight, Large for gestational age, Diabetic pregnant women

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Başvuru tarihi : 19.01.2022
Kabul tarihi :22.02.2022

INTRODUCTION

Diabetes mellitus (DM), which affects a significant portion of women of reproductive age, is defined as an increase in blood glucose level due to insufficient insulin production or ineffectiveness of insulin. Hyperglycemia in pregnancy (HIP) is the most common metabolic disorder and consists of gestational diabetes mellitus (GDM) or pregestational diabetes mellitus (PGDM). The frequency of HIP has been reported as 15.8% globally (1). PGDM refers to type 1 DM and type 2 DM diagnosed before pregnancy. While PGDM constitutes approximately 13-21% of DM in pregnancy, GDM constitutes the remaining part (2).

DM causes a significantly high risk of adverse maternal, fetal, and neonatal outcomes such as polyhydramnios, large for gestational age (LGA), fetal growth restriction (FGR), stillbirth, and neonatal's hypoglycemia, hypocalcemia, hypomagnesemia, polycythemia, hyperbilirubinemia, respiratory distress. The primary cause of these risks is hyperglycemia. Fetal hyperinsulinemia due to maternal hyperglycemia causes fetal weight gain. Insulin is one of the main factors that ensure fetal growth, and it has a mitogenic effect by stimulating food intake in insulin-sensitive tissues (3).

Large for gestational age, which you often see in newborns of diabetic pregnant women, causes birth traumas such as shoulder dystocia and increases the risk of cesarean delivery. It was aimed to estimate the birth weight by examining the fasting glucose, 1st -hour postprandial glucose, and Hemoglobin A1c levels in pregnant women diagnosed with PGDM and GDM at 28th and 32nd gestational weeks.

MATERIALS AND METHODS

In our clinic, a two-stage approach is adopted to diagnose GDM. According to the American College of Obstetricians and Gynecologists, a 100 g oral glucose tolerance test (OGTT) is performed for pregnant women whose serum glucose is 140 mg/dl and above, one hour after the 50 g glucose challenge test (GCT) at 24 to 28 weeks of gestation. GDM is diagnosed according to the Carpenter and Coustan criteria (4). A 100 g OGTT is given after at least eight hours of fasting to pregnant. Fasting 95 mg/dl, 180 mg/dl for one hour, 155 mg/dl for two hours, and 140 mg/dl for three hours, at least two values above these threshold values make the diagnosis of GDM (5).

Exclusion criteria were the mother's systemic disease other than DM, medical treatment history other than insulin, smoking, multiple pregnancy, and fetal anomaly. A total of 105 pregnant women diagnosed with 66 GDM, 39 PGDM (7 of type 1 DM and 32 of type 2 DM) were included in our study. All participants' age, obstetric histories, pre-pregnancy body mass index (BMI), gestational weight gain (GWG), gestational weeks, fasting and 1st-hour postprandial glucose, HbA1c, a gestational week at delivery, newborn weight and percentile, and 1st and 5th minute Apgar score were found in hospital records and noted. LGA birth weight was defined as infant weight above the 90th percentile for gender and gestational age.

In this retrospective study, hospital records of pregnant women with DM who applied to the Perinatology unit of Ankara City Hospital were analyzed from April 2021 to December 2021. Our study was approved by Ankara City Hospital Medical Research Ethics Department (E2-22-1251).

Statistical analysis

The sample size was calculated with G Power software (version 3.1; Franz Foul, Universitat Kiel, Kiel, Germany). The effect size was 0.80 (large) for the sample size, the p-value was 0.05, and the power was 95%. It was planned to include at least 74 patients, 37 cases for each group. Statistical analyses were performed using SPSS 17 software (SPSS, Inc., Chicago, IL, United States). To express the quantitative data, statistical methods such as descriptive frequency, percentage, mean, standard deviation, median, and interquartile ranges (IQRs). The normal distribution of the variables was evaluated with the Kolmogorov Smirnov test. Statistical comparisons between groups were used with an independent t-test for normal distribution variables. It was done using the Mann-Whitney U test for the variables not having a normal distribution. Chi-square test and Fisher's exact test were used to compare categorical data. Receiver operating characteristic (ROC) curve analysis was used to predict newborn birth weight. The p-value < 0.05 was regarded as statistically significant.

RESULTS

One hundred and five pregnant women were included in our study. The socio-demographic, clinical characteristics, biochemical data, and perinatal outcomes were presented in Table 1. 25 newborns in the GDM group and 18 newborns in the PGDM group were LGA. Maternal clinical characteristics and biochemical data of LGA and AGA newborns in GDM and PGDM groups are given in Tables 2 and 3.

Table 1: Socio-demographic, clinical characteristics, biochemical data, and perinatal outcomes of all participants

	GDM (n=66)	PGDM (n=39)	p value
Age (years)	33±6	31±5	.085*
Gravidity	3±1	3±1	.364*
Parity	1±1	1±1	.245*
Gestational age (Weeks)	30.6±1.4	30.2±1.8	.687*
Pre-pregnancy BMI (kg/m²)	29.1±4.8	28.4±3.7	.074*
GWG (kg)	9±3	10±4	.452*
HbA1c (%)	5.8±0.7	6.9±1.5	<.001*
Fasting glucose (mg/dl)	85±16.5	99.2±25	<.001*
1st-hour postprandial glucose (mg/dl)	138.1±28.9	145±45	<.001*
GA at delivery (weeks)	37±2	37±2	.775*
Birth weight (grams)	3157±590	3422±656	.087*
Birth weight (percentile)	69.3±25.6	75±23.3	.154*
LGA	25 (37.9%)	18 (46.2%)	.405†
1st minute APGAR score	7 (7-8)	7 (7-8)	.645‡
5th minute APGAR score	9 (9-10)	9 (9-9)	.795‡

Values are presented as mean± standard deviation, median (IQRs (Inter Quartile Ranges)), or as counts (percentage)

* Independent t-test

† Chi-square test

‡ Mann Whitney U tes

Table 2: Clinical characteristics and biochemical data of LGA and AGA groups of pregnant women with GDM

	LGA (n=25)	AGA (n=41)	p value
HbA1c (%)	7.6 (7.2-8.7)	5.7 (5.1-6.3)	.327‡
Fasting glucose (mg/dl)	114 (94-126)	88 (78-93)	.027‡
1st-hour postprandial glucose (mg/dl)	167 (157-212)	114 (111-127)	.016‡
Pre-pregnancy BMI (kg/m²)	28.4 (27.7-32.2)	28.3 (26.9-30.4)	.247‡
GWG (kg)	10 (9-12)	9 (8-10)	.015‡

Values are presented median (IQR (Inter Quartile Range))

‡ Mann Whitney U test

Table 3: Clinical characteristics and biochemical data of LGA and AGA groups of pregnant women with PGDM

	LGA (n=18)	AGA (n=21)	p value
HbA1c (%)	7.6 (7.1-8.9)	5.8 (5.3-6.7)	<.001‡
Fasting glucose (mg/dl)	114 (94-126)	88 (78-93)	<.001‡
1st-hour postprandial glucose (mg/dl)	167 (157-212)	114 (111-127)	<.001‡
Pre-pregnancy BMI (kg/m²)	27.6 (25.2-29.7)	27.7 (26.5-30.4)	.364‡
GWG (kg)	11(8-12)	12 (8-12)	.813‡

Values are presented median (IQR (Inter Quartile Range))

‡ Mann Whitney U test

ROC curves for LGA prediction in GDM and PGDM groups are presented in Figures 1 and 2. We performed ROC curve analysis to fasting glucose, 1st-hour postprandial glucose, and GWG predicting LGA in the GDM group (AUC: 0.663, %95 CI [0,526, 0,800], AUC: 0.678, %95 CI [0,540, 0,816], AUC: 0.677, %95 CI [0,548, 0,805], respectively). In addition we also ROC curve analysis to determined to fasting glucose, 1st-hour postprandial glucose, and HbA1c predicting LGA in the PGDM group (AUC: 0.889, %95 CI [0,782, 0,996], AUC: 0.893, %95 CI [0,737, 1,000], AUC: 0.931, %95 CI [0,807, 1,000], respectively).

Figure 1: Fasting glucose, 1st-hour postprandial glucose, and GWG predicting LGA in the GDM group

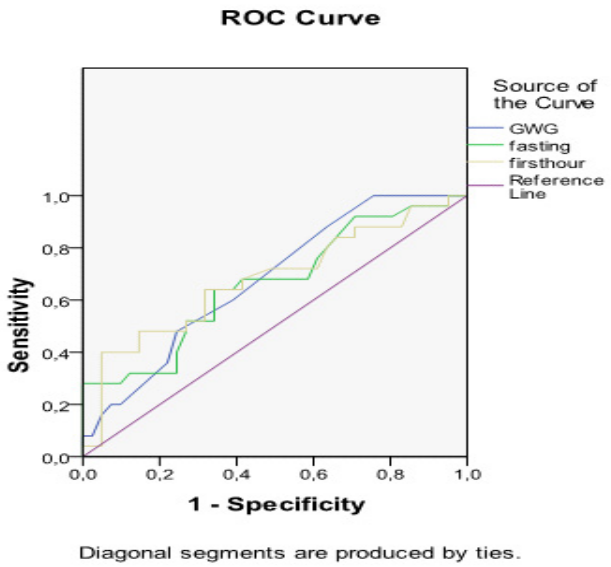
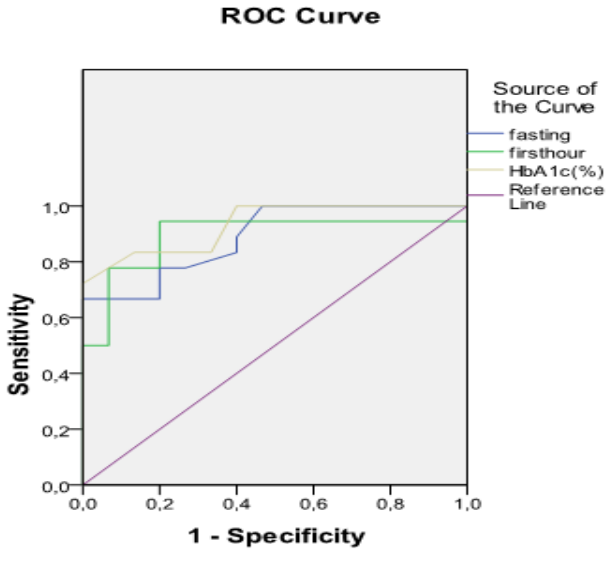


Figure 2: Fasting glucose, 1st-hour postprandial glucose, and HbA1c predicting LGA in the PGDM group



DISCUSSION

The present study showed that fasting glucose, 1st-hour postprandial glucose, and HbA1c values measured at 28th and 32nd gestational weeks were significantly higher in the PGDM group than in the GDM group, and the GWG and pre-pregnancy BMI values were similar. In addition, HbA1c, 1st-hour postprandial glucose, and fasting glucose were more significant for LGA prediction in the PGDM group, respectively. Also, we found that 1st-hour postprandial glucose, GWG, and fasting glucose were more significant for LGA prediction in the GDM group, respectively.

Fasting and postprandial glucose tests are inexpensive and easy to apply. It also reflects the immediate changes in glucose. A study comparing type 1 DM and the control group found that the postprandial blood glucose measured in the third trimester was the strongest predictor for macrosomia (6). In addition, other studies have demonstrated the importance of postprandial blood glucose similarly (7, 8). The present study showed that for the predictive performance of LGA of 1st-hour postprandial glucose, a sensitivity of 64% and a specificity of 68% were achieved with a cut-off value of 140.5 mg/dl in the GDM group. In addition, for the predictive performance of LGA of 1st-hour postprandial glucose, a sensitivity of 94% and a specificity of 80% were achieved with a cut-off value of 128.5 mg/dl in the PGDM. On the other hand, for the fasting glucose, a sensitivity of 78% and a specificity of 80% were achieved with a cut-off value of 93.5 mg/dl in the PGDM. Our study showed that postprandial glucose was significantly predictive of LGA, especially in PGDM compared to the GDM group. We also showed that postprandial blood glucose significantly predicted LGA relative to fasting blood glucose in the PGDM group.

HbA1c is a commonly used test in chronic glycemic control, reflecting the average blood sugar level in the last one to two months, especially in pregnant women with PGDM. Due to the increase in hemodilution and erythrocyte destruction rate during pregnancy, the HbA1c value is lower in pregnant women than in non-pregnant women (9). It has not been shown that the use of the HbA1c test, which will be performed every 4-5 weeks in pregnant women with GDM, as a glycemic control parameter may be of value (10, 11). Birth weight is significantly correlated with HbA1c measured at different time points in the PGDM group (12, 13). For example, in a prospective study, the HbA1c value measured in the third trimester of 289 pregnant women with Type 1 DM was the strongest predictor for macrosomia (14). Significant deviations in serum glucose values in the GDM group are less than in the PGDM group (15, 16). For this reason, the evidence for a relationship between HbA1c and birth weight in the GDM group is weaker. Many studies have looked at HbA1c at the time of OGTT and have shown a weak association of HbA1c with infant birth weight in the early period. However, the relationship between HbA1c at the time of birth and macrosomia has been demonstrated more strongly (17). Therefore, HbA1c may be measured close to delivery for birth weight prediction in the GDM group. Similarly, in our study, HbA1c strongly predicted LGA in the PGDM group. The present study showed that for the predictive performance of LGA of the HbA1c, a sensitivity of 93% and a specificity of 87% were performed with a cut-off value of 6.55 in the PGDM. Since it predicts LGA weakly in the GDM group, HbA1c measurement may be planned close to birth, especially in the GDM group.

The risk of GDM is increased, especially in pre-pregnancy obese or overweight women, and GWG should be followed carefully. In studies, excessive GWG was associated with cesarean delivery, hypertension, LGA, inability to lose weight gained after birth, and an increased risk of diabetes (18, 19). The present study showed that for the predictive performance of LGA of GWG, a sensitivity of 60% and a specificity of 61% were performed with a cut-off weight of 11.5 kg in the GDM. On the other hand, for the fasting glucose, a sensitivity of 64% and a specificity of 66% were achieved with a cut-off value of 84.5 mg/dl in the GDM. Our study demonstrated that GWG is more valuable than fasting glucose and HbA1c in LGA prediction in pregnant women with GDM. In addition, glycemic control and GWG should be followed closely.

Limitation

One of the study's limitations was its retrospective design and the calculation of the pre-pregnancy BMI of the pregnant women according to their self-reported weights. Also, maternal glycemic markers were measured only once and had no repetitive measurements. In addition, the number of pregnant women with Type 1 DM included in the study was very low (n=7).

CONCLUSİON

Glycemic control is critical in pregnant women with both PGDM and GDM. The risk of LGA may be reduced by closely monitoring HbA1c and postprandial glucose in PGDM and postprandial glucose and GWG in GDM. By minimizing fetal overgrowth,

the risk of childhood obesity and metabolic syndrome that may develop in the long term may be reduced, and the cardiometabolic profile may be improved. For this reason, the parameters that will predict LGA in the early stages of pregnancy are very valuable.

REFERENCES

1. Deputy NP, Kim SY, Conrey EJ, Bullard KM. Prevalence and Changes in Preexisting Diabetes and Gestational Diabetes Among Women Who Had a Live Birth - United States, 2012-2016. MMWR Morb Mortal Wkly Rep. 2018;67(43):1201-7.

2. Yuen L, Saeedi P, Riaz M, Karuranga S, Divakar H, Levitt N, et al. 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.

3. Pedersen J. Weight and length at birth of infants of diabetic mothers. Acta Endocrinol (Copenh). 1954;16(4):330-42.

4. ACOG Practice Bulletin No. 190: Gestational Diabetes Mellitus. Obstet Gynecol. 2018;131(2):e49-e64.

5. Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. Am J Obstet Gynecol. 1982;144(7):768-73.

6. Combs CA, Gunderson E, Kitzmiller JL, Gavin LA, Main EK. Relationship of fetal macrosomia to maternal postprandial glucose control during pregnancy. Diabetes Care. 1992;15(10):1251-7.

7. Parfitt VJ, Clark JD, Turner GM, Hartog M. Maternal postprandial blood glucose levels influence infant birth weight in diabetic pregnancy. Diabetes Res. 1992;19(3):133-5.

8. Persson B, Hanson U. Fetal size at birth in relation to quality of blood glucose control in pregnancies complicated by pregestational diabetes mellitus. Br J Obstet Gynaecol. 1996;103(5):427-33.

9. Jovanovic L, Savas H, Mehta M, Trujillo A, Pettitt DJ. Frequent monitoring of A1C during pregnancy as a treatment tool to guide therapy. Diabetes Care. 2011;34(1):53-4.

10. Lapolla A, Dalfrà MG, Bonomo M, Castiglioni MT, Di Cianni G, Masin M, et al. Can plasma glucose and HbA1c predict fetal growth in mothers with different glucose tolerance levels? Diabetes Res Clin Pract. 2007;77(3):465-70.

11. Lowe LP, Metzger BE, Dyer AR, Lowe J, McCance DR, Lappin TR, et al. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study: associations of maternal A1C and glucose with pregnancy outcomes. Diabetes Care. 2012;35(3):574-80.

12. Herranz L, Pallardo LF, Hillman N, Martin-Vaquero P, Villarroel A, Fernandez A. Maternal third trimester hyperglycaemic excursions predict large-for-gestational-age infants in type 1 diabetic pregnancy. Diabetes Res Clin Pract. 2007;75(1):42-6.

13. Damm P, Mersebach H, Råstam J, Kaaja R, Hod M, McCance DR, et al. Poor pregnancy outcome in women with type 1 diabetes is predicted by elevated HbA1c and spikes of high glucose values in the third trimester. J Matern Fetal Neonatal Med. 2014;27(2):149-54.

14. Evers IM, de Valk HW, Mol BW, ter Braak EW, Visser GH. Macrosomia despite good glycaemic control in Type I diabetic pregnancy; results of a nationwide study in The Netherlands. Diabetologia. 2002;45(11):1484-9.

15. Yu H, Qi X, Wang X. Application of glycated hemoglobin in the perinatal period. Int J Clin Exp Med. 2014;7(12):4653-9.

16. Cahill AG, Tuuli MG, Colvin R, Cade WT, Macones GA. Markers of Glycemic Control and Neonatal Morbidity in High-Risk Insulin-Resistant Pregnancies. Am J Perinatol. 2016;33(2):151-6.

17. Karcaaltincaba D, Yalvac S, Kandemir O, Altun S. Glycosylated hemoglobin level in the second trimester predicts birth weight and amniotic fluid volume in non-diabetic pregnancies with abnormal screening test. J Matern Fetal Neonatal Med. 2010;23(10):1193-9.

18. Cheng YW, Chung JH, Kurbisch-Block I, Inturrisi M, Shafer S, Caughey AB. Gestational weight gain and gestational diabetes mellitus: perinatal outcomes. Obstet Gynecol. 2008;112(5):1015-22.

19. Siega-Riz AM, Viswanathan M, Moos MK, Deierlein A, Mumford S, Knaack J, et al. A systematic review of outcomes of maternal weight gain according to the Institute of Medicine recommendations: birthweight, fetal growth, and postpartum weight retention. Am J Obstet Gynecol. 2009;201(4):339.e1-14.