



Postpartum Metabolic Outcomes and Related Factors in Women with Gestational Diabetes Mellitus History

Gestasyonel Diabetes Mellitus Öyküsü Olan Kadınlarda Postpartum Metabolik Sonuçlar ve İlişkili Faktörler

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Abstract

Objective: This study aimed to investigate early and late postpartum glycemic abnormalities and related factors in women with a history of gestational diabetes mellitus (GDM). **Material and Methods:** This study included 152 women aged 18-40 years who were diagnosed with GDM either by one- or two-step oral glucose tolerance test (OGTT). Sociodemographic characteristics, body mass index (BMI), biochemical parameters, and OGTT results of the participants were recorded from files. In addition, BMI, fasting plasma glucose, lipid parameters, and glycosylated hemoglobin (HbA1c) levels were measured, and OGTT was performed between 4 and 12 weeks after postpartum and at the first year. **Results:** The mean age of the participants was 31.86±6.096 years, and their mean BMI was 26.23±3.67 kg/m². In the early postpartum period (4-6 weeks) after 75 g OGTT, 70.4% of patients had normal glucose tolerance (NGT), 25% had prediabetes (preDM), and 4.6% had diabetes mellitus (DM). In the late postpartum period, 48.0% of patients had NGT, 45.4% had preDM, and 6.6% had DM. BMI and HbA1c levels were significantly higher in patients with both preDM and DM than women with NGT in both early and late periods (p<0.05). In addition, BMI before and 1 year after pregnancy and HbA1c level between 4 and 6 weeks after delivery were independent risk factors for the development of dysglycemia (OR: 1.004, p<0.001; OR: 2.848, p<0.001; and OR: 4.437, p=0.016, respectively). **Conclusion:** Women with GDM have a high risk of developing preDM and type 2 DM in the first year after delivery.

Keywords: Gestational diabetes mellitus; postpartum period; hyperglycemia

Özet

Amaç: Bu çalışmanın amacı, gestasyonel diabetes mellitus (GDM) öyküsü olan kadınlarda, erken ve geç postpartum dönemde glisemik anormallik oranı ve ilişkili faktörleri değerlendirmektir. **Gereç ve Yöntemler:** Çalışmaya 18-40 yaş arasında, 24-28. haftada tek basamaklı ya da iki basamaklı yaklaşımla GDM tanısı konmuş ve doğum yapmış olan 152 kadın alındı. Katılımcıların sosyodemografik özellikleri, beden kitle indeksi (BKİ), biyokimyasal verileri ve oral glukoz tolerans testi (OGTT) sonuçları dosyalarından kaydedildi. Ayrıca postpartum 4-12. hafta ile 1. yılda BKİ, açlık plazma glukozu, lipid parametreleri, glikozile hemoglobin (HbA1c) seviyeleri ölçüldü ve 75 g OGTT yapıldı. **Bulgular:** Katılımcıların ortalama yaşı 31,86±6,096 ve BKİ 26,23±3,67kg/m² idi. Postpartum erken dönemde (4-6. hafta) 75 g OGTT sonrası %70,4 normal glukoz toleransı (NGT), %25,0 prediyabet (preDM) ve %4,6 diabetes mellitus (DM), geç dönemde (1. yıl) ise %48,0 oranında NGT, %45,4 preDM ve %6,6 DM saptandı. BKİ ve HbA1c seviyeleri, hem erken hemde geç dönemde NGT'li kadınlara kıyasla hem preDM hem de DM'lilerde anlamlı düzeyde daha yüksek saptandı (p<0,05). Ayrıca disglisemi gelişimi için gebelik öncesi ve 1 yıl sonraki BKİ ile gebelik sonrası 4-6. haftadaki HbA1c seviyesi bağımsız risk faktörleri idi (sırasıyla, OR: 1,004, p<0,001, OR: 2,848, p<0,001 ve OR: 4,437, p=0,016). **Sonuç:** GDM'li kadınların doğumdan sonraki ilk yılda preDM ve tip 2 DM geliştirme riskleri yüksektir.

Anahtar kelimeler: Gestasyonel diyabet; postpartum periyod; hiperglisemi

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Peer review under responsibility of Turkish Journal of Endocrinology and Metabolism.

Received: 06 Apr 2021 **Received in revised form:** 21 Jun 2021 **Accepted:** 24 Jun 2021 **Available online:** 24 Sep 2021

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Introduction

Gestational diabetes mellitus (GDM) is a common metabolic complication of pregnancy. GDM prevalence increases in parallel with the rates of obesity and type 2 diabetes mellitus (T2DM) and has been reported at a rate of 8-20% according to the diagnostic criteria used (1,2). Having a history of GDM is a strong predictor of several metabolic disturbances. Women with a history of GDM show a high risk for T2DM, and it has been reported that these women have a 7-10 times increased risk for T2DM compared with normoglycemic women (3). T2DM develops in approximately 5% of women in the first 6 months and in 10% within 1-2 years after birth in patients who have GDM in pregnancy (4). Approximately 70% of women with a history of GDM may develop T2DM if no intervention is provided (5). Therefore, for the subsequent monitoring and management of women with GDM, it is necessary to determine the risk factors for postpartum glucose abnormalities and screen those who are at risk of developing dysglycemia after birth (6,7).

At present, the most sensitive test recommended in postpartum screening is the 75 g oral glucose tolerance test (OGTT). Compared with fasting plasma glucose (FPG) and glycated hemoglobin (HbA1c), OGTT is required for the maximum detection of prediabetes (preDM) and diabetes mellitus (DM) cases (8). If FPG alone is performed, 30-40% of T2DM cases and impaired glucose tolerance (IGT) can go undetected (9). Sufficient evidence does not exist about the use of HbA1c as a screening test (10). Other indicators that can predict the development of preDM and T2DM in the future in women with GDM are pregestational body mass index (BMI), ethnic characteristics, higher plasma glucose (PG) level during pregnancy, detection of GDM in early weeks of pregnancy, need for insulin treatment during pregnancy, multiparity, advanced maternal age, and HbA1c during pregnancy (11-13). Strategies to reduce the risk of progression to T2DM are a crucial public health priority for women with previous GDM. However, this can be done by identifying people at high risk through postpartum follow-up. Therefore, in this study, we aimed to evaluate the rate of dysglycemia development in

the early and late postpartum periods and the factors associated with dysglycemia in women who were diagnosed with GDM using either a one-or two-step approach.

Material and Methods

This study is a cross-sectional study conducted in Kahramanmaraş Sütçü İmam University (KSU) Faculty of Medicine, Department of Endocrinology and Metabolic Diseases. The study was approved by the Ethics Committee of KSU, dated 25.12.2019 and numbered 01, and a written consent form was obtained from all participants. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Study Design and Inclusion Criteria

The study included 165 women aged 18-40 years who were diagnosed with GDM either by a one-or two-step approach. After obtaining the consents of the volunteers to be included in the study, their sociodemographic characteristics, gestational week at the time of diagnosis, age, height, pregestational weight, BMI, GDM treatment, birth type, birth number, baby's birth weight, and additional diseases were scanned from archive files and recorded. In addition, FPG, creatinine, alanine aminotransferase (ALT), lipid parameters, fasting insulin and HbA1c levels, and OGTT results were recorded from their files. Moreover, 13 women were excluded because of lack of data, and the study continued with 152 women. BMI, FPG, lipid parameters, fasting insulin, and HbA1c levels of the participants included in the study were measured, and 75 g OGTT was performed between 4 and 12 weeks and the first year after delivery.

Exclusion Criteria

Patients with type 1 DM and T2DM before pregnancy; smokers and alcohol users; those with serious concomitant disease (nondiabetic disease that will significantly limit life expectancy); those who use drugs that affect glucose metabolism; and those with hypothyroidism or hyperthyroidism, renal dysfunction, liver failure, morbid obe-

sity, mental retardation, and severe psychiatric disease were excluded from the study. In addition, women below the age of 18 years and above 40 years were excluded from the study.

Anthropometric Measures

Weight was measured with an accuracy of at least 0.1 kg, and measurements were made with light clothing. Height (m) was measured with bare feet while standing using a wall-mounted gauge with an accuracy of at least 0.1 cm. BMI was calculated as weight/height² (kg/m²).

Biochemical Measurements

Blood samples for biochemical parameters were taken from the antecubital vein between 08.00 and 09.00 in the morning after 8-10 h of overnight fast. Glucose, ALT, creatinine, and lipid parameters were measured using the spectrophotometric method and Advia 1800 Chemistry System (Siemens Healthcare GmbH, Erlangen, Germany). HbA1c was studied using high pressure liquid chromatography (HPLC) method with an HPLC device and commercial kit (Bio-rad, Hercules, California, USA). Insulin was measured using the chemiluminescence method with a hormone analyzer and commercial kit (Siemens Healthcare GmbH, Erlangen, Germany).

Normal reference values were as follow: FPG 70-100 mg/dL, total cholesterol 0-200 mg/dL, triglyceride 0-150 mg/dL, high-density lipoprotein 26-86 mg/dL, low-density lipoprotein 0-130 mg/dL, ALT 7-45 U/L, creatinine 0.5-0.9 mg/dL, fasting insulin 6-27 uIU/mL, and HbA1c 4-5.6%.

Diagnosis of Gestational Diabetes Mellitus

GDM was diagnosed between 24 and 28 weeks of pregnancy by using either a one-or two-step approach (7). In the one-step approach, after at least 8-10 h of fasting and drinking 75 g of glucose mixed into 300 mL of water, fasting and first and second hours glucose levels were measured. GDM was diagnosed when one of the threshold values (FPG \geq 92 mg/dL, OGTT first hour PG \geq 180 mg/dL, and OGTT second hour PG \geq 153 mg/dL) was exceeded.

In the two-step approach, the prescreening test was performed by measuring PG at any

time of the day 1 h after drinking 50 g of glucose. If the first hour PG was between 140 and 179 mg/dL, OGTT was performed the next day after fasting for at least 8-10 h with 100 g glucose to make a definitive diagnosis of GDM. In OGTT, if two of four values were higher (FPG \geq 95 mg/dL, first hour PG \geq 180 mg/dL, second hour PG \geq 155 mg/dL, and third hour PG \geq 140 mg/dL), GDM was diagnosed. In addition, after the 50 g glucose challenge test, if the first hour PG value was \geq 180 mg/dL, 100 g OGTT was not performed, and GDM was confirmed.

Postpartum Oral Glucose Challenge Test

OGTT was performed for all participants between 4 and 12 weeks and the first year after delivery. Food intake, smoking, and excessive physical activity were not allowed during OGTT. Following at least 8-10 h of fasting and drinking 75 g of glucose mixed into 300 mL of water, FPG and second hour PG levels were measured. Normal glucose tolerance (NGT) was established when FPG level was $<$ 100 mg/dL and OGTT second hour PG was $<$ 140 mg/dL, impaired fasting glucose (IFG) was confirmed when FPG was 100-125 mg/dL, IGT was defined as OGTT second hour glucose between 140 and 199 mg/dL, and DM was diagnosed if FPG \geq 126 mg/dL and OGTT second hour glucose \geq 200 mg/dL (7).

Insulin Resistance Index

The insulin resistance (IR) index homeostasis model assessment (HOMA-IR) was calculated using the following formula for all participants based on fasting insulin and FPG levels at postpartum 4-12 weeks and the first year.

HOMA-IR: FPG (mg/dL) \times fasting plasma insulin (μ IU/mL)/405.

According to this formula, HOMA-IR score of 2.7 indicates high IR (14).

Statistical Analysis

Normally distributed values were expressed as mean \pm standard deviation. The data were analyzed using SPSS (Statistical Package for Social Sciences) version 25 package program (IBM Corp. Released 2017Armonk, NY, USA). For the application of parametric tests, the Kolmogorov-Smirnov test was used to determine whether the samples had

normal distribution and whether the variances were homogeneous. The patients were divided into three groups according to the glucose profile in the postpartum early and late periods, and one-way analysis of variance test was used to compare the NGT, preDM, and DM groups. The data that differed between the groups were evaluated by the post hoc analysis. Scheffe's method was used for determining significant differences in the post hoc analysis because variance analysis was homogeneous and the number of groups was three, but the sample size was not equal. The chi-square test was used to evaluate the relationship between frequency distributions of categorical variables. Logistic regression analysis was performed to determine the effects of demographic and laboratory variables on the development of postpartum preDM/DM. Relative proportions were expressed as odds ratio and confidence interval. A p value of <0.05 was considered statistically significant.

Results

The sociodemographic characteristics and data of the 24-28th week of pregnancy of 152 women included in the study are shown in Table 1. A total of 205 patients participated in the study. However, the study was completed with 152 patients who underwent OGTT in both early and late stages. The average age of the participants was 31.86±6.096 years, and the pregestational BMI was 26.23±3.67 kg/m². GDM was diagnosed using the single-step test in 27.6% of the patients and the two-step test in 72.4% of the patients. In addition, 53.9% of the participants received only medical nutrition treatment (MNT), whereas 46.1% were given MNT and insulin treatment. When the rates of delivery were examined, 46.7% of the patients had a normal vaginal delivery, whereas 53.3% had a cesarean section, and history of macrosomic birth was found in 15.8%.

Postpartum Early Evaluation

The comparison of the demographic and laboratory characteristics of women with NGT, preDM, and DM in the early postpartum period (4-6 weeks) is shown in Table 2. In addition, 85.7% of women with DM in the early postpartum period were receiving MNT and

Table 1. The sociodemographic characteristics and the data of the 24th-28th week of pregnancy (n=152).

Parameters	
Mean±SD	
Age (year)	31.86±6.096
Pregestational BMI (kg/m ²)	26.23±3.67
Education, n, (%)	
Elementary school	130 (85.5)
High school	22 (14.5)
Family history of diabetes, n, (%)	69 (45.4)
GDM diagnosis criteria	
One-step approach, n, (%)	42 (27.6)
OGTT ₇₅ PG ₀	98.64±17.09
OGTT ₇₅ PG _{1s}	154.28±41.46
OGTT ₇₅ PG _{2s}	129.24±33.78
Two-step approach, n, (%)	110 (72.4)
OGTT ₅₀ PG _{1s}	174.33±22.97
OGTT ₁₀₀ PG ₀	93.20±11.20
OGTT ₁₀₀ PG _{1s}	173.17±36.90
OGTT ₁₀₀ PG _{2s}	144.04±34.58
OGTT ₁₀₀ PG _{3s}	118.55±31.84
Treatment for GDM	
Medical nutrition therapy, n, (%)	82 (53.9)
Medical nutrition and insulin therapy, n, (%)	70 (46.1)
Type of Delivery, n, (%)	
NVD	71 (46.7)
C/S	81 (53.3)
Macrosomia (≥4000 g) n, (%)	24 (15.8)
Systolic BP (mmHg)	113.93±14.04
Diastolic BP (mmHg)	70.99±8.89
FPG (mg/dL)	94.83±11.37
T-C (mg/dL)	202.54±41.99
LDL-C (mg/dL)	128.27±31.02
HDL-C (mg/dL)	48.33±8.56
TG (mg/dL)	204.55±64.06

SD: Standard deviation; BMI: Body mass index; GDM: Gestational diabetes mellitus; OGTT: Oral glucose tolerance test; PG: Plasma glucose; NVD: Normal vaginal delivery; C/S: Cesarean section; BP: Blood pressure; FPG: Fasting plasma glucose; T-C: Total cholesterol; LDL-C: Low-density lipoprotein; HDL-C: High-density lipoprotein; TG: Triglyceride.

insulin treatment during GDM, and it was significantly higher than the other groups (p=0.039). The rate of macrosomia was also significantly higher in the DM group than that in the NGT and preDM groups (p=0.019). In addition, FPG levels increased from NGT to DM groups, and the difference between them was statistically significant

Table 2. The comparison of the demographic and laboratory characteristics of women with NGT, prediabetes, and diabetes in the early postpartum period (4-6 weeks).

Parameters	NGT (n=107, 70.4%)	PreDM (n=38, 25.0%)	DM (n=7, 4.6%)	p value
Age (year)	31.65±5.88	32.05±6.60	34.00±6.92	0.603
BMI (kg/m ²)	27.62±3.24	29.76±4.95*	28.22±1.58*	0.011
GDM diagnosis criteria n, (%)				
One-step approach	37 (34.6)	19 (50.0)	3 (42.9)	0.235
Two-step approach	70 (65.4)	19 (50.0)	4 (57.1)	
Hypertension, n, (%)	7 (6.5)	5 (13.2)	1 (14.3)	0.274
Hyperlipidemia, n, (%)	12 (11.2)	3 (7.9)	1 (14.3)	0.620
Family history of diabetes, n, (%)	46 (43.0)	18 (47.4)	5 (71.4)	0.349
Treatment for GDM, n, (%)				
MNT	56 (52.3)	25 (65.8)	1 (14.3)	0.039
MNT and insulin therapy	51 (47.7)	13 (34.2)	6 (85.7)**	
Type of delivery, n, (%)				
NVD	50 (46.7)	19 (50.0)	2 (28.6)	0.637
C/S	57 (53.3)	19 (50.0)	5 (71.4)	
Macrosomia, n, (%)	16 (15.0)	4 (10.5)	4 (57.1)**	0.019
FPG (mg/dL)	91.76±18.68	93.39±14.82*	116.43±32.41*¶	0.004
T-C (mg/dL)	202.64±42.81	203.87±48.96	218.43±43.57	0.661
LDL-C (mg/dL)	122.44±34.15	125.58±31.71	115.57±28.87	0.740
HDL-C (mg/dL)	50.08±14.52	48.39±10.36	44.00±12.27	0.451
TG (mg/dL)	173.29±84.57	171.50±80.87	184±90.94	0.937
HbA1c (%)	5.23±0.47	5.52±0.44*	6.11±0.56*¶	0.000
Fasting insulin (mIU/mL)	12.82±6.03	14.53±6.65	13.73±5.84	0.341
HOMA-IR	2.91±0.14	3.35±0.25	3.99±0.78	0.094

*ANOVA, Scheffe test; the significant difference between normal glucose tolerance-prediabetes and normal glucose tolerance-diabetes mellitus groups ($p<0.05$). ¶ANOVA, Scheffe test; the significant difference between prediabetes-diabetes mellitus groups ($p<0.05$). **Chi-square test; the significant difference between groups ($p<0.05$). NGT: Normal glucose tolerance; PreDM: Prediabetes; DM: Diabetes mellitus; BMI: Body mass index; GDM: Gestational diabetes mellitus; OGTT: Oral glucose tolerance test; PG: Plasma glucose; NVD: Normal vaginal delivery; C/S: Cesarean section; BP: Blood pressure; FPG: Fasting plasma glucose; T-C: Total cholesterol; LDL-C: Low-density lipoprotein; HDL-C: High-density lipoprotein; TG: Triglyceride; HbA1c: Glycosylated hemoglobin; HOMA-IR: Homeostasis model assessment-insulin resistance.

($p=0.004$). In post hoc analysis, FPG was significantly higher in the DM group than in the NGT and preDM groups ($p=0.004$ vs. $p=0.012$). When the HbA1c levels were compared, a significant difference was observed between the groups ($p<0.001$). HbA1c levels were significantly higher in the preDM and DM groups than in the NGT group ($p=0.002$ vs. $p<0.001$) and in the DM group than in the preDM group ($p=0.005$). A significant difference was observed between the three groups in terms of BMI ($p=0.025$). In addition, BMI was significantly higher in women with both preDM and DM than in those with NGT ($p=0.011$ vs. $p=0.048$) (Figure 1A).

Postpartum Late Evaluation

The comparison of demographic and laboratory characteristics of women with NGT, preDM, and DM in the postpartum late period (first year) is shown in Table 3. The rate of macrosomia was 40.0% in the DM group and significantly higher than in the NGT and preDM groups ($p=0.023$). In addition, FPG and HbA1c levels were increasing from NGT to DM groups, and the difference between them was statistically significant ($p<0.001$). In post hoc analysis, FPG and HbA1c levels were significantly higher in the preDM and DM groups than in the NGT group ($p<0.001$) and in the DM group than the preDM group

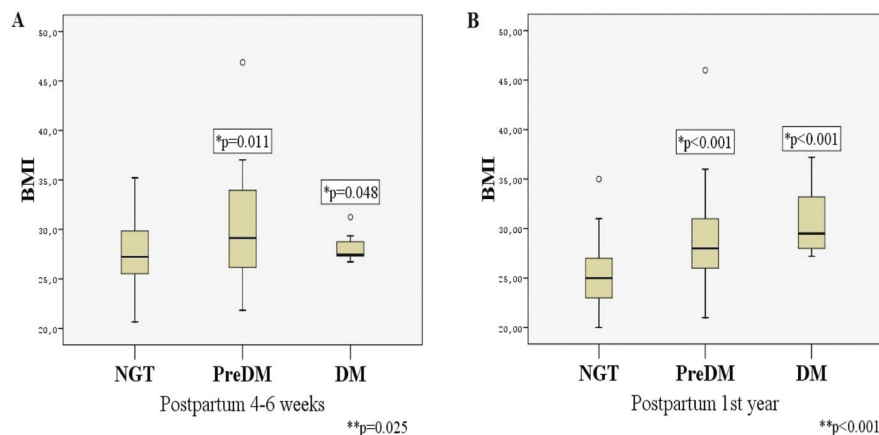


Figure 1. Change in body mass index of women with normal glucose tolerance and dysglycemia in the postpartum early (A) and late (B) periods.

BMI: Body mass index; NGT: Normal glucose tolerance; PreDM: Prediabetes; DM: Diabetes mellitus.

*p; ANOVA, Scheffe test; significant difference between normal glucose tolerance (NGT)-prediabetes (preDM) and normal glucose tolerance-diabetes mellitus (DM) groups ($p < 0.05$)

**p; significant difference between three groups ($p < 0.05$)

Table 3. The comparison of demographic and laboratory characteristics of women with NGT, prediabetes, and diabetes in the postpartum late period (first year).

Parameters	NGT (n=73, 48.0%)	PreDM (n=69, 45.4%)	DM (n=10, 6.6%)	p value
Age (year)	30.95±6.02	32.64±6.02	33.20±6.73	0.198
BMI (kg/m ²)	24.96±2.80	28.80±3.99*	30.72±3.41*	0.000
GDM diagnosis criteria, n, (%)				
One-step approach	27 (37.0)	29 (42.0)	3 (30.0)	0.726
Two-step approach	46 (63.0)	40 (58.0)	7 (70.0)	
Hypertension, n, (%)	3 (4.1)	8 (11.6)	2 (20.0)	0.091
Hyperlipidemia, n, (%)	6 (8.2)	9 (13.0)	1 (10.0)	0.641
Family history of diabetes, n, (%)	33 (45.2)	29 (42.0)	7 (70.0)	0.289
Treatment for GDM, n, (%)				
MNT	36 (49.3)	43 (62.3)	3 (30.0)	0.092
MNT and insulin therapy	37 (50.7)	26 (37.7)	7 (70.0)	
Type of delivery, n, (%)				
NVD	30 (41.1)	38 (55.1)	3 (30.0)	0.146
C/S	43 (58.9)	31 (44.9)	7 (70.0)	
Macrosomia, n, (%)	14 (19.2)	6 (8.7)	4 (40.0)**	0.023
FPG (mg/dL)	89.55±12.30	100.46±15.34*	130.20±26.43*¶	0.000
T-C (mg/dL)	185.68±38.26	189.99±28.19	184.90±37.67	0.731
LDL-C (mg/dL)	120.48±32.62	123.13±27.22	117.00±25.77	0.772
HDL-C (mg/dL)	49.67±9.37	47.81±9.28	49.10±10.27	0.497
TG (mg/dL)	140.11±67.93	158.55±67.81	159.60±80.01	0.253
HbA1c (%)	5.33±0.28	5.77±0.34*	6.67±1.24*¶	0.000
Fasting insulin (mIU/mL)	13.85±6.02	15.92±6.53	14.65±5.98	0.146
HOMA-IR	3.07±0.17	3.96±0.21*	4.69±0.65*	0.001

*ANOVA, Scheffe test; the significant difference between normal glucose tolerance-prediabetes and normal glucose tolerance-diabetes mellitus groups ($p < 0.05$). ¶ANOVA, Scheffe test; the significant difference between prediabetes-diabetes mellitus groups ($p < 0.05$). **Chi-square test; the significant difference between groups ($p < 0.05$). NGT: Normal glucose tolerance; PreDM: Prediabetes; DM: Diabetes mellitus; BMI: Body mass index; GDM: Gestational diabetes mellitus; OGTT: Oral glucose tolerance test; PG: Plasma glucose; NVD: Normal vaginal delivery; C/S: Cesarean section; BP: Blood pressure; FPG: Fasting plasma glucose; T-C: Total cholesterol; LDL-C: Low-density lipoprotein; HDL-C: High-density lipoprotein; TG: Triglyceride; HbA1c: Glycosylated hemoglobin; HOMA-IR: Homeostasis model assessment-insulin resistance.

($p < 0.001$). In addition, a significant difference was observed between the groups in terms of HOMA-IR ($p = 0.001$). HOMA-IR was significantly higher in the preDM and DM groups than in the NGT group ($p = 0.007$ vs. $p = 0.016$). The significant difference between the three groups in terms of BMI is shown in Figure 1B. BMI was significantly higher in preDM and DM groups than NGT group ($p < 0.001$).

Postpartum Early and Late Glycemic Variation Rate

In the early postpartum period (4-6 weeks), after 75 g OGTT, 70.4% of patients had NGT, 25% had preDM (IFG or IGT), and 4.6% had DM. In the late postpartum period (first year), after 75 g OGTT, 48.0% of patients had NGT, 45.4% had preDM, and 6.6% had DM (Figure 2).

Factors Affecting Postpartum Dysglycemia

The women included in the study were evaluated in terms of demographic and metabolic factors that may affect the development of preDM/DM in the postpartum period (Table 4). Pregestational BMI, BMI at postpartum in the first year, and increase in HbA1c levels at postpartum 4-6 weeks were independent risk factors for preDM/DM (OR: 1.004, $p < 0.001$; OR: 2.848, $p < 0.001$; and OR: 4.437, $p = 0.016$, respectively).

Discussion

We found that 25% of patients had preDM (IFG/IGT) and 4.6% had DM in the early postpartum period (4-6 weeks), and 45.4% had preDM, and 6.6% had DM in the late postpartum period (first year). In addition, BMI increases before and after pregnancy and early postpartum HbA1c levels are in-

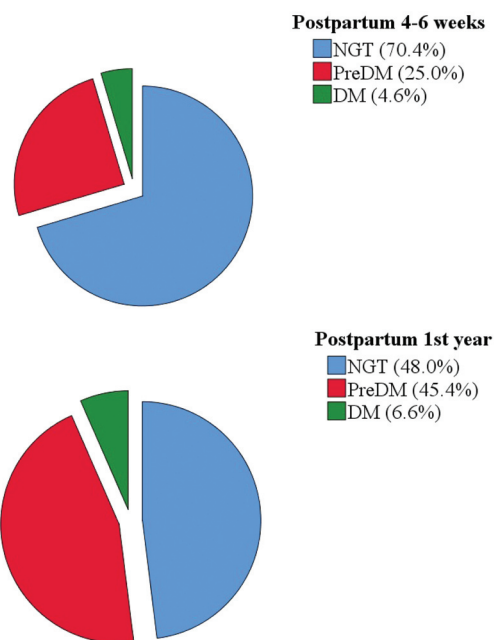


Figure 2. Postpartum early and late period dysglycemia rates. NGT: Normal glucose tolerance; PreDM: Prediabetes; DM: Diabetes mellitus.

dependent risk factors for the development of T2DM in the future.

Glucose metabolism disorders (preDM/DM) are common in the postpartum period in pregnant women with gestational diabetes. However, the rates of postpartum glucose metabolism disorder vary considerably because of the differences in the study population, the diagnostic criteria used in the diagnosis of GDM and the time of diagnosis, and the follow-up periods after birth. O'Sullivan et al. (15) showed that 52% of women developed T2DM within 6-7 years after GDM pregnancy. Jacob et al. (16) found that the risk of developing dysglycemia was 1.9

Table 4. The factors associated with the development of postpartum dysglycemia.

Parameters	PreDM/DM		
	OR	CI 95%	p value
Pregestational BMI	1.004	(0.922-1.094)	0.000
Postpartum BMI1st year	2.848	(1.997-4.062)	0.000
Postpartum HbA1c4-6 weeks	4.437	(1.321-14.905)	0.016

*Non-significant variables in the multivariable logistic regression analysis were not indicated in the table. PreDM: Prediabetes; DM: Diabetes mellitus; BMI: Body mass index; HbA1c: Glycosylated hemoglobin.

times higher in women with GDM in a follow-up period of 4-8 years after the pregnancy than pregnant women with NGT. Weinert et al. (13) reported T2DM in 3.7% and preDM (IFG/IGT) in 20.4% of women when they evaluated 108 women with GDM at the postpartum sixth week with OGTT, FPG, and random PG measurement. In a study of Wang et al. (17), 583 women with GDM were evaluated using the World Health Organization criteria with 75 g OGTT in postpartum 6-12 weeks. IGT was reported in 29.9% of the patients and T2DM in 2.9%. We included GDM patients who were diagnosed with either a one- or two-step approach. We reevaluated the patients with 75 g OGTT at postpartum 4-6 weeks and the first year. Accordingly, 25% of patients had preDM (IFG and/or IGT), and 4.6% had DM in the early postpartum period (4-6 weeks), and 45.4% had preDM, and 6.6% had DM in the late period (first year). Thus, we believe that GDM is a crucial risk factor for the development of T2DM in the future in line with the literature, and the risk increases as time progresses. However, the difference in our prevalence rates was because of the differences in our study population, the diagnostic criteria we used, and the time of diagnosis.

Postpartum T2DM frequency is affected by BMI, weight gain after pregnancy, family history of DM, FPG during and after pregnancy, postpartum IR and insufficient β cell secretion, and the need for pharmacological treatment during pregnancy (11-13). In our study group, a significant difference in pregestational BMI was observed between groups (NGT/preDM/DM) both in the early and late postpartum periods. Pregestational BMI was significantly higher in the DM and preDM groups than in the NGT group. In addition, pregestational BMI and postpartum first year BMI were independent risk factors for the development of dysglycemia. Palardo et al. (18) showed that prepregnancy BMI is an independent risk factor for DM in their study where they evaluated 788 women with GDM 3-6 months after pregnancy. Moreover, they suggested that the risk of DM increased eight times in those with a BMI of >27 kg/m². In addition, Jang et al. (19) reported a 40% increase in T2DM risk for every 1 kg increase in prepregnancy

weight. Our findings and the current evidence suggest that pre- and postpregnancy weight gain is a crucial risk factor for the development of postpartum T2DM. Studies have reported that insulin use because of GDM poses an independent risk for postpartum glucose abnormalities (20,21). Cheung et al. (22) reported a three-fold increase in the risk of T2DM in women with GDM using insulin compared with those who do not. We found that insulin use during GDM was significantly higher in the DM group than in the NGT group in the early postpartum period. Bakiner et al. (21) also reported higher IFG incidences in sixth postpartum week OGTT in insulin users than diet alone. In addition, we found that FPG and HbA1c levels were significantly higher in the preDM/DM groups than the NGT group in the postpartum early and late periods. This indicates that patients with significant hyperglycemia during GDM and using insulin therapy should be particularly careful in terms of developing DM in the future. Peripheral IR and pancreatic beta-cell dysfunction are pathogenetic mechanisms responsible for GDM and T2DM, and they can also affect glucose metabolism in the postpartum period (23,24). We found that HOMA-IR, which is the IR index, was significantly higher in the preDM and DM groups than the NGT group in the postpartum late period. This supports that, similar to the literature, the postpartum IR may be a risk predictor of developing DM in the future.

The incidence of postpartum glucose abnormality in patients with GDM also depends on how GDM is defined. The incidence of DM and preDM reported between 6 and 12 weeks postpartum before the introduction of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria was approximately 1.2-4.5% and 12.2-36.0%, respectively (25). After the widespread adoption of IADPSG criteria for the diagnosis of GDM, the incidences of postpartum preDM and DM reported in women with GDM have decreased mainly because of the lower thresholds in IADPSG criteria. Wang et al. (26) found that the incidence of postpartum preDM and DM in women with GDM was 29.9% and 2.9% after using IADPSG criteria. We included patients diagnosed with GDM both in one-

(27.6%) and two-step approaches (72.4%). No significant difference was observed between the groups in terms of the development of dysglycemia after pregnancy in terms of the GDM diagnosis method used. This may be because of the relatively low number of patients diagnosed with the one-step approach.

The purpose of postpartum screening is to determine any existing glucose abnormalities (IFG, IGT, and DM) (27). Both isolated IFG and IGT predict future T2DM and cardiovascular risk (28,29). There has been a controversy about the feasibility and effectiveness of different glucose tests in postpartum screening. The higher stability and reproducibility of FPG measurement compared with the OGTT suggested that it can be applied more easily and widely for clinical screening and diagnosis (28). However, in the meta-analysis of 13 studies comparing FPG and OGTT, the sensitivity of FPG as a screening test was lower than OGTT (30). Although HbA1c is a valuable test in monitoring the treatment, it is not recommended because of the lack of standardization in postpartum screening. However, Ekelund et al. (31) showed that HbA1c $\geq 5.7\%$ and FPG ≥ 5.2 mmol/L were associated with a 4-6 fold increased risk of developing diabetes within five years after pregnancy. We used 75 g OGTT in postpartum screening and divided the patients into groups accordingly (NGT, preDM, and DM). We also evaluated postpartum early and late FPG and HbA1c levels. Moreover, FPG and HbA1c levels were significantly higher in preDM and DM groups than in the NGT group in early and late evaluations. We found that HbA1c, which was examined in the early postpartum period, was an independent risk factor in predicting dysglycemia. We believe that FPG and HbA1c, which are studied using standardized methods, can be used in the evaluation of glucose abnormalities after pregnancy.

Conclusion

Therefore, women with GDM have a high risk of developing preDM and T2DM in the future. Increased BMI before and after pregnancy and early postpartum HbA1c level are

independent risk indicators of developing dysglycemia. Therefore, we believe that lifestyle modifications and pharmacological interventions should be planned early in women with a GDM history to prevent progression to T2DM.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Songül Işıқтаş, Ayten Oğuz, Kamile Gül, Murat Şahin; Design: Ayten Oğuz, Kamile Gül, Murat Şahin; Control/Supervision: Ayten Oğuz, Kamile Gül, Murat Şahin; Data Collection and/or Processing: Songül Işıktan, Gül İnci Torun, Ayten Oğuz; Analysis and/or Interpretation: Songül Işıқтаş, Gül İnci Torun, Ayten Oğuz; Literature Review: Songül Işıқтаş, Ayten Oğuz; Writing the Article: Songül Işıқтаş, Ayten Oğuz, Murat Şahin; Critical Review: Ayten Oğuz, Kamile Gül; References and Fundings: Songül Işıktan, Ayten Oğuz, Kamile Gül.

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