Original Article

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Evaluation of the Effects of Preeclampsia and Gestational Diabetes Mellitus on Endothelial Function

Preeklamsi ve Gestasyonel Diyabet Öyküsünün Endotel Fonksiyona Etkisinin Değerlendirilmesi

Ömür ALBAYRAK, Mehmet Ata TOPÇUOĞLU

Bolu Abant İzzet Baysal University Training and Research Hospital, Department of Gynecology and Obstetrics, Bolu, Türkiye

ABSTRACT

Objective: Gestational diabetes mellitus (GDM) and preeclampsia are the most common medical complications of pregnancy. Both GDM and preeclampsia are risk factors for cardiovascular diseases (CVD) and atherosclerosis. Flow-mediated dilatation (FMD) is a good ultrasonographic marker of early atherosclerotic changes used to measure endothelial function. In this study; we evaluated FMD, an indicator of endothelial function, and investigated whether there was an increased risk of CVD in patients with a history of preeclampsia or GDM.

Methods: The study was carried out with 104 patients who gave birth in the Obstetrics and Gynecology Clinic of Bolu Abant İzzet Baysal University Training and Research Hospital between January 2016 and January 2017. Thirty four patients with a history of preeclampsia, 37 patients with a history of GDM, and 33 patients with uncomplicated deliveries were included in the study. All patients in the study had only one live birth and their age range was between 20 and 30 years. Demographic data, cardiovascular risk markers, obstetric data, laboratory tests and FMD change (%) measurements of all patients were compared. Mean and standard deviation values of the obtained data were calculated.

Results: The mean FMD change (%) in the group of patients with a history of preeclampsia was 9.8±3.1. It was 10.32±2.50 in the group of patients with a history of GDM and it was 13.19±3.03 in the control group. A statistically significant difference was found between the control group and GDM and preeclampsia groups in terms of FMD change (%) (<0.001). There was a significant negative correlation between FMD change (%) and systolic blood pressure, diastolic blood pressure, the amount of proteinuria, and glucose, low-density lipoprotein and total cholesterol levels.

ÖZ

Amaç: Gestasyonel diabetes mellitus (GDM) ve preeklampsi gebeliğin en sık medikal komplikasyonlarındandır. Gestasyonel diabet ve preeklampsi hem kardiyovasküler hastalıklar (KVH) hem de ateroskleroz için risk faktörüdür. Akım aracılı dilatasyon (FMD), endotel fonksiyonunu ölçmek için kullanılan, erken aterosklerotik değişikliklerin iyi bir ultrasonografik belirtecidir. Bu çalışmada; endotel fonksiyonlarının bir göstergesi olan FMD değerlendirilerek preeklampsi veya GDM öyküsü olan hastalarda artmış bir KVH riskinin olup olmadığını araştırdık.

Yöntemler: Çalışmamız Ocak 2016 ile Ocak 2017 tarihleri arasında Bolu Abant İzzet Baysal Üniversitesi Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği'nde doğum yapmış olan 104 hasta ile gerçekleştirildi. Preeklampsi öyküsü olan 34 hasta, GDM öyküsü olan 37 hasta ve komplikasyonsuz doğum yapmış 33 hasta çalışmaya dahil edildi. Olgu kontrol çalışması olarak dizayn edildi. Çalışmadaki tüm hastalar sadece 1 canlı doğum yapmış, yaş aralıkları 20 ile 30 arasında olacak şekilde belirlendi. Tüm hastaların demografik verileri, kardiovasküler risk belirteçleri, obstetrik verileri, laboratuvar tetkikleri ve FMD değişim (%) ölçümleri karşılaştırıldı.

Bulgular: Her üç grup FMD değişim (%) açısından karşılaştırıldığında preeklampsi öyküsü olan hasta grubu ortalaması 9,8±3,1, GDM öyküsü olan hasta grubu ortalaması 10,32±2,50, kontrol grubu hasta ortalaması 13,19±3,03 saptandı. Kontrol grubu ile GDM ve preeklampsi grupları arasında FMD değişimi (%) açısından istatistiksel olarak anlamlı farklılık saptandı (p<0,001). FMD değişim (%) değerleri ile sistolik tansiyon, diastolik tansiyon, glukoz, düşük dansiteli lipoprotein ve total kolesterol düzeyleri ve proteinüri miktarı ile anlamlı negatif korelasyon mevcuttu.

Address for Correspondence: Ömür Albayrak, Bolu Abant İzzet Baysal University Training and Research Hospital, Department of Gynecology and Obstetrics, Bolu, Türkiye
E-mail: omuralbayrak@gmail.com **ORCID ID:** orcid.org/0000-0003-2323-3037

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ABSTRACT

Conclusion: The use of FMD change (%) measurement in patients with a history of GDM and preeclampsia can be used as a predictive marker for CVD, and early detection of risk can be time-consuming in terms of prevention. Demonstrating that GDM and preeclampsia cause increased cardiovascular risk in women's lives will raise awareness of taking measures to reduce the risk in this group of patients.

Keywords: Preeclamsia, gestational diabetes mellitus, endothelial function, flow-mediated dilatation

ÖZ

Sonuç: Gestasyonel diabetes mellitus öyküsü ve preeklampsi öyküsü olan hasta grubunda FMD değişiminin (%) ölçümü KVH açısından prediktif bir markır olarak kullanılabilir ve erken yaşta risk tespiti yapılabilmesi önlem alma açısından zaman kazandırıcı olabilir. GDM ve preeklampsinin kadınların yaşamlarında ilerleyen dönemde artmış kardiyovasküler riske neden olduğunun gösterilmesi, bu grup hastalarda riski azaltma yönünde önlemlerin alınması konusunda farkındalık oluşturacaktır.

Anahtar Sözcükler: Preeklamsi, gestasyonel diyabetes mellitus, endotel fonksiyon, akım aracılı dilatasyon

Introduction

Gestational diabetes mellitus (GDM) is a varying degree of carbohydrate intolerance that begins during pregnancy or is diagnosed during pregnancy (1). GDM causes short- and long-term complications for both mother and fetus. It should be advised to educate patients for symptoms of hyperglycemia and patients should come to control if they experience such symptoms. Macrovascular and microvascular complications of diabetes are known (2). It is obvious that both type 1 DM and type 2 DM increase the risk of cardiovascular diseases (CVD) (3). Insulin resistance in patients with GDM decreases nitric oxide (NO) activity in the vascular endothelium, leading to endothelial dysfunction (4). However, endothelial dysfunction and accelerated atherosclerosis in diabetic patients are thought to play a key role in the formation of cardiovascular complications (5).

Preeclampsia is defined as hypertension (HT) (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg) that occurs after the middle of the second trimester of pregnancy and is accompaniedby newly emerging proteinuria (≥300 mg/24 hours) (6). Preeclampsia is not only a hypertensive condition, but a complex and multisystemic syndrome that concerns all systems of the body (7). The incidence of preeclampsia increases due to increase in maternal age, obesity, diabetes, HT and renal diseases. Although its etiology is not known precisely, it is anticipated to be caused by inadequate trophoblast invasion and widespread endothelial damage caused by vasospasm in the uteroplacental vascular bed. The cause of vascular endothelial dysfunction is unknown (8). There is increasing evidence that women with a history of preeclampsia during pregnancy are more likely to develop CVD later in life (9).

Endothelial dysfunction is by definition functional and reversible changes of endothelial cells due to the availability of NO in the endothelial cells and the oxidative stress disorder. It is seen in various pathological conditions such as endothelial dysfunction, atherosclerosis, hypercholesterolemia, diabetes, HT, heart failure, smoking, aging and obesity. Obesity is closely associated with the risk of CVD. Inflammation and impaired endothelial function can improve with weight loss. It functions to keep the endothelial vessel relatively dilated in basal conditions. However, the endothelium has the capacity to react to various physical stimuli such as shear stress (10). Blood vessels dilate in response to tearing stress, which is called flow-mediated dilation (FMD) (11). FMD is a good ultrasonographic marker of early atherosclerotic changes used to measure endothelial function, showing the vasodilation response of peripheral arteries against physical stimuli (12). The endothelium-dependent response is mainly regulated by the release of NO from the endothelium.

In this study; by evaluating FMD, which is an indicator of endothelial functions, we investigated whether there was an increased risk of CVD in patients with a history of preeclampsia or GDM.

Methods

Our study started with the approval of Bolu Abant İzzet Baysal University Ethics Committee (decision number: 2019/85, date: 11.04.2019). Written informed consents were obtained from all patients included. A total of 104 patients who were followed up at Obstetrics and Gynecology Clinic of Bolu Abant İzzet Baysal University Training and Research Hospital were included in the study. The study consisted of three groups. Thirty-four patients with a pre-history and at least 24 months from birth, 37 patients with GDM history, 33 patients with normal pregnancy follow-up and no pregnancy complications and additional diseases. Patients with a prior history of chronic disease (DM, HT), patients with a history of smoking, patients with a history of myocardial infarction, patients with chronic obstructive pulmonary disease, asthma, cor pulmonale, those with systemic disease and pregnant women using drugs for systemic disease, pregnants with multiple pregnancy, pregnancy cholestasis, gestational dermatosis, polyhydramnios, placenta previa, or detachment of the placenta, patients with thyroid dysfunction during pregnancy, pregnant women with rheumatological or autoimmune disease, and patients with the presence of peripheral or coronary artery disease were not included. The diagnostic criteria for preeclampsia are; systolic blood pressure ≥140 mmHg occurring after 20 weeks of gestation; diastolic blood pressure ≥90 mmHg and presence of proteinuria (≥300 mg/24h, urinary protein creatinine ratio ≥0.3 or 1+ protein in spot urine) or thrombocytopenia (<100,000/mm^3), renal dysfunction (creatinine ≥1.2 mg/dL and serum creatinine level increased by at least 2 times), liver dysfunction (AST-ALT >2 times of normal level), pulmonary edema or cyanosis, headache, blurred vision. The 24-hour protein level of all patients in the preeclampsia group was recorded. In all

pregnant women, oral glucose tolerance tests (OGTT) was performed with 50 grams of glucose for GDM screening at 24-28 weeks. In the screening test, women whose blood glucose was found to be 140-180 mg/dL at the first hour after drinking 50 grams of glucose were subjected to a 3-hour OGTT with 100 grams of glucose to make a definitive diagnosis of GDM.

The patient files were scanned retrospectively and pregnant women with a diagnosis of preeclampsia and GDM and pregnant women with normal follow-up were called by phone. GDM screening of all patients, history of preterm birth, abortion or in utero fetal loss, history of preeclampsia, smoking, drug use, dieting, hyperandrogenemia findings, obstetric, gynecological, medical and surgical resumes and family history (DM, HL in family, HT, CAD etc.) were questioned and detailed anamnesis was obtained. Height, weight and weight gain during pregnancy were recorded in all three groups. The pregnants were weighed without shoes and with light clothes on them (kg), and their height was measured without shoes and a hat, and their hair was measured without a flat bun (cm). Body mass indexes (BMI) of the patients were calculated according to the formula (BMI = body weight (kg)/height (m^2) = kg/m^2). All these data were noted on the patient evaluation form. The blood pressure of each patient in the control and study groups was measured in the clinic using the standard measurement technique. The measurement of the tension was assessed with brachial artery blood pressure after 5 minutes of rest while sitting, while the cuff was at the level of the heart. If there was a difference in systolic or diastolic blood pressure >5 mmHg at least twice in the measurements, it was deemed appropriate to repeat with two additional measurements. Each repeat was made by giving 30 minutes of rest and recorded.

All blood samples were taken on an empty stomach, using vacutaine from the antecubital area. HbA1c, glucose, low-density lipoprotein (LDL), very low density lipoprotein (VLDL), high-density lipoprotein (HDL), total cholesterol, and triglyceride levels were measured in maternal serum.

Ultrasonographic Evaluation of The Brachial Artery

Brachial artery Doppler ultrasonography examination was performed in the cardiology clinic of Bolu Abant İzzet Baysal University Training and Research Hospital, Faculty of Medicine, Cardiology Clinic for all patients in the study and control group. For brachial artery doppler ultrasonography examination, Philips EPIQ 7 device (Philips Medical Systems, Bothell, WA, USA) and a 12 L Doppler ultrasonography probe in the echocardiography laboratory were used in all patients and the control group. All echocardiographic procedures were performed by a single processor. The study was performed in a quiet and controlled environment, followed by a 8-12 hour fasting period, and the patients were placed in a supine position. Patients were advised to avoid exercise and not to take antioxidants such as caffeine, high-fat foods, and vitamin C in the last 4-6 hours. The transducer was placed on the right brachial artery tract 4-5 cm above the elbow, and the image was taken longitudinally in the region where the best image could be taken and enlarged. In this position, the projection of the transducer edge was marked on the skin with a ballpoint pen. The brachial artery diameter (intima to intima) was measured three times, and the average of these three measurements was recorded as the basal diameter. The cuff of the sphygmomanometer was connected to the forearm and inflated at least 50 mmHg above the systolic artery pressure, and after holding it for 5 minutes, the cuff was suddenly lowered, and the transducer was placed at the point marked with the pen, and the artery diameter at 60 sec (endothelium dependent vasodilator response) was recorded. The difference between the diameter measured after the reactive hyperemia and the basal diameter was taken as FMD. [FMD = 100x (radial diameter after reactive hyperemia)/basal diameter].

Statistical Analysis

The data were evaluated in the statistical package program IBM SPSS Statistics for Windows, Version 20.0 (Chicago, IL, USA: IBM Corp.). Number (n), percentage (%), average, median (minimum-maximum) values were given. Data were presented as mean arithmetic tools and standard deviations were calculated for each group. Kolmogorov-Smirnov test was used to evaluate the distribution of numerical variables. One-way analysis of variance (ANOVA) was used for comparing multiple groups with homogeneous distribution, and post-hoc Tukey test was used for comparisons between subgroups.

Kruskal-Wallis test was used for comparisons of nonparametric data belonging to multiple groups, and Bonferroni corrected Mann-Whitney U test was used for post-hoc analysis. The degree of relationship between continuous variables was calculated using the correlation analysis of Pearson or Spearman where appropriate.

Results

Our study was conducted with a total of 104 patients, including 37 patients with a history of of GDM, 34 patients with preeclampsia and 35 controls.

Demographic characteristics of the participants are shown in Table 1. The mean gestational age was found as 25.41±2.53 (year) in pregnant women with a history of GDM and 25.35±2.67 (year) in pregnant women with preeclampsia, while the mean age was 26±3.01 (year) in the control group (Table 1). There was a significant difference between the groups in terms of weight and BMI. This is because insulin resistance and obesity are more common in the GDM group. Although this affects endothelial function, the fact that the FMD value is lower than the control group may also be related to this situation. There was no statistically significant difference between the three groups in terms of average age, average height, family history, occupation, gravida, parity, number of abortions, time after delivery, and type of delivery ($p<0.05$) (Table 1).

Obstetric data of the previous pregnancies of all three patient groups are given in Table 2. All patients in the study were selected as having had 1 live birth. Patients who had given birth more than one or had a history of still birth were excluded from the study. The mean time elapsed after birth was 28.50±3.03

Table 1. GDM History, preeclampsia history and demographic findings of the control group

		Patients with a history of preeclamsia	Patients with a history of GDM	Control group	p-value
Age		25.35±2.67	25.41±2.53	26±3.01	0.561
Height		162.88±5.08	163.65±5.82	162.7±6.7	0.771
Weight		63.29±7.67	81.30±12.38	70.39±10.06	**<0.001**
BMI		23.86±2.81	30.25±3.72	26.58±3.50	**<0.001**
DM in the family (+)		3 (8.8%)	8 (21.6%)	3 (9.1%)	
HT in the family (+)		9 (26.5%)	1 (2.7%)	0 (0%)	
DM + HT + in the family		1 (2.9%)	4 (10.9%)	2 (6.1%)	0.082
No family history		21 (61.8%)	24 (64.9%)	28 (84.8%)	
Profession	**Housewife**	14 (41.2%)	17 (45.9%)	15 (45.5%)	
	Officer	10 (29.4%)	10 (27%)	8 (24.2%)	0.889
	Worker	10 (29.4%)	10 (27%)	10 (30.3%)	

GDM: Gestational diabetes mellitus, BMI: Body mass index, DM: Diabetes mellitus, HT: Hypertension

Table 2. GDM history, preeclampsia history, and obstetric data from previous pregnancies of the control group

		Patients with a history of preeclampsia	Patients with a history of GDM	Control group	p-value
Gravida		1.79±1.09	1.35±0.58	1.36±0.69	0.142
Number of abortions		0.79±1.09	0.35±0.58	0.36±0.69	0.142
The time elapsed after childbirth		28.50±3.03	28.62±3.51	28.66±3.38	0.927
Week of birth		35.15±3.15	37.3±5.18	39.39±1.34	**<0.001****
Baby birth weight		2494.32±760	3676.59±684	3315.30±238	**<0.001****
Mode of birth	**Normal birth**	15 (44.1%)	20 (51.1%)	23 (69.7%)	
					0.107
	Cesarean	19 (55.9%)	17 (45.9%)	10 (30.3%)	

GDM: Gestational diabetes mellitus, **: <0.01 compared to controls

months in the preeclampsia group and 28.62±3.51 months in the GDM group. It was found to be 28.66±3.38 in the control group. The postpartum periods in each of the 3 groups were selected as between 24 months and 36 months. The average postpartum time between the groups was found to be close to each other. The mean birth week of the patients in the patient group with a history of preeclampsia was 35.15±3.15, the mean birth week of the patients in the patient group with a history of GDM was 37.3±5.18, and the mean birth week of the patients in the control group was 39.39±1.34. There was a statistically significant difference between the weeks of birth in all three groups (p<0.001). When the groups were compared in terms of birth forms, 44.1% of the preeclampsia group, 51.1% of the GDM group and 69.7% of the control group had a normal birth (Table 2).

As seen in Table 3; the mean systolic blood pressure and diastolic blood pressure in patients with a history of GDM was 116.16±6.48/76.95±5.50, 121.3±8.8/78.6±5.9 in patients with preeclampsia and 111.97±7.63/71.67±7.04 in the control group. There was a statistically significant difference in terms of systolic and diastolic blood pressure averages in all three groups (p<0.001). Glucose and HbA1c values of all three patient groups were; 79.5±7.5, 5.1±0.3, 84.78±7.20, 5.62±0.27 in the GD group, 79.94±8.34, 5.01±0.36 in the control group. A statistically significant difference was found between the group with a history of GDM and the other two groups in terms of glucose and HbA1c values (p=0.007). LDL, HDL, VLDL, total cholesterol level averages were 138±41.5, 49.7±10.2, 138±41.5, 219.8±48 in the preeclampsia group; 126.49±36.57, 50.48±16.51, 33.78±15.69, 207.86±48.15 in the GDM group; and 117.09±37.31, 53.03±14.14, 32.48±17.71, 198.64±50.90 in the control group, respectively. There was no statistically significant difference between the groups in terms of the levels of those 4 parameters. The mean triglyceride levels were 208±110, 164.35±86.08 and 141.00±74.24 in the preeclampsia, GDM and control groups, respectively. There was a statistically significant difference between the three groups (p=0.005) (Table 3).

The mean FMD changes (%) were 9.8±3.1, 10.32±2.50 and 13.19±3.03 in the preeclampsia, GDM and control groups, respectively (Table 3). A statistically significant difference was found between the control group and GDM and preeclampsia groups in terms of FMD change (%) (p<0.001) (Table 3).

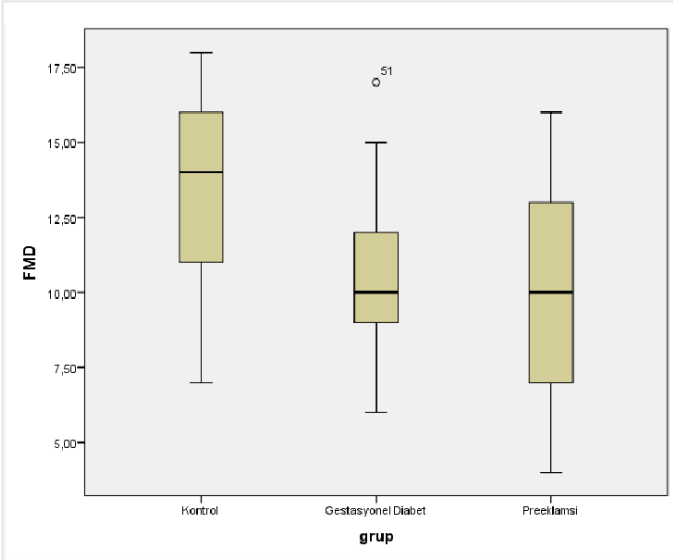
Table 3. Cardiovascular risk markers by groups (physical examination, laboratory, ultrasound parameters)

	Patients with a history of preeclampsia	Patients with a history of GDM	Control group	p-value
Systolic blood pressure	121.3±8.8	116.16±6.48	111.97±7.63	**<0.001****
Diastolic blood pressure	78.6±5.9	76.95±5.50	71.67±7.04	**<0.001****
Glucose	79.5±7.5	84.78±7.20	79.94±8.34	**0.007***
HbA1c	5.1±0.3	5.62±0.27	5.01±0.36	**<0.001****
LDL	138±41.5	126.49±36.57	117.09±37.31	0.087
HDL	49.7±10.2	50.48±16.51	53.03±14.14	0.59
VLDL	39±17.5	33.78±15.69	32.48±17.71	0.168
Total cholesterol	219.8±48	207.86±48.15	198.64±50.90	0.213
Triglyceride	208±110	164.35±86.08	141.00±74.24	**0.005***
FMD change (%)	9.8±3.1	10.32±2.50	13.19±3.03	**<0.001****

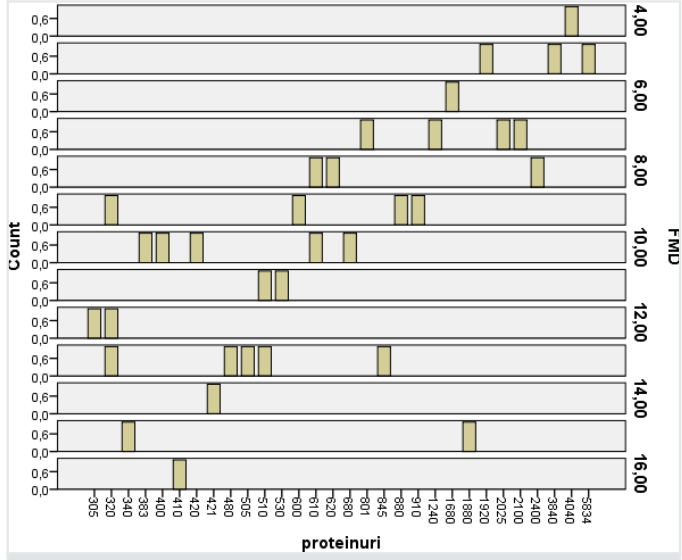
GDM: Gestational diabetes mellitus, FMD: Flow-mediated dilatation, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, VLDL: Very low density lipoproteins

As seen in Graphic 1, among all groups, the lowest was in the preeclampsia group and the highest was in thecontrol group. The lowest and highest FMD change (%) values were 4 and 16 in the preeclampsia group, 7 and 18 in the control group, and lowest value was 6 in the GDM group (Graphic 1).

As seen in Graphic 2, it was observed that FMD change (%) rate gradually decreased as the amount of proteinuria increased in the patient group with a preeclampsia history.



Graphic 1. FMD change (%) of case and control groups
FMD: Flow-mediated dilatation



Graphic 2. Relationship between proteinuria amount and FMD change (%)
FMD: Flow-mediated dilatation

Discussion

Endothelial dysfunction is an important predictor of future CVD development. In this study; FMD, which is an indicator of endothelial functions, was evaluated and it was investigated whether there was an increased risk of CVD in patients with a history of preeclampsia or GDM. Investigating the effects of having a history of GDM or preeclampsia on the endothelium is important in order to predict and prevent macrovascular events that may result in mortality. In our study, the demographic data, obstetric data, laboratory parameters, and endothelial structure by using FMD of the preeclampsia, GDM and control groups were compared.

The FMD measurement has been studied many times before in HT, preeclampsia, metabolic and CVD groups. The decrease in this value, which is accepted as a marker of subclinical atherosclerosis, is considered significant. In many studies conducted in patients with preeclampsia and GDM, FMD measurements were found to be significantly lower compared to normotensive and normoglycemic pregnant women (13). The originality of our study was the careful selection of patient groups. Since FMD measurement was affected by the age factor, the age range was limited and healthy women between the ages of 20 and 30 were included in the study. However, only patients who had a live birth were included in the study. When the literature was reviewed, the same number of births and no study of the patient population with a similar age range were seen. In our study, women with similar age group who had a history of preeclampsia, GDM history and who did not experience these two conditions during pregnancy were compared in terms of laboratory and FMD change (%) in terms of showing cardiovascular risk ratio. FMD in the group with a history of preeclampsia was significantly lower than the group without a history of preeclampsia. When all three groups were compared in terms of FMD change (%), the mean of the patient group with a preeclampsia history was 9.8±3.1, the mean of the patient group with a history of GDM was 10.32±2.50, and the mean of the control group was 13.19±3.03. A statistically significant difference was found between the control group and GDM and preeclampsia groups in terms of FMD change (%) (<0.001). Among all groups, the lowest was in the preeclampsia group and the highest was in the control group.

In the study of Tarim et al. (14), there was no difference between the groups with and without GDM interms of total cholesterol, HDL, LDL and insulin levels. Triglyceride and fasting glucose levels were significantly higher in the group with a history of GDM (14). In our study, a significant difference was found between the patient group with a history of GDM and the control group in terms of glucose, HbA1c and FMD change (%) values. In our study, there was a statistically significant difference between the group of patients with preeclampsia and the control group in terms of systolic blood pressure, diastolic blood pressure, triglyceride level and FMD change (%).

There are studies in the literature that have different results from our study. Women with a history of preeclampsia and gestational HT in previous pregnancies and healthy women who had a healthy pregnancy were compared in terms of endothelial dysfunction 2-12 years after their pregnancy in the study by Mangos et al. (15). FMD values were similar in women with a history of preeclampsia or gestational HT. However, in this study, the periods after delivery were accepted for 10 years and could not beabstracted from other parameters that might affect the FMD measurement of the patients after birth.

In our study, we found a significant negative correlation between FMD change (%) and systolic and diastolic blood pressure, glucose, LDL, total cholesterol, and triglyceride levels and amount of proteinuria in the preeclampsia and GDM groups. In particular, we found that FMD change (%) decreased more as the proteinuria amount increased in patients with pre-eclampsia. While there was no difference in terms of LDL, HDL, VLDL, and total cholesterol levels; glucose and triglyceride levels were significantly higher in the group with a history of GDM. In addition, in our study, HbA1c was found tobe significantly higher in the GDM group. This is important in terms of showing the relationship between glucose level and HbA1c and increased cardiovascular risk. The distribution of factors such as age, height, family history of DM or HT, CAD, gravida, parity, abortion number in GDM, preeclampsia and control groups were determined. This suggests that the resulting endothelial dysfunctional directly related to a history of GDM.

Low FMD change detected in patients complicated with GDM or preeclampsia during their pregnancy indicate that having GDM or preeclampsia carries a risk for CVD and that these patients should be followed up. Although many studies conducted in patients with a history of GDM or with a preeclampsia history have shown low FMD values; there are also studies in the literature that show opposite results. It would be appropriate to conduct prospective studies covering large patient series or meta-analysis with current studies. In addition to FMD measure's advantages such as being cheap, simple and easy to apply, repeatability, no risk for the patient, it should not be forgotten that it has difficulties such as difficult to display, the necessity of keeping the probe fixed throughout the measurement, the measurement requires experience, and there is still no consensus on the measurement technique.

Study Limitations

This study has potential limitations. In our study, it is a negative situation that the number of patients is small and there are patients who have given birth in a single hospital. In addition, we believe that the fact that the patients do not have the same weight may affect the FMD change. A study with a larger sample group and patients with similar demographic data will be more meaningful.

Conclusion

The FMD measurement was significantly lower in women with a preeclampsia or GDM history during pregnancy than in the control group. Significant results can be interpreted that FMD measurement increases the risk of developing CVD in women with a history of preeclampsia or GDM. The FMD change in the premenopausal patient group can be used as a predictive marker for CVD, and early risk detection can be time-saving. If an increased cardiovascular risk is detected in these patients, we can ensure that the patient takes measures to reduce this risk. Counseling can be given to this patient group on lifestyle changes, diet, weight control, blood pressure monitoring.

Demonstrating that GDM - causes increased cardiovascular risk in women in the future will create awareness in taking measures to reduce risk in this group of patients.

Ethics

Ethics Committee Approval: Our study started with the approval of Bolu Abant İzzet Baysal University Ethics Committee (decision number: 2019/85, date: 11.04.2019).

Informed Consent: Written informed consents were obtained from all patients included.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ö.A., M.A.T., Concept: Ö.A., M.A.T., Design: Ö.A., M.A.T., Data Collection or Processing: Ö.A., Analysis or Interpretation: Ö.A., M.A.T., Literature Search: Ö.A., M.A.T., Writing: Ö.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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