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Evaluation of epicardial fat tissue thickness and aortic stiffness in patients with gestational diabetes mellitus

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Abstract

Objective: We aimed to assess the relationship between gestational diabetes mellitus and coronary artery disease by measuring epicardial fat tissue thickness and aortic stiffness in pregnant women diagnosed with gestational diabetes mellitus.

Methods: 28 pregnant women diagnosed with gestational diabetes mellitus and 25 pregnant women without gestational diabetes mellitus were included in the research. Body mass index, laboratory values, blood pressure measurements and obstetric history findings of the study population were recorded. All participants of the study population were evaluated with transthoracic echocardiography between 24 and 28 weeks of gestational period. The measurement of epicardial fat tissue thickness was taken and aortic stiffness index was also calculated.

Results: The age, gravidity, parity and obstetric history of the two groups were similar. Epicardial fat tissue thickness was found significantly higher in gestational diabetes mellitus group than control group (0.416 cm and 0.336 cm, respectively; p<0.001). However, no significant difference was found in aortic stiffness measurements of the two groups (p=0.079).

Conclusion: According to the results of our study, epicardial fat tissue thickness was found to be statistically significantly higher in pregnant women with gestational diabetes mellitus compared to the control group. The fact that no difference was detected in other cardiovascular parameters suggests that measurement of epicardial fat tissue thickness in gestational period may be a beneficial adjunctive tool in early detection of gestational diabetes mellitus.

Keywords: Gestational diabetes mellitus, epicardial fat tissue, aortic stiffness.

Özet: Gestasyonel diabetes mellitus hastalarında epikardiyal yağ dokusu kalınlığı ve aortik sertliğin değerlendirilmesi

Amaç: Çalışmamızda, gestasyonel diabetes mellitus tanısı almış gebelerde epikardiyal yağ dokusu kalınlığını ve aortik sertliği ölçerek gestasyonel diabetes mellitus ile koroner arter hastalığı arasındaki ilişkiyi değerlendirmeyi amaçladık.

Yöntem: Çalışmaya gestasyonel diabetes mellitus tanısı almış 28 gebe ve gestasyonel diabetes mellitusu olmayan 25 gebe dahil edildi. Çalışma popülasyonunun vücut kitle indeksi, laboratuvar değerleri, kan basıncı ölçümleri ve obstetrik hikaye bulguları kaydedildi. Çalışmaya katılan tüm olgular gebeliğin 24 ve 25. haftaları arasında transtorasik ekokardiyografi ile değerlendirildi. Epikardiyal yağ dokusu kalınlığı ölçümü alındı ve aortik sertlik indeksi hesaplandı.

Bulgular: Yaş, gravida, parite ve obstetrik hikaye bakımından iki grup benzerdi. Epikardiyal yağ dokusu kalınlığı, kontrol grubuna kıyasla gestasyonel diabetes mellitus grubunda anlamlı şekilde daha yüksekti (sırasıyla 0.336 cm ve 0.416 cm; p<0.001). Ancak, iki grubun aortik sertlik ölçümleri arasında hiçbir anlamlı fark yoktu (p=0.079).

Sonuç: Çalışmamızın sonuçlarına göre epikardiyal yağ dokusu kalınlığı, kontrol grubuna kıyasla gestasyonel diabetes mellituslu gebelerde istatistiksel olarak anlamlı şekilde daha yüksekti. Diğer kardiyovasküler parametrelerde hiçbir farklılığın bulunmaması, gestasyonel dönemde epikardiyal yağ dokusu kalınlığı ölçümünün gestasyonel diabetes mellitusun erken tespitinde faydalı bir ek araç olabileceğine işaret etmektedir.

Anahtar sözcükler: Gestasyonel diabetes mellitus, epikardiyal yağ dokusu, aortik sertlik.

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Introduction

Gestational diabetes mellitus (GDM) is a carbohydrate tolerance disorder that was detected during gestational period.[1,2] The incidence of GDM varies from 1% to 14%.[3,4] GDM is not only a pregnancy-related disease, but also patients with GDM have the risk of 17.06 % for studies with follow-up of one to five years developing type 2 diabetes mellitus.[5] Insulin resistance is the main cause of GDM and it is also related with cardiovascular diseases.[3] Insulin resistance leads to chronic inflammation, which results in atherosclerosis, which also makes pregnant women a candidate for cardiovascular disease.[6] It is aimed to predict cardiovascular risk in women complicated with GDM by detecting preclinical markers of atherosclerosis before the development of type 2 DM.

Epicardial fat tissue is the visceral adipose tissue of the heart and is derived from brown adipose tissue during embryogenesis, which creates a defensive system against cardiac hypothermia.[7,8] The defensive system is to absorb free fatty acids when they are high in the circulatory system and work as an energy resource as the energy demand increases.[9] Epicardial adipose tissue secretes many proinflammatory and proatherogenic cytokines including vasoactive peptides so it is metabolically very active. These cytokines were found to be associated with obesity, hypertension and coronary heart disease.[10,11] Epicardial fat tissue thickness (EFTT) is a useful and noninvasive method for predicting cardiovascular diseases. EFTT measurement is practical, inexpensive and effective. EFTT can be evaluated very well by transthoracic echocardiography. It has also been reported to increase in patients with diabetes mellitus and insulin resistance.[12] There are also researches investigating the relationship between GDM and EFTT.[13,14] But these studies have reported some conflicting results.

The impact of cardiovascular risk factors on circulatory system has been the subject of many studies. As a result of the structural changes in the large vessels due to these risk factors, it is now clear that these vessels are stiffened, in other words, they are exposed to "stiffness". It has been found that this process directly affects cardiovascular morbidity and mortality, especially with "stiffness" studies in large vessels in the literature.[15] EFTT has been also found to be related with arterial stiffness.[16] In most studies examining the aortic stiffness, the pulse wave velocity (PWV) was used as the "stiffness" index that was measured invasively or non-invasively in these studies.[17,18] Aortic stiffness is usually measured with echocardiography. Aortic "strain", beta index and aortic "distensibility" calculated by echocardiographic aortic diameter and sphygmomanometric blood pressure measurements have been proposed to measure aortic stiffness.[19] In this research, our goal was to find the relationship between GDM and coronary artery disease by measuring EFTT and aortic stiffness in pregnant women with GDM.

Methods

The ethical approval was obtained from the Clinical Research Ethics Committee of Muğla Sıtkı Koçman University School of Medicine for the study (Ethics Committee Approval Number 25.05.2015 / 12). Two-step GDM screening was performed to diagnose GDM in pregnant women between 24 and 28 weeks of gestation who applied to the Gynecology and Obstetrics outpatient clinic of Muğla Sıtkı Koçman University Hospital. First, 50-g oral glucose tolerance test (OGTT) was applied on the pregnant women as screening test. 100-g OGTT was applied to those whose 1st hour blood glucose level was over 140 g/dl as diagnostic test. Among the 100-g OGTT results, 28 patients were confirmed as GDM and included in GDM group (study group). Threshold levels of 100-g OGTT were determined according to The National Diabetes Data Group (NDDG) standards (fasting value: 105 mg/dL, 1st hour value: 190 mg/dL, 2nd hour value: 165 mg/dL and 3rd hour value: 145 mg/dL).[20] 25 patients were included in the control group whose 50-g OGTT's within normal limits (control group). Laboratory values, height (cm), weight (kg), blood pressure measurements and obstetric history findings of the patients were recorded.

Transthoracic echocardiography examination was performed in all participants between 24 and 28 weeks of gestation using a 2.5–3.5 MHz ultrasound probe in the left lateral lying position (Vivid 7, GEVingmed Ultrasound AS, Horten, Norway). All echocardiographic scans were performed by a cardiologist expert in echocardiography, who was blinded to the patient's clinical data and digitally recorded including at least three heartbeats. Standard echocardiographic measurements such as left atrium size, left ventricle diameter, left ventricular wall thickness and left ventricular ejection fraction were performed in accordance with the American Echocardiography Association guidelines. Epicardial adipose tissue was detected as an area of relatively low echogenicity located between the right ventricle and the inner leaf of the pericardium. The thickest EFT was measured in the end-systolic phase of the cardiac cycle, parallel to the aortic valve from this area.[21] The aortic strain, distensibility and aortic stiffness index (ASI) were taken as aortic elasticity parameters.[22]

The following formulas were used to calculate these parameters:

Aortic Strain (%) = (systolic diameter-diastolic diameter) × 100 / diastolic diameter,

Aortic Stiffness Index (ASI) = ln (systolic pressure / diastolic pressure) / aortic strain,

Distensibility ($cm^2.dyn^{-1}$) = (2 × aortic strain) / (systolic pressure - diastolic pressure)

The normal distribution suitability of continuous variables was analyzed using Shapiro-Wilk test. Independent samples t test (for normal data) and Mann-Whitney U test (for not normally distributed data) were used for comparison of two independent groups, and mean and standard deviation were given as descriptive statistics. The obtained data were evaluated using SPSS for Windows version 22.0 (SPSS Inc., Chicago, IL, USA). Differences were considered significant at a p-value of less than 0.05.

Results

The clinical characteristics and laboratory findings of the groups included in the study are presented in **Table 1**. The participants in two groups were similar in terms of age, gravidity, parity and obstetric history of abortion, smoking, gestational diabetes mellitus. Fasting blood glucose levels and 50-g OGTT results of the groups were statistically significantly different (p=0.003 and p<0.001, respectively). There was a significant difference between the 1st hour and 2nd hour blood glucose levels of the patients who underwent 100-g OGTT in the groups (p<0.001 and p=0.006, respectively). Body mass index values were found to be higher in the GDM group compared to the control group (24.7 and 29.6, respectively).

EFTT was significantly higher in the GDM group compared to the control group (0.336 and 0.416 respectively, p<0.001) (**Table 2**). While there was no difference in systolic blood pressures between the groups, diastolic blood pressures of patients with GDM were found to be higher (p=0.009). In multivariate linear regression analysis, a weak correlation was found between diastolic blood pressure and EFTT (p=0.04, r=0.307). However, there was no significant difference in aortic stiffness measurements between the

Table 1. Demographic characteristics of the study population.

	GDM group (n=28) Mean±SD	Control group (n=25) Mean±SD	p-value
Age (years)	26±0.4	21±0.5	0.297*
Body mass index (kg/m²)	29.6	24.7	0.001*
Gravidity	2.4±1.3	2.4±1.3	0.741†
Parity	0.8±0.9	1.1±1.1	0.235†
No. of abortions	0.5±0.8	0.2±0.5	0.260†
GDM history n (%)	5 (17.8)	2 (8)	0.290†
Family history of GDM n (%)	3 (1.2)	1 (4)	0.317†
Smoking n (%)	3 (1.2)	2 (8)	0.978†
Systolic blood pressure (mmHg)	116±14	110±13	0.123†
Diastolic blood pressure (mmHg)	72±11	64±8	0.009*
Fasting blood glucose (mg/dl)	94±16	82±10	0.003†
50-g OGTT 1st hour (mg/dl)	176±23	123±26	<0.001†
100-g OGTT 1st hour (mg/dl)	189±13	144±12	<0.001†
100-g OGTT 2nd hour (mg/dl)	152±17	125±12	0.006†
100-g OGTT 3rd hour (mg/dl)	115±19	103±20	0.151†
Serum creatinine (mg/dl)	0.5±0.1	0.5±0.1	0.946†

*Mann-Whitney U test; †Independent samples t-test.

Table 2. Transthoracic echocardiographic findings of study population.

	GDM group (n=28) Mean±SD	Control group (n=25) Mean±SD	p-value
EF (%)	63±2.6	62±2.8	0.334*
Aortic systolic diameter (mm)	2.5±2.4	2.4±2.4	0.292†
Aortic diastolic diameter (mm)	2.3±2.5	2.2±2.3	0.155†
AD	0.4±0.3	0.5±0.2	0.285†
AS (%)	6.3±0.7	6±0.4	0.415†
ASI	9.6±7.3	11.1±3.7	0.079†
EFTT (cm)	0.416±0.1	0.336±0.1	<0.001†

AD: aortic distensibility; **AS:** aortic strain; **ASI:** aortic stiffness index; **EF:** ejection fraction; **EFTT:** epicardial fat tissue thickness. *Mann-Whitney U test; †Independent samples t-test.

groups (p=0.079). There was no difference in left ventricular diameters of the groups in terms of ejection fraction. Aortic measurement units such as aortic systolic diameter, aortic diastolic diameter, AD, AS, ASI were similar between the groups (**Table 2**).

To further explore the independent predictor(s) of GDM, regression analysis was performed based on risk factors affecting GDM (**Table 3**). After adjusting for all covariates, EFTT was independently associated with GDM [odds ratio (OR)= 2.166, 95% confidence interval (CI)= 1.063–4.399, p=0.019].

Discussion

In our research, EFTT was significantly higher in patients with gestational diabetes mellitus. However, there was no significant difference in aortic stiffness measurements between two groups.

In recent studies, it has been reported that EFTT measurement by transthoracic echocardiography can be utilized as an early sign of increased cardiovascular risk. Many studies have found increased EFTT associated with metabolic syndrome and coronary heart disease.[12,23–25] Prior researches revealed a significant association between EFTT, fasting blood glucose and DM.[12,26,27] In the study of Çalışkan et al., the relationship between EFTT and glucose intolerance in women with GDM history was investigated. EFTT measured by echocardiography was found to be significantly increased in 62 women with previous GDM compared to the control group.[28] In this research, it was reported that high EFTT may indicate the existence of atherosclerosis in women with prior GDM. In another study, the mean EFTT was detected higher in pregnant women with GDM compared to the control group. In the same study, significant correlations were found between EFTT, BMI and postprandial serum glucose levels.[29] These results were comparable with another study that showed that postprandial glucose and BMI are associated with maternal EFTT in regression models.[13] In a recent systematic review and meta-analysis, each unit increment in BMI (kg/m^2) was associated with a higher risk of coronary heart disease in women.[30] Also obesity is a major risk factor for Type 2 DM, in fact, 85.2% of people with Type 2 DM are overweight or obese.[31] As expected, BMI of the GDM group was higher in our study.

Table 3. Independent predictors of gestational diabetes in multivariate logistic regression analysis.

Variables	Odds ratio	95% confidence interval	p-value
Body mass index	1.177	0.982–1.410	0.077
Diastolic blood pressure	1.035	0.961–1.115	0.360
EFTT	2.166	1.063–4.399	0.019

EFTT: epicardial fat tissue thickness.

Yavuz et al. measured both maternal and fetal EFTT in pregnant women with GDM at the second trimester, and fetal and maternal EFTT were found to be significantly higher in patients with GDM compared to non-gestational diabetes mellitus.[14] In addition, fetal EFTT was measured by fetal echocardiography in this study. It was determined that fetal EFTT was an independent predictor for serum glucose values after glucose tolerance test. In our study, the increased EFTT rates in gestational diabetic women support these data.

In a prospective study conducted by Moodley et al., it was shown that pregnant women with pregestational and gestational diabetes mellitus had more arterial stiffness compared to non-diabetic pregnant women, but this variability did not cause a deterioration in placental or fetal cardiovascular parameters.[32] In our study, no difference was found between the two groups in terms of arterial stiffness. The reason for not showing a difference between the study and control groups in terms of arterial stiffness may be that the cardiovascular evaluation of the patients with gestational diabetes mellitus was performed as soon as they were diagnosed. However, despite this, the difference between the two groups in terms of EFTT without arterial involvement in our study shows that EFTT may stand out as an early marker.

In the study of Altınet et al. conducted in 44 cases with gestational hypertension and 46 healthy pregnant women, maternal EFTT was higher than the control group, but the carotid intima-media thickness was not different between the two groups.[33] Patients with gestational diabetes were excluded in this study. However, we found similar results with Altınet et al.'s study. This result may have been caused by the presence of the risk factors of gestational diabetes mellitus that predispose to gestational hypertension in these patients in our study.

The limitation of our study is that patients cannot be categorized in terms of treatment modalities after diagnosis of GDM and cannot be evaluated with cardiovascular examinations at regular intervals according to this categorization. The EFTT, AD, AS, ASI are the parameters that have been studied in the literature in terms of cardiovascular risk assessment in pregnant women with gestational diabetes mellitus. According to the results of our study, EFTT was found to be statistically significantly higher in pregnant women with gestational diabetes compared to the control group, but the fact that no difference was detected in other cardiovascular parameters suggests that EFTT may be an early diagnostic tool for GDM that can be checked before gestational diabetes mellitus screening.

Conclusion

In conclusion, BMI and EFTT were higher in GDM group but only EFTT was independent predictor of GDM. Screening of groups at risk for GDM with EFTT at the beginning of pregnancy may improve treatment modalities that can help to intervene before cardiovascular damage occurs. Randomized prospective studies are needed to use EFTT as a cardiovascular parameter at the beginning of pregnancy or after GDM detection.

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Compliance with Ethical Standards: The authors stated that the standards regarding research and publication ethics, the Personal Data Protection Law and the copyright regulations applicable to intellectual and artistic works are complied with and there is no conflict of interest.

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