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The Modified Myocardial Index for Evaluation of Fetal Cardiac Function in Gestational Diabetes Mellitus

Gestasyonel Diyabetli Gebelerde Modifiye Myokardiyal Index ile Fetal Kardiyak Fonksiyonun Değerlendirilmesi

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ÖZ

Amaç: Modifiye Miyokardiyal Performans İndeksi (Mod-MPI) miyokar fonksiyonunu değerlendirmek için kullanılan yeni bir yöntemdir. Annede Gestasyonel Diyabet (GDM) varlığı fetusun miyokard fonksiyonunu etkileyebilir ve Mod-MPI değerinin değişmesine neden olabilir. Biz bu çalışmamızda GDM tanısı olan gebelerde fetusun kalp fonksiyonun Mod-MPI ile değerlendirmeyi ve sağlıklı gebeler ile karşılaştırmayı amaçladık.

Gereç ve Yöntem: Bu prospektif vaka kontrol çalışmaya ; 30 GDM tanılı , 30 sağlıklı olmak üzere toplam 60 gebe dahil edildi. Çalışma grubunun demografik özellikleri kaydedildi. Mod-MPI ve Obstetric Doppler parametereleri her fetus için deneyimli bir Perinatoloji uzmanı tarafından hesaplandı. İki grubun sonuçları karşılaştırıldı.

Bulgular : İki grup arasında yaş, parite ve BMI açısından fark izlenmedi. GDM tanılı gebelerde ortalama Mod-MPI değeri sağlıklı gebelere oranla daha yüksek bulundu. Her iki grup arasında Obstetrik Doppler parametreleri açısında fark izlenmedi.

Sonuç: GDM tanılı gebelerde Mod-MPI'ın klinik yönetimine faydası literatürde belirsizdir. Gelecekte GDM'li anne fetüslerinde kalp fonksiyonunun göstergesi olarak Mod-MPI kullanımının faydasını değerlendirmek için daha fazla sayıda vaka içeren prospektif çalışmalara ihtiyaç duyulmaktadır.

Anahtar Kelimeler : Gestasyonel Diyabet, Kardiyak Fonksiyon, Mod-MPI, Doppler

ABSTRACT

Objectives: The modified myocardial performance index (ModMPI) is a new technique that is used to assess myocardial function. Gestational Diabetes can affect myocardial function and may lead to change Mod –MPI value. We aimed to evaluate fetal cardiac function with Mod-MPI in pregnant with GDM and compare with healthy pregnant.

Material and Methods: Totally 60 pregnant; 30 with GDM and 30 without disease were included into this prospective case control study. Demographic characteristics of the study group were recorded. Mod-MPI and obstetric Doppler parameters were calculated for each fetus by an experienced perinatologist. The results of the two groups were compared.

Results : There was no difference in terms of demographic characteristics, age, parity and BMI between the groups. The mean Mod-MPI value was found significantly higher in pregnant with GDM when compared with healthy pregnant. The obstetric Doppler parameters were found similar between groups.

Conclusion: The utility of the ModMPI in GDM pregnant is unclear in literature. Future prospective studies with larger number of cases are needed to evaluate the utility of the ModMPI as a predictor of cardiac function in fetuses of GDM mothers

Keywords : Gestational Diabetes, Cardiac Function, Mod-MPI, Doppler

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INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as glucose intolerance that starts during pregnancy or when first noticed during pregnancy. Although it may vary depending on ethnicity, weight, age, and diagnostic criteria, it is seen in approximately 6-7% of pregnancies (1). Diabetogenic hormones secreted from the placenta cause insulin resistance and hyperglycemia during pregnancy and GDM develops in women who do not have an adequate pancreatic response to this hormones. Maternal hyperglycemia affects placental blood flow and fetal growth (2). GDM causes fetal morbidities such as polyhydramnios, macrosomia, hyperbilirubinemia, neonatal hypoglycemia, hypocalcemia and hypomagnesemia. Obesity, metabolic syndrome, hypertension and diabetes in future have been shown to increase in these babies born from pregnancies with GDM (3).

Although it is known that pre-gestational diabetes mellitus (PDM) increases the risk of congenital heart defects, morphological changes like cardiac hypertrophy and systolic and diastolic dysfunction have been seen in both PDM and GDM as a result of the fetus being exposed to high glucose levels during the intrauterine period (4). There is growing concern that in utero cardiac dysfunction may cause future cardiovascular diseases (5,6).

Tsutsumi et al. first described the myocardial performance index (MPI), a measure of the overall function of the myocardium, using Doppler ultrasound in 1999 (7). Systolic function is evaluated with isovolumetric contraction time (ICT) and ejection time (ET), whereas diastolic function is evaluated with isovolumetric relaxation time (IRT). The MPI is defined as the sum of ICT and IRT divided by ET (7). Recently, a modification of myocardial performance index (Mod-MPI) described by Hernandez-Andrade et al. based on Doppler echoes of the mitral valve (MV) and aortic valve (AV) clicks, which is associated with a lower variation and better inter- and intra-observer agreement than the MPI (8). It is hypothesized that pathological conditions in pregnancy that influence fetal cardiac functions may change fetal MPI levels.

In this study, we aimed to evaluate Mod-MPI and Obstetric Doppler parameters in pregnant with GDM and compare them with pregnant women without disease.

MATERIALS AND METHOD

This prospective cohort study was performed at the Etlik City Hospital, a tertiary center in Ankara, Turkey between 01.06.2023-01.09.2023. Pregnant with diagnosis of GDM and healthy pregnant women that matched for age and gestational week without GDM during the same time period were included in the study. Local Ethical Committee of the Hospital approved the study (Ethics Number: AEŞH-EK1-2023-224). The universal principles of the Helsinki Declaration were applied and informed consent was obtained from all participants.

A total of 60 pregnant women between 28-38 week of gestation were recruited for the study, 30 of whom were diagnosed with GDM and 30 healthy pregnant women with the same gestational age served as the control group. The analysis determined that a total sample size of 28 pregnant women would be necessary to meet the desired statistical parameters: a Type II error rate (β) of 0.25, a Type I error rate (α) of 0.05, and a power level of 80%.

All pregnant women in the study group were diagnosed with GDM following a (+) screening with 50 g oral GTT (>140 mg/dl) between 24-28 weeks and a fasting diagnostic test of 100 g OGTT performed where Carpenter-Coustan criteria of 2 or more abnormal values were used for diagnosis. Insulin therapy was recommended for patients whose fasting plasma glucose level was 105 mg/dl or two-hour postprandial plasma glucose level was above 120 mg/dl despite diet during follow-up (9). Pregnant women with insulin therapy for glucose control were included to the study.

Pregnant women with pre-existing chronic systemic disease, multiple gestation and fetuses with malformation or diagnosis of intrauterine growth retardation (defined as estimated fetal weight of <10th percentile or abdominal circumference of <10th percentile) and pregnant women with obstetric complications (e.g., preeclampsia, premature rupture of membranes) were excluded from the study.

Demographic information including age, parity, gestational age, and body mass index (BMI) were recorded at first evaluation of the pregnant. The first day of the last menstrual period (LMP) and the first trimester USG measurement of the crown-rump length (CRL) were used to calculate gestational age. The estimated date was modified to ultrasound dating if the difference between LMP and ultrasound dating was greater than seven days (10).

All sonographic examinations were performed transabdominal using the GE Volusion S-10 with a 3.5-MHz convex transducer by the same perinatology specialist. Sonographic assessment of fetal anatomy, maximal measurement of deepest vertical amniotic fluid (MVP) pocket, fetal biometry, estimated fetal weight

(EFW), and umbilical artery (UA), Middle Cerebral Artery (MCA) Doppler measurements (RI, resistance index; PI, pulsatility index; S/D, systolic/diastolic ratio) were performed according to the guidelines of the International Society of Ultrasound in Obstetrics and Gynecology (26). UA Doppler measurements were made from a free-floating portion of the umbilical cord away from the fetus and placenta. After locating the circle of Willis, MCA Doppler sampling was performed from the proximal segment 2 mm following the MCA branching, in the axial section of the fetal brain, without applying pressure to the fetal head and with the angle of insonation close to 0 degrees. During the examination, attention was given to the maternal position to prevent the development of supine hypotension.

The fetal left ventricle ModMPI measurement was performed as described by HernandezAndrade et al. (8). The Doppler sample was applied to the lateral wall of the ascending aorta after an apical four-chamber image was obtained, capturing the aortic and mitral valves as well as their opening and closing clicks. Doppler's gain was adjusted for optimal visualization of valve clicks. The Doppler angle of insonation was kept as low as 0 degrees but no more than 30 degrees. The Ewave (early ventricular filling) and Awave (active atrial filling) were obtained.

ICT was calculated from the start of mitral valve closure until the opening of the aortic valve. IRT was calculated from the time of aortic valve closure to mitral valve opening. The ET was measured from the time of opening to closing of the aortic valve and the ModMPI was calculated as (ICT + IRT)/ET. The measurements were taken without fetal movement and while the fetal heart rate was within the usual range (120-160 bpm). To avoid intra-observer differences, measurements were only obtained when at least 3 successively comparable waves were seen.

Statistical Analyses

Data were processed using IBM SPSS 26.0 software (SPSS Inc., Chicago, Ill., USA) and descriptive statistics and frequency tables were utilized to interpret the results.

Kolmogorov–Smirnov test was used for distribution and variance homogeneity. The Independent Sample t-Test and the Paired Sample Test were used to compare the parameters with a normal distribution in independent and dependent groups, respectively. For parameters with a non-normal distribution, the Mann-Whitney U test was employed for independent groups and the Wilcoxon test for dependent groups. a p value of 0.05 or lower was considered as statistically significant.

RESULTS

This study involved a total of 60 pregnant women—30 with GDM and 30 without disease. Demographic factors in terms of age, gravidity, parity, BMI, and gestational week at assessment of study were similar between groups. Table 1 shows the demographics characteristics of the study group.

Table 1: Demographic Characteristics of the Study Groups

Variable	GDM (n=30)	Control (n=30)	P value
Age (years)	28.14 ± 4.26	27.27± 4.17	0.43
Gravidity (numbers)	2.0 ± 0.6	1.97 ± 1.12	0.66
Parity	1.07 ± 0.7	0.73 ± 0.8	0.10
Abortus	0.64 ± 0.9	0.27 ± 0.6	0.09
GW at Study Assessment	33.6 ± 3.46	33.7 ± 3.13	0.85
BMI (kg/m2)	30.28 ± 3.40	28.55 ±4.67	0.11

Abbreviations: GW, Gestational Week; BMI, Body Mass Index; $p < 0.05$ was considered statistically significant.

There was no statistically significant difference ICT (24.04 ± 7.10, 25.20 ± 7.83; p= 0.55) IRT (37.54 ± 11.65, 41.13 ± 13.08; p=0.27), and ET (169.21 ± 14.6, 173.07 ± 15.46; p=0.33) value in GDM group and control group. The mean Mod-MPI value of GDM group was significantly higher in GDM group when compared with control group (0.41± 0.08, 0.38±0.07; p= 0.002). The cardiac function parameters of the groups were presented in Table 2.

Table 2: Cardiac Function Parameters of the Study Groups

Variable	GDM Group (n=30)	Control group (n=30)	P value
UA RI	0.62 ±0.10	0.60 ±0.06	0.29
UA PI	0.93 ±0.19	0.96 ±0.35	0.66
UA S/D	2.65 ±0.51	2.54 ±0.35	0.33
MCA PI	1.89 ±0.53	1.93 ±0.65	0.66
CPR	2.03 ±0.9	2.01 ±1.1	0.78

Abbreviations: UA, Umbilical Artery; S/D, Systole/Diastole; MCA, Middle Cerebral Artery; CPR, Cerebro-Placental Ratio; PI, Pulsatility Index; RI, Resistance Index. $p<0.05$ was considered statistically significant.

Obstetric Doppler parameters of UA and MCA were found similar between groups. There was also no significant difference between groups in terms of CPR. The obstetric Doppler parameters of the study population were shown in Table 3.

Table 3: Fetal Peripheral Doppler Parameters of the Study Groups

Variable	GDM Group (n=30)	Control group (n=30)	P value
UA RI	0.62 ±0.10	0.60 ±0.06	0.29
UA PI	0.93 ±0.19	0.96 ±0.35	0.66
UA S/D	2.65 ±0.51	2.54 ±0.35	0.33
MCA PI	1.89 ±0.53	1.93 ±0.65	0.66
CPR	2.03 ±0.9	2.01 ±1.1	0.78

Abbreviations: UA, Umbilical Artery; S/D, Systole/Diastole; MCA, Middle Cerebral Artery; CPR, Cerebro-Placental Ratio; PI, Pulsatility Index; RI, Resistance Index. $p<0.05$ was considered statistically significant.

DISCUSSION

In this study, we aimed to determine whether there was variability in fetal left ventricular mod-MPI value in fetuses of pregnant with GDM and we also aimed to evaluate fetal circulation with using common Doppler Ultrasonography and compare with healthy pregnant women. We found that mean mod-MPI value was significantly higher in pregnant with GDM when compared with healthy pregnant.

GDM is defined as abnormal glucose tolerance seen in pregnancy for the first time and macrosomia, hyperbilirubinemia, neonatal hypoglycemia, hypocalcaemia, hypomagnesaemia, respiratory distress and polyhydramnios, and increased risk of birth trauma, and stillbirth are most common fetal complications of GDM and especially seen in pregnant with poor glycemic control (11). Fetus is also at risk for future development of cardiovascular disease, metabolic syndrome and type 2 DM in adulthood (12,13). The role of ultrasound in pregnant women with GDM is important in terms of antepartum maternal and fetal monitoring, detection of maternal and fetal risks, evaluation of fetal growth and well-being, and to determine delivery type and delivery timing (14).

Several fetal and pregnancy-associated diseases may have an impact on fetal cardiac function and Mod‐MPI is one of the newer techniques used to evaluate cardiac function. In the presence of pathological conditions such as preeclampsia, fetal hydrops, fetal anemia, twin-to-twin transfusion syndrome, fetal growth restriction and maternal DM, MPI levels are expected to change (15). Studies have demonstrated that higher fetal cardiac afterload is associated with higher MPI level, and it is known that both hypervolemia and placental vascular resistance may contribute to higher cardiac afterload (16).

Falkensammer et al. reported a mean left fetal cardiac MPI of 0.41 that remained constant throughout pregnancy (17) and similiarly Eidem et al. and Friedman et al also showed that MPI value do not change throughout pregnancy and reported mean value as 0.35 and 0.53 respectively in their studies (18,19). However Tsutsumi et al showed a gradual decrease in the left MPI with advancing gestation (7). The Mod-MPI marginally rises from 0.35 at 19 weeks to 0.37 at 39 weeks of gestation, according to Hernandez- Andrade et al., whose method was employed in our investigation (8). In our study, mean MPI value was 0.41± 0.08 in study group.

Both systolic and diastolic dysfunction is evaluated with MPI by ICT and IRT respectively (20). In the case of pathological circumstances, the IRT is the MPI component that has had the earliest influence. Ventricular wall compliance rises during advanced gestation and cardiac maturation; and expresses as an increase in relaxation capacity, which enhances heart diastolic function (21). IRT is predicted to rise when pathologic circumstances are present. Pooransari et al. showed prolonged IRT in GDM pregnant when compared with normal group (22). However there was no statistically significance between groups in terms of IRT in our study. Pooransari et al. and Sanhal et al. found increased MPI level in pregnant with GDM compared with healthy pregnant (22,23). Increased MPI in fetuses of diabetic mothers may be due to damage to the myocardium of high glucose levels. We also found increased MPI level in pregnant with GDM than pregnant without disease in our study consistent with the results of previous studies.

Doppler USG is increasingly being used in high-risk pregnancies; and it is critically important for monitoring and assessing the health of the fetus (24). Contrary to fetal growth restriction, the pathophysiology of placental vascular resistance in diabetic pregnancies may be caused by hyperglycemia, which can also cause polycythemia, which can reduce blood flow to the fetus and cause hypoxia (25). Hyperglycemia can also increase the thromboxane/prostacyclin ratio in the placenta and umbilical vessels (24). There are conflicting data in the obstetric Doppler USG findings of pregnant women with GDM in the literature. In their study on pregnant women with GDM, Pietryga M et al. found abnormal umbilical artery velocity in 5% according to gestational week and abnormal uterine artery Doppler findings in 16% in pregnant with GDM; however they did not find a relationship between HbA1c and vascular impedance (2). Leung et al. evaluated UA and MCA with Doppler USG in pregnant women with GDM and reported that UA-PI, MCA-PI and MCA-Vmax values are not useful in estimating abnormal pregnancy outcomes in pregnant women with GDM (24). In their Doppler study conducted in pregnant women with GDM, Dantas et al. concluded that the ratio of UA PI, MCA PI and CPR did not differ in pregnant with GDM compared to pregnant women without disease (14). In our study obstetric Doppler parameters of UA and MCA were similar in pregnant with GDM and without disease. CPR value also did not differ between groups.

The strength of this study was, this was a prospective study, and an experienced and same operator calculated all the Mod-MPI values and we used the modified technique described by

Hernandez‐Andrade et al., which increased the reproducibility of the measurements and decreased intra‐observer variability. The limitation of this study was we could not evaluate perinatal and neonatal outcome and not evaluate the pregnant serially in terms of MPI and Doppler values. The small number of cases was also another limitation.

CONCLUSION

We evaluated the Mod-MPI and fetal obsteric Doppler values in pregnant with GDM and compared with healthy pregnant. We found that Mod-MPI value of pregnant with GDM were significantly higher than healthy pregnant without disease however we found obstetric Doppler parameters similar between groups. When pathological condition such as maternal increased blood glucose influence fetal cardiac function and as a result Mod-MPI, it may be important to decide the time of birth of these fetuses. However multicenter prospective studies with larger number of cases and with serial measurements are needed; to evaluate the utility of the Mod‐MPI as a predictor of cardiac function in fetuses of GDM mothers and to evaluate the relationship of fetal high blood glucose levels with fetal hypoxic changes and its effect on the obstetric Doppler measurements.

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Conflict of Interest : None

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