CORRELATION OF MATERNAL BLOOD, CORD BLOOD AND PLACENTAL TISSUE MALONDIALDEHYDE LEVELS WITH FETOMATERNAL DOPPLER VALUES IN PREECLAMPTIC PREGNANT WOMEN

PREEKLAMPTİK GEBELERDE MATERNAL KAN, KORDON KANI VE PLASENTAL DOKUDA MALONDIALDEHİT DÜZEYLERININ FETOMATERNAL DOPPLER DEĞERLERİ İLE KORELASYONU

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Received/Geliş Tarihi	Accepted/Kabul Tarihi	Published/Yayın Tarihi
13.12.2022	20.12.2022	30.12.2022

To cite this article / Bu makaleye atıfta bulunmak için:

Tanriverdi EC, Tanriverdi HA, Akça ASD. Correlation of maternal blood, cord blood and placental tissue malondialdehyde levels with fetomaternal doppler values in preeclamptic pregnant women. Atatürk Üniversitesi Tıp Fakültesi Cerrahi Tıp Bilimleri Dergisi. 2022; 1(3): 89-96

This work is derived from the specialization thesis of Esra Çınar Tanrıverdi.

Part of the study presented as an oral presentation at the 7. International Congress of Family Medicine (Edirne, Edirne, Turkey, 21 - 25 March 2018).

Abstract

Objective: In this study, it was aimed to evaluate the correlation of malondialdehyde (MDA) levels in maternal blood, fetal blood, and placental bed with fetomaternal Doppler values in preeclamptic pregnant women. **Methods:** The study was carried out with a total of 74 cases, of whom 52 were healthy and 22 were pregnant with preeclampsia. Malondialdehyde levels were measured in maternal blood, cord blood, and placenta tissues of the pregnant women. Doppler sonographic measurements were carried out for the uterine and umbilical arteries. Doppler values and MDA levels of preeclamptic and healthy pregnant women were compared. **Results:** Malondialdehyde levels in maternal blood and placental tissue in preeclamptic pregnant women were significantly higher than healthy pregnant women ($p<0.05$). Although umbilical artery and umbilical vein MDA levels were higher in the study group than in the control group, they were not statistically significant ($p>0.05$). Doppler sonographic indexes in the umbilical and uterine arteries were significantly higher in the preeclamptic group than in the control group ($p<0.05$). When all patients were evaluated, there was no significant correlation between maternal and placental malondialdehyde values and umbilical and uterine artery Doppler values. **Conclusion:** Malondialdehyde levels and fetomaternal Doppler values in blood and placental tissue were significantly higher in preeclamptic pregnant women compared to the control group. However, no significant correlation was found between MDA levels and Doppler values.

Keywords: Oxidative stress, lipid peroxidation, malondialdehyde, Doppler sonography, placental insufficiency, preeclampsia

Özet

Amaç: Bu çalışmada preeklamptik gebelerde maternal kan, fetal kan ve plasental yataktaki malondialdehit (MDA) düzeylerinin fetomaternal Doppler değerleri ile korelasyonunun değerlendirilmesi amaçlanmıştır. **Materyal ve Metod:** Çalışma 52 sağlıklı, 22 preeklamptik gebe olmak üzere toplam 74 olgu ile yürütüldü. Gebelerin maternal kan, kordon kanı, plasenta dokularında MDA düzeyleri ölçüldü. Uterin ve umbilikal arterlerde Doppler sonografik ölçümler yapıldı. Preeklamptik ve sağlıklı gebelerin Doppler değerleri ile MDA düzeyleri karşılaştırıldı. Veriler SPSS programında analiz edildi. İstatistiksel anlamlılık düzeyi $p<0.05$ kabul edildi. **Bulgular:** Preeklamptik gebelerde maternal kan ve plasental dokudaki MDA seviyeleri, sağlıklı gebelere göre anlamlı şekilde yüksekti ($p<0.05$). Umbilikal arter ve umbilikal ven MDA düzeyleri çalışma grubunda, kontrol grubuna göre daha yüksek bulunsa da istatistiksel olarak anlamlı değildi ($p>0.05$). Umbilikal arter ve uterin arterlerdeki Doppler sonografik indeksler, preeklamptik grupta kontrol grubuna göre anlamlı şekilde daha yüksekti ($p<0.05$). Tüm hastalar değerlendirildiğinde maternal ve plasental malondialdehit değerleri ile umbilikal ve uterin arter Doppler değerleri arasında anlamlı bir korelasyon saptanmadı. **Sonuç:**Preeklamptik gebelerde, kan ve plasental dokudaki MDA düzeyleri ve fetomaternal Doppler değerleri kontrol grubuna göre anlamlı şekilde daha yüksek bulunmuş, ancak MDA düzeyleri ile Doppler değerleri arasında anlamlı bir korelasyon saptanmamıştır.

Anahtar Kelimeler: Oksidatif stres, lipid peroksidasyonu, malondialdehit, Doppler sonografi, plasental yetmezlik, preeklampsi

1. INTRODUCTION

Preeclampsia is a multisystemic syndrome with hypertension and proteinuria that occurs after the 20th week of pregnancy. It is a pregnancy-specific disease (1, 2). It is still among the most important causes of maternal and neonatal mortality and morbidity in developing countries (3-5).

The cause of preeclampsia has not been fully determined (1). Many factors are blamed on its etiology, and one of the hypotheses put forward is oxidative stress and endothelial cell damage. The lack of placental perfusion seen in preeclampsia initiates circulatory events that cause endothelial cell damage (3). Accordingly, an imbalance between oxidative stress and antioxidant defense systems causes damage to the placental wall. It has been suggested that an increase in malondialdehyde (MDA) production due to lipid peroxidation may lead to preeclampsia (6-8). As a result, placental insufficiency occurs. Early detection of preeclampsia is of great importance for maternal and fetal health.

Oxidative stress is the intersection of the factors that cause the clinical features of preeclampsia and leads to endothelial cell dysfunction. Free radicals attract polyunsaturated fatty acids to the cell membrane, initiate lipid peroxidation, and cause the release of free radicals mediated by lipid peroxidation, thereby causing endothelial damage (9, 10). Some products are formed during lipid peroxidation and the measurement of these products is used as an indicator of oxidative stress. Malondialdehyde is the most widely used one among them (11).

Doppler ultrasonography (USG) is a noninvasive method that can be used in fetal hemodynamic studies. It helps to identify the risky fetus in high-risk pregnancies, which enables it to be used as a screening test (12, 13). Impairment of placental perfusion occurs long before the onset of clinical signs of preeclampsia and can be detected by Doppler sonography. In this respect, Doppler USG is an important tool in the prediction of preeclampsia and adverse perinatal outcomes (14, 15).

Since the uterine artery represents the maternal condition, it is the most used vessel in the Doppler sonographic evaluation of PE (16, 17). On the other hand, the umbilical artery is mostly used to evaluate fetal status (18-20). Doppler sonographic examination of the utero-fetoplacental vasculature allows evaluation of perfusion in both compartments and has a better risk estimation. It is known that the risk of developing hypertensive complications in antenatal follow-up can be estimated by uterine artery Doppler sonographic examination to be performed in the second trimester. The presence of pathological findings in both A. uterina indicates a high risk for preeclampsia, most likely due to impaired perfusion of fetal vessels (21).

The presence of end-diastolic flow in the A. umbilicalis Doppler sonography indicates a high obstetric risk. The degree of Doppler sonographic pathologies is proportional to the degree of fetal intrauterine threat. Therefore, a reverse flow in the A. umbilicalis is a sign of serious perinatal problems. At this time, a backward flow is observed in the fetal vessels at the end-diastolic stage. In the presence of such a finding, perinatal mortality is very high. This finding reflects a dangerous situation for the fetus. Most fetuses with reverse flow can experience intrauterine death in a few days. The end-diastolic block is also a serious condition. These fetuses have a significantly increased risk for serious perinatal pathologies and neuromotor disabilities. Perinatal mortality is significantly higher in cases with the reverse flow (21). Preeclampsia poses a significant risk to the mother and fetus. Patients with placental insufficiency usually have decreased flow amounts or at least altered flow curves. Thanks to the information obtained about the deficiencies in placental function through Doppler sonography, fetal damage can be prevented by planning a perinatal approach (21).

In this study, we aimed to investigate the correlation between MDA levels and fetomaternal Doppler values in maternal blood, fetal blood, and placental tissue in preeclamptic patients.

2. MATERIAL AND METHOD

2.1. Ethical Consent

The ethical permission required for the study was obtained from Bülent Ecevit University Clinical Research Ethics Committee (Issue: 2005/02-10). The study was conducted in accordance with the principles of the Helsinki Declaration.

2.2. Study design and participants

The study was a prospective study in which 22 preeclamptic and 52 normal pregnant women who were admitted to the pregnant outpatient clinic were included. The preeclamptic pregnant patients were determined as the study group, whilst the normal pregnant women were accepted as the control group. Participants were given detailed information about all transactions to be carried out and their written consent was obtained. The diagnosis of preeclampsia was made according to the criteria of the American College of Obstetricians and Gynecologists (ACOG) after the 20th gestational week, at least two blood pressure values measured at intervals of six hours were 140/90 mmHg or above, proteinuria was 1+ / 2+ in the urine analysis with a dipstick or 300 mg or more in 24-hour urine was detected (22). Having a metabolic or systemic disease, antihypertensive drug use, smoking, and alcohol use, and non-volunteering were determined as exclusion criteria. Since placental bed biopsy was planned to be taken during delivery, healthy-term pregnant women who did not have a

systemic or chronic disease and who were planned to undergo cesarean section for other reasons (such as elective, presentation anomalies) were included in the control group. Multiple pregnancies and those with congenital or structural malformations were excluded from the study.

2.3. Procedure

Gestational age was determined by the last menstrual period and ultrasonographic biometry. Gestational age, birth weight, placental weight, mode of delivery, perinatal mortality, 1st and 5th minute Apgar score, umbilical and uterine artery Doppler results, MDA values in placental tissue and maternal blood were examined in terms of demographic characteristics of the participant.

2.3.1. Doppler measurements

Doppler measurements of the umbilical artery and both uterine arteries were performed transabdominally using a 3.5 MHz Probe (GE Logiq 7®, Penta Elektronik, Ankara, Turkey) in all pregnant participants. Umbilical artery measurements were taken in a free umbilical cord cycle. The maximum and end-diastole flow velocities in the systole were marked in three separate waves and the systole/diastole (S/D) ratio was calculated and averaged. At the same time, resistance index (RI) and pulsatility index (PI) values were calculated. Early diastolic "notch" in uterine arteries and PI, RI, and S/D values in umbilical and uterine arteries were measured in waveform. All Doppler measurements were performed by the same person within 24 hours of birth. In the study group, S/D ratios above the percentile of 95% according to gestational age were considered pathological. In the control group, since they were all termly pregnant, an S/D value above 3 was considered pathological. Notch monitoring in uterine arteries, end-diastolic flow loss in umbilical and uterine arteries, and reverse flow monitoring were considered pathological for both groups (16, 21).

2.3.2. Taking and storing blood samples

5 cc of peripheral venous blood was taken from all pregnant women within 3 days before delivery. After birth, approximately 2 cc of blood was taken from the cord from both the umbilical artery and vein following the clamping of the cord. Following the clamping of the cord after birth, a blood sample was taken from the cord and fetal blood gas was evaluated. After waiting for 30 minutes for blood samples to coagulate in sterile tubes, centrifuged for 3000 cycles and 30 minutes, separated the serums, and stored at -80 degrees until the time of analysis.

2.3.3. Malondialdehyde (MDA) measurement

In our study, lipid peroxidation was evaluated as an indicator of oxidative stress (23, 24). Lipid peroxidation was evaluated based on the reaction of MDA with Thiobarbituric acid (TBA). 0.2 ml 8.1% SDS (Sodium dodecyl sulfate), 1.5 ml NaOH (Sodium Hydroxide) with pH = 3.5 adjusted 20% acetic acid, 1.5 ml 0.8% TBA were added to 0.2 ml serum and the volume was completed to 4 ml with distilled water. After incubating for 60 minutes in a 95ºC water bath, it was cooled with water, and added 1 ml of distilled water. 5ml n-butanol was mixed by adding pyridine (15/1, v/v) mixture. The absorbance of the organic layer at 532 nm was measured in Shimadzu Ultraviolet 1600 spectrophotometer by centrifugation at 4000 rpm for 10 minutes. 1,1,3,3 tetraethoxypropane was used as standard. Blood MDA concentrations were assessed in nmol/ml (25).

Placental bed biopsy was taken in the form of approximately 3 mm 3 samples with scissors or a scalpel after the placenta was removed during cesarean section. Care was taken to ensure that the biopsy specimens included decidua and superficial myometrial tissue. The samples taken were kept in Eppendorf tubes at – 80 degrees until the day of analysis.

Placental tissues were homogenized with 1.15% KCl solution by weighing their weight and turning them into 10% tissue homogenate. 0.2 ml of 8.1% SDS (Sodium dodecyl sulfate), 1.5 ml of NaOH (Sodium Hydroxide) with pH = 3.5 adjustment of 20% acetic acid, 1.5 ml of 0.8% TBA (Thiobarbituric acid) were added to 0.2 ml homogenate and the volume was completed to 4 ml with distilled water. After incubating for 60 minutes in a 95ºC water bath, it was cooled with water, and added 1 ml of distilled water. 5ml n-butanol was mixed by adding pyridine (15/1, v/v) mixture. The absorbance of the organic layer at 532 nm was measured in Shimadzu Ultraviolet 1600 spectrophotometer by centrifugation at 4000 rpm for 10 minutes. 1,1,3,3 tetraethoxypropane was used as standard. Tissue MDA concentrations were evaluated as nmol/g tissue weight.

2.4. Statistical Analysis

Patient data were collected with hospital computer automation system records and patient information sheets and analyzed using SPSS 15 (SPSS Inc., USA) statistical program. In the comparison of continuous measurements such as age, gravida, and parity of the patients, Student's t-test was used for parameters with normal distribution and equal variances. Mann-Whitney U test was used to compare measurements without normal distribution in nonparametric data. In all statistical calculations, the significance limit was accepted as $p<0.05$.

3. RESULTS

3.1 Demographic characteristics and findings on MDA levels

Demographic characteristics of pregnant women are presented in Table 1. There was no statistically significant difference between the study and control group in terms of maternal age, gravida, parity, and abortus numbers ($p>0.05$ for the whole).

Gestational age, birth weight, and placental weight were significantly lower in the preeclampsia group than in the control group ($p<0.001$ for all). Apgar values (1st and 5th min) were also significantly lower in the preeclampsia group than in the control group ($p=0.001$). Cord blood gas values were also significantly lower in the PE group ($p=0.01$).

MDA levels in both maternal blood and placental tissue were statistically significantly higher in the study group than in the control group ($p<0.05$, Figure 1). Although umbilical artery and umbilical vein MDA levels were higher in the preeclamptic group than in the control group, they were not statistically significant ($p>0.05$). Comparisons between groups are shown in Table 1. The comparison of MDA levels in the preeclamptic and control group is shown in Figure 1.

Table 1: Comparison of various characteristics of preeclampsic and healthy pregnant women

	Control Mean±SD	Preeclampsia Mean±SD	p
Age	29.1±4.2	29.1±6.4	0.28
Gravida	1.8±1.0	3.0±3.2	0.56
Parity	0.7±0.8	1.2±1.5	0.15
Abort	0.1±0.6	0.4±0.9	0.39
Gestation period according to LMP (days)	264.2±15.0	229.6±35.9	0.00
Sonographically gestation period (days)	261.2±13.8	214.8±31.5	0.00
Placenta weight (g)	580 ± 124	372±153	0.00
Birth weight (g)	3236 ± 632	1691±920	0.00
Apgar 1st minute	9.1±1.3	4.2±3.6	0.00
Apgar 5th minute	9.8 ± 0.5	6.3±3.9	0.00
Cord blood PH	7.38 ± 0.3	7.35±0.5	0.01
MDA maternal blood (nmol/ml)	57.35 ±24.5	99.8±45.4	0.00
MDA placenta (nmol/g tissue)	30.3±14.5	45.9±23.9	0.00
MDA umbilical artery (nmol/ml)	32.8±21.2	34.6±7.7	0.36
MDA umbilical vein (nmol/ml)	26.2±14.0	30.9±13.3	0.17

Figure 1: Comparison of MDA levels in maternal blood and placental tissue

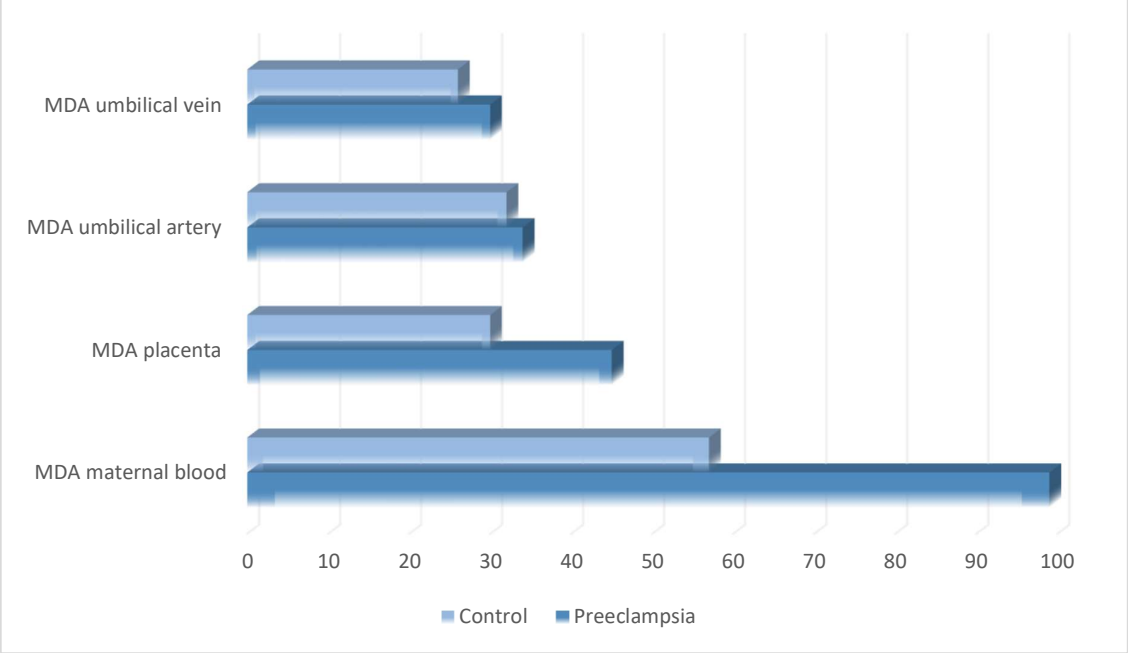

Table 2: Comparison of umbilical and uterine artery Doppler values

	Control Mean ± SD	Preeclampsia Mean ± SD	p
Umbilical artery S/D	2.5 ± 0.5	4.4 ± 3.5	.00
Umbilical artery RI	0.59 ± 0.08	1.03 ± 0.78	.00
Umbilical artery PI	0.84 ± 0.18	1.82 ± 1.62	.00
Right uterine artery S/D	1.97 ± 0.65	2.69 ± 0.98	.00
Right uterine artery RI	0.45 ± 0.15	0.61 ± 0.19	.00
Right uterine artery PI	0.59 ± 0.25	0.86 ± 0.29	.00
Left uterine artery S/D	0.18 ± 0.46	0.86 ± 0.29	.00
Left uterine artery RI	0.45 ± 0.15	0.59 ± 0.22	.01
Left uterine artery PI	0.57 ± 0.24	0.79 ± 0.33	.00

SD Standard deviation

Tablo 3: The frequency of pathological Doppler in the groups

	Control %	Preeclampsia %
Pathological Doppler in the umbilical artery	0	42
End Diastolic Block in the umbilical artery	0	21
Reverse current in the umbilical artery	0	0
Notch in the right uterine artery	3	42
Notch in the left uterine artery	7	42

3.2. Doppler values

All Doppler values measured in the umbilical artery were statistically significantly higher in the PE group than in the control group ($p<0.05$ for all). All Doppler values measured in the right uterine artery were significantly higher in the PE group than in the control group ($p<0.05$ for all). All Doppler values measured in the left uterine artery were higher in the PE group than in the control group. The difference between the groups for S/D, PI, and RI values was statistically significant ($p<0.05$ for all parameters).

While pathological Doppler was detected in the umbilical artery in 42% of the study group, no pathological Doppler value was detected in any pregnant woman in the control group. End diastolic flow loss (EDB) in the umbilical artery was 21% in the study group, while no patients in the control group had end-diastolic flow loss. In both the study group and the control group, no reversal flow was observed in any patient. The notch rate was significantly higher in the preeclamptic group than in the control group. The incidence of notches in uterine arteries was 3% in the right uterine artery, and 7% in the left uterine artery for the control group whereas incidences of notches in the right and left uterine arteries were 42% in the study group. In all cases, the notch was bilateralized (Table 3).

There was a statistically significant correlation between maternal blood and placental MDA values ($R = 0.35$, $p<0.05$).

There was no correlation between maternal blood MDA levels and umbilical artery PI values. ($R= 076$, $p= 0.750$, Figure 3). However, there was a negative correlation between the right uterine artery PI values ($R= -0.138$, $p= 0.558$). Although there was a positive correlation with left uterine artery PI values, it was not statistically significant. ($R= 0.004$ $p= 0.987$). Although there was a positive correlation between placental MDA levels and umbilical artery and left uterine artery PI values, it was not statistically significant. (Respectively $R=0.393$, $p=0.087$; $R= 0.025$, $p= 0.920$). There was a statistically insignificant negative correlation between placental MDA levels and right uterine artery PI levels.

4. DISCUSSION

Preeclampsia is a pregnancy-specific syndrome. Lack of placental perfusion in preeclampsia leads to the formation of circulatory factors that cause endothelial cell damage. (3)

In this study, we aimed to investigate whether there is a correlation between malondialdehyde levels and maternal Doppler values in preeclamptic pregnant women and to evaluate its availability in the clinic. Our study results show that maternal blood, fetal blood, and placenta MDA levels are significantly higher in preeclamptic pregnant women than in healthy pregnant women and that these findings are accompanied by a disorder in Doppler values.

Oxidative stress is the intersection of factors that cause the clinical features of preeclampsia and leads to endothelial cell dysfunction. Free radicals initiate lipid peroxidation by attracting polyunsaturated fatty acids to the cell membrane, leading to the release of free radicals mediated by lipid peroxidation, thereby causing endothelial damage. (9, 26, 27)

Preeclampsia is still a disease of theories and the role of oxidative stress in the etiology is of interest. However, a consensus on systemic oxidative stress has not been reached yet.

Several products are formed during lipid peroxidation and the measurement of these products is used as an indicator of lipid peroxidation. MDA is the most widely used of these (11). Our study results showed that MDA; an indicator of lipid peroxidation, was significantly higher in both plasma and placental beds of preeclamptic women than in the control group. In the literature, it is reported that serum lipid peroxide levels of preeclamptic pregnant patients are higher than in normal pregnant women and antioxidant activity is lower in preeclamptic pregnant patients compared to normal pregnant women (9, 28). Various studies have reported a significant increase in lipoperoxidation products in the plasma of preeclamptic women similar to our results (26, 29). In one study, MDA was examined in the amniotic fluids taken in the mid-trimester of preeclamptic women and it was not found to be different from the healthy pregnant control group. In this study where contradictory results to other studies were obtained, blood MDA levels were not controlled, and only amniotic fluid was examined (30). A meta-analysis reports that MDA levels were significantly higher in preeclamptic pregnant women than in healthy pregnant women (28). In another study, it was reported that the level of MDA in amniotic fluids of preeclamptic women was lower than in controls (31). These differences may have been influenced by measurement techniques, sample size, and severity of preeclampsia. In our study, although MDA levels in the umbilical artery and especially in the vein were higher in the PE group than in the control group, the difference between the groups was not statistically significant.

Preeclampsia is known as nulliparous disease. In our results, it is thought that the lower number of pregnancies in the control group is that the majority of the pregnant participants in this group consisted of health individuals who were planned by elective cesarean section. When the gestational ages were compared, the gestational age determined according to SAT and sonographically in preeclampsia was found to be significantly lower than the control group. In this difference, it is thought that earlier termination of pregnancy plays an important role due to the weight of clinics of preeclamptic patients and/or intrauterine fetal distress.

Pathologic vascularization is known to lead to a decrease in uteroplacental perfusion and placental weight (21). In our study, placental weight was significantly lower in the control group than in the PE group. As a result, the difference between gestational weeks is thought to be effective as well as placental dysfunction. In our study, newborn weight, placenta weight, 1st and 5th min Apgar values, and cord blood gas values were significantly lower in the PE group.

The aim of Doppler USG in preeclampsia is to detect early pregnancies that will develop PE (32). Doppler sonographic pathologies are proportional to the degree of fetal intrauterine threat (21). In our study, the rate of pathological Doppler in the umbilical artery was found to be 42% in the study group, while no pathological Doppler value was detected in the umbilical artery in the control group.

The appearance of reverse flow in the umbilical artery is a sign of serious perinatal problems. End diastolic block is also a serious condition. In these fetuses, there is a significantly increased risk of severe perinatal pathologies and neuromotor disabilities. Perinatal mortality is significantly higher in cases with the reverse flow (21). In our study, no reverse flow was observed neither in the PE group nor the control group. End diastolic flow loss in the umbilical artery was found to be 21% in the study group. In the control group, no end-diastolic flow loss was observed in any patient.

In our study, the incidence of notches in the uterine artery was 42% in the preeclamptic group. In the control group, no notches were observed in any of the patients. The presence of pathological findings in both a.uterinas indicates a high risk of preeclampsia, most likely as a result of disruption of perfusion of fetal vessels (21). In our study, the bilateral notch detected in all preeclamptic cases was remarkable. In one study, notch was detected in uterine artery in 20% of preeclamptic pregnant patients, RI and PI values of the uterine artery were not associated with PE, but abnormal umbilical artery Doppler values were detected in the preeclamptic group (13).

In our study, to evaluate the relationship between the results of oxidative stress (lipid peroxidation) and Doppler measurements and whether there is a correlation between them, the correlation of MDA results in maternal blood and placental tissue with PI values measured among themselves and on Doppler sonography was examined. The existence of this type of correlation is important in terms of creating

the possibility of using Doppler sonography and oxidative stress markers interchangeably.
In our study, to evaluate the relationship between oxidative stress (MDA level) and Doppler measurements and whether there was a correlation between them, the correlation of MDA results in maternal blood and placental tissue with PI values measured among themselves and on Doppler sonography was examined. The existence of this type of correlation is important in terms of creating the possibility of using Doppler sonography and oxidative stress markers interchangeably. However, although there was some correlation between MDA levels and Doppler values, it was not statistically significant.

Limitations

The most important limitations of our study are that the number of study groups is low and preeclamptic pregnant participants are not classified according to the severity of the disease.

Conclusion

The findings of the study show us that MDA levels in maternal blood and placental tissue are significantly higher in preeclamptic patients compared to healthy pregnancies. In addition, there is a correlation between MDA values in maternal blood and placental tissue. Accordingly, an increase in MDA in maternal blood is accompanied by an increase in MDA in placental tissue. Prediction of oxidative stress markers may be a predictor of the development of preeclampsia.
Although it does not have statistical significance, when we consider that oxidative stress is correlated with fetomaternal Doppler values, it is possible to say that new horizons are opened in the evaluation of pregnancies with the risk of placental dysfunction. However, these data should be interpreted carefully due to the small number of patients included in the study.
For future studies, we recommend large-scale and larger sample research on the subject.

Funding: No financial support was received for the study.

Conflict of interest: There is no conflict of interest between the authors.

Acknowledgments: We would like to thank Prof. Dr. Şerefden Açıkgöz for contributing to the analysis of blood and tissue samples and Prof. Dr. Mustafa Başaran for contributing to the statistical analysis of the data.

5. REFERENCES

1. Gestational Hypertension and Preeclampsia. "ACOG practice bulletin, number 222." Obstet Gynecol. (2020); 135(6): e237-e260.
2. Young BC, Levine RJ, Karumanchi SA. Pathogenesis of preeclampsia. Annual review of pathology. 2010;5:173.
3. Sibai B, Dekker G. Kupferminc M. Pre-eclampsia Lancet. 2005;365(9461):785-99.
4. Tranquilli AL, Landi B, Giannubilo SR, Sibai BM. Preeclampsia: No longer solely a pregnancy disease. Pregnancy Hypertension: an International Journal of Women'S Cardiovascular Health. 2012;2(4):350-7.
5. Duley L, editor The global impact of pre-eclampsia and eclampsia. Seminars in perinatology; 2009: Elsevier.
6. Brett SE, Jiang BY, Turner C, Ritter JM, Chowienczyk PJ. Elevation of plasma homocysteine by methionine loading increases the diastolic blood pressure response to exercise. Journal of hypertension. 2006;24(10):1985-9.
7. Roberts JM, editor Pathophysiology of ischemic placental disease. Seminars in perinatology; 2014: Elsevier.
8. Nelson DM, Kay H, Wang Y. The placenta: from development to disease: John Wiley & Sons; 2011.
9. Luppi P, DeLoia JA. Monocytes of preeclamptic women spontaneously synthesize pro-inflammatory cytokines. Clinical immunology. 2006;118(2-3):268-75.
10. Hubel CA. Oxidative stress in the pathogenesis of preeclampsia. Proceedings of the Society for Experimental Biology and Medicine. 1999;222(3):222-35.
11. Kim YJ, Park H, Lee HY, Ahn Y-m, Ha EH, Suh SH, et al. Paraoxonase gene polymorphism, serum lipid, and oxidized low-density lipoprotein in preeclampsia. European journal of obstetrics & gynecology and reproductive biology. 2007;133(1):47-52.
12. Alfirevic Z, Stampalija T, Medley N. Fetal and umbilical Doppler ultrasound in normal pregnancy. Cochrane Database of Systematic Reviews. 2015(4).
13. Lopez-Mendez MA, Martinez-Gaytan V, Cortes-Flores R, Ramos-Gonzalez RM, Ochoa-Torres MA, Garza-Veloz I, et al. Doppler ultrasound evaluation in preeclampsia. BMC research notes. 2013;6(1):1-6.
14. Yu J, Shixia C, Wu Y, Duan T. Inhibin A, activin A, placental growth factor and uterine artery Doppler pulsatility index in the prediction of pre-eclampsia. Ultrasound in obstetrics & gynecology. 2011;37(5):528-33.
15. Arauz JFR, León JCR, Velásquez PR, Jiménez GÁ, Pérez CJM. Umbilical artery Doppler velocimetry and adverse perinatal outcome in severe

pre-eclampsia. Ginecología y Obstetricia de México. 2008;76(08):440-9.
16. Gomez O, Martinez J, Figueras F, Del Rio M, Borobio V, Puerto B, et al. Uterine artery Doppler at 11–14 weeks of gestation to screen for hypertensive disorders and associated complications in an unselected population. Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2005;26(5):490-4.
17. Schwarze A, Nelles I, Krapp M, Friedrich M, Schmidt W, Diedrich K, et al. Doppler ultrasound of the uterine artery in the prediction of severe complications during low-risk pregnancies. Archives of gynecology and obstetrics. 2005;271(1):46-52.
18. Newnham JP, Patterson LL, James IR, Diepeveen DA, Reid SE. An evaluation of the efficacy of Doppler flow velocity waveform analysis as a screening test in pregnancy. American journal of obstetrics and gynecology. 1990;162(2):403-10.
19. Skotnicki MZ, Flig E, Urban J, Hermann TW. Doppler examinations in the prognosis of birth status of the newborn. Medical Science Monitor. 2000;6(3):MT611-MT5.
20. Cruz-Martinez R, Figueras F. The role of Doppler and placental screening. Best practice & research Clinical obstetrics & gynaecology. 2009;23(6):845-55.
21. Werner S, Obstetri KA. Jinekolojide Renkli Doppler Sonografi çeviri editörü Ertan Kubilay, Tanrıverdi H. Alper Nobel Tıp Kitabevleri. 2003:131-36.
22. ACOG. American College of Obstetricians and Gynecologists. Hypertension in Pregnancy. American College of Obstetricians and Gynecologists Washington, DC; 2013.
23. Wasowicz W, Neve J, Peretz A. Optimized steps in fluorometric determination of thiobarbituric acid-reactive substances in serum: importance of extraction pH and influence of sample preservation and storage. Clinical chemistry. 1993;39(12):2522-6.
24. Esterbauer H, Cheeseman KH. [42] Determination of aldehydic lipid peroxidation products: malonaldehyde and 4-hydroxynonenal. Methods in enzymology. 186: Elsevier; 1990. p. 407-21.
25. Mohseni R, Karimi J, Tavilani H, Khodadadi I, Hashemnia M. Carvacrol downregulates lysyl oxidase expression and ameliorates oxidative stress in the liver of rats with carbon tetrachloride-induced liver fibrosis. Indian Journal of Clinical Biochemistry. 2020;35(4):458-64.
26. Adiga U, D'souza V, Kamath A, Mangalore N. Antioxidant activity and lipid peroxidation in preeclampsia. Journal of the Chinese Medical Association. 2007;70(10):435-8.
27. Veronica M, Jaime L, Alvaro C. Antioxidant activity and lipid peroxidation in preeclampsia. Biol Res. 2006;39:229-36.
28. Gupta S, Aziz N, Sekhon L, Agarwal R, Mansour G, Li J, et al. Lipid peroxidation and antioxidant status in preeclampsia: a systematic review. Obstetrical & gynecological survey. 2009;64(11):750-9.
29. Aydın S, Benian A, Madazli R, Uludağ S, Uzun H, Kaya S. Plasma malondialdehyde, superoxide dismutase, sE-selectin, fibronectin, endothelin-1 and nitric oxide levels in women with preeclampsia. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2004;113(1):21-5.
30. Çelik H, Sapmaz E, Kılınç N, Çıkım G, Tuğ N, Parmaksız C, et al. Dergi Kimliği. Perinatoloji Dergisi. 2002;10(3):3.
31. Bogavac M, Lakic N, Simin N, Nikolic A, Sudji J, Bozin B. Biomarkers of oxidative stress in amniotic fluid and complications in pregnancy. The Journal of Maternal-Fetal & Neonatal Medicine. 2012;25(1):104-8.
32. Myatt L, Clifton RG, Roberts JM, Spong CY, Hauth JC, Varner MW, et al. The utility of uterine artery Doppler velocimetry in prediction of preeclampsia in a low-risk population. Obstetrics & Gynecology. 2012;120(4):815-22.