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Renal artery Doppler findings in fetuses of mothers with preeclampsia

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ABSTRACT

Objectives: Preeclampsia (PE), which affecting multi-organ systems, is one of the most common causes of feto-maternal morbidity and mortality. The fetal kidney is one of the vulnerable organs in PE caused by sustained vasospasm of the renal arteries. In this study, it was aimed to reveal the changes in the renal vascular bed with renal artery Doppler examinations in fetuses of pregnant women with PE.

Methods: Fifty-five pregnant women with PE and 60 healthy pregnant women were included in this prospective study. Multiple pregnancies, those who did not want to participate in the study, and those with other co-morbidities were excluded from the study. Fetal renal artery Doppler studies included renal artery systolic/diastolic (S/D) ratio, pulsatility index (PI) and resistance index (RI) of the control and PE groups, and findings such as week of birth and birth weight were recorded and analyzed statistically.

Results: Fetal renal artery PI values were found to be higher in pregnant women with PE compared to the control group (2.93 in the patient group, 2.28 in the control group, $p < 0.001$). There was no significant difference between RI values and S/D ratios between the two groups. In the preeclampsia group, gestational week and baby weight at birth were significantly lower.

Conclusions: Due to preeclampsia, hypoxia occurs in peripheral tissues and organs at the maternal level. Fetal organs are also affected by these hypoxic conditions. Doppler is an extremely useful examination tool in the evaluation of the status of peripheral organs such as the kidney. This study suggests that PE increases the resistance of renal arteries in fetuses of mothers with PE compared to fetuses of mothers without PE, which may contribute critically to kidney disease later in life.

Keywords: Preeclampsia, Doppler, fetal renal artery

Preeclampsia (PE), which increases morbidity and mortality in mothers and fetuses due to a multi-systemic disease involving more than one organ, is a picture that occurs with proteinuria, thrombocytopenia, kidney failure, liver failure, pulmonary edema, and brain/visual symptoms [1, 2]. The treatment of preeclampsia, the etiology of which has not been fully elucidated, has not yet been found. The only known definitive solution is delivery and separation of the placenta, which is thought to play a role in the etiology [3].

PE causes a higher risk of chronic hypertension, cardiovascular disease [4], chronic kidney disease [5] and end-stage renal disease [6] on maternal health not

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only during pregnancy but also in subsequent years. Fetuses of mothers with PE have a higher lifetime risk for pulmonary, cardiovascular, and metabolic diseases, systemic vascular dysfunction, and obesity [7-9]. Additionally, hypoxia caused by placental pathology in PE reduces nephrons in the fetal kidneys, which may affect the long-term health of fetuses at lifetime risk [10]. Some animal experiments have shown that this damage causes a decrease in size of fetal kidneys and glomerular number [7, 11].

Doppler ultrasonography is one of the most appropriate examination methods to show vascular resistance anomalies in fetal kidneys due to preeclampsia, since it does not contain ionizing radiation and is a noninvasive method. Resistance index (RI) and pulsatile index (PI) values, which mean high values measured by Doppler examination, show increased resistance in the vascular bed, are the best indicators of resistance in the vascular bed [12].

In this study, it was aimed to reveal the changes caused by PE in the fetal renal vascular bed by Doppler examination measurements made from fetal renal arteries in pregnancies complicated by PE.

METHODS

A prospective study was conducted between March-2021 and December-2021 in a tertiary hospital with PE and control group to evaluate the changes caused by PE in fetal renal vascular bed with Doppler examination measurements made from fetal renal arteries. Ethical approval was obtained from the local institutional ethics committee (number E-2021/87).

Written informed consent was obtained from all participants before the examination. Fifty-five patients with preeclampsia and 60 normal pregnant women were included in the study. The diagnosis of PE was made according to the guidelines of the International Federation of Gynecology and Obstetrics for the Study of Hypertension in Pregnancy. As a result of the data scans, the routine laboratory, ultrasonographic measurements and birth follow-up data of the pregnant women who applied to the hospital were recorded. Gestational age was confirmed by first trimester sonographic measurements of pregnancy.

Inclusion criteria were women with a singleton pregnancy complicated with PE, and the control group consisted of mothers of matched gestational age. Fetal anomaly, accompanying maternal comorbidity (such as diabetes, ischemic heart disease, kidney disease and autoimmune diseases), multiple pregnancies, pregnant women with smoking and alcohol use, and pregnant women who did not want to participate in the study were excluded.

All patients underwent an ultrasonographic examination using a Mindray Resona 7 ultrasound (Mindray Bio-Medical Electronics Co., Ltd., Shenzhen, China), diagnostic apparatus with a 1,2-6 MHz convex abdominal probe. Fetal renal artery Doppler assessments were performed by a fetal medicine specialist (HAS) using a method similar to that previously described by Azpurua *et al*. [4]. The ultrasound parameters were performed gestational weeks in between 27-40. All pregnant women were placed in the supine position and respiratory levels were kept constant to avoid noise and artifacts.

The color Doppler range (1.5 to 2.0 mm) was in-

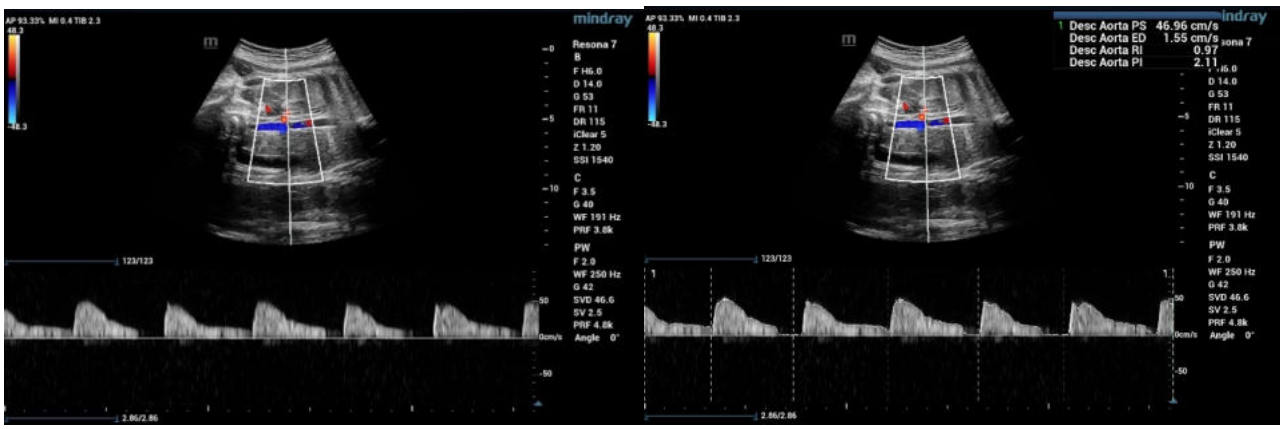

Fig. 1. Fetal renal artery doppler imaging.

serted into the lumen of the renal artery, just after the aortic outlet, in the midsection of the renal artery before intrarenal branching (Fig. 1)

The scan plane was set in the range of 30°-60°. Low filter (50-75Hz) settings were used to preserve the end-diastolic values of the renal artery waveform. Renal artery PI, RI, and systolic diastolic (S/D) velocity ratios were measured.

Statistical Analysis

The IBM SPSS Statistics program (Version 11.0, SPSS; Chicago, IL, USA) was used for the statistical evaluation of the data obtained in this study. The Shapiro-Wilk test was used to test whether the variables of the patient and control groups fit the normal distribution, and the variables that fit the normal distribution were given as mean ± standard deviation values, and the variables that did not fit the normal distribution were given as their median (minimum-maximum) values. "Mann Whitney U" and "Independent Sample t" tests were used to analyze the differences between the two groups.

Table 1. Demographic data averages of the study and control groups

Variables	Preeclamptic Patient (n = 55)	Control Group (n = 60)
Age (years)	30.16	30.05
Weight (kg)	81.83	79.93
Height (cm)	162.63	159.21
Gravity	2.61	2.73
Parity	1.1	1.26
Living child	1.03	1.16

RESULTS

Table 1 shows the demographic characteristics. Maternal age and demographic characteristics were similar between the study and control groups (Table 1). It was found that the renal artery Doppler PI values of the fetuses of mothers with PE were higher than the control group (2.93 in the patient group, 2.28 in the control group, $p < 0.001$). Week of birth and fetal weight at birth were significantly lower in the PE group ($p < 0.001$). The RI and S/D values of the participants did not differ between the patient and control groups ($p > 0.05$) (Table 2).

DISCUSSION

In the normal physiology of the fetus, the renin-angiotensin system activity is high in early pregnancy, so urine production is low due to high resistance in the renal arteries during early pregnancy. In the later weeks of pregnancy, renal artery resistance decreases due to low renin-angiotensin system activity and this causes an increase in urine production [6, 13].

In PE high systemic vascular resistance and low cardiac output are seen, which causes hypoxia in peripheral tissues and organs. Animal experiments show an increased risk of impaired fetal kidney development due to increased renal vascular tone due to hypoxia, therefore an increase in Doppler values of the fetal renal artery was expected. These changes in the kidney may be the cause of hypertension in both childhood

Table 2. The values belonging to both groups and the analyses

Variables	Preeclamptic Patient (n = 55)	Control Group (n = 60)	*p* value
RI	0.87 (0.67-0.98)	0.85 (0.61-0.99	0.569
PI	2.93 (1.47-3.72)	2.28 (1.43-3.71)	**< 0.001**
Renal arter S/D	9.9 (6.21-21.3)	11.8 (6.3-22.4)	0.083
Birth Weight (g)	1949.47 ± 803.02	2704.9 ± 735.57	**< 0.001**
Week of Birth	34.71 (27-40.28)	37.14 (26.85-41.28)	**< 0.001**

The RI, PI and S/D values belong to fetal renal arteries. RI = Resistance index, PI = pulsatility index, S/D = systolic/diastolic ratio

$p < 0.05$, *Mann Whitney *U* test, ** Independent Sample *t* test

and adulthood of fetuses with PE [9, 11].

Our study is similar to the fact that fetal renal blood flow Doppler indexes are higher in pregnant women with PE compared to normal pregnancy. When PI, RI values and S/D ratios obtained in fetal renal artery Doppler examinations were compared with the control group, an increase was observed in fetal PI values in patients with PE, but no significant difference was found in RI and S/D values.

Our results are also in line with the results of another study, Boubred *et al*. [14] showed that PI indices in the renal arteries increased in the PE animal group compared to the control group. This increase in PI indices is explained as the deterioration of the balance between vasoconstrictive factors and vasorelaxing factors, including the renin-angiotensin system (RAS) and renal sympathetic nervous system [14].

Several other studies have shown similar results to our study and these studies also explained this increase in renal artery tension in PE, the imbalance of vasoconstrictors, and the increased vascular sensitivity to angiotensin II induced by placental hypoxia [15, 16].

Although the pathophysiological mechanisms responsible for PE are not yet known, it has been described in some studies that prenatal hypoxia has a significant effect on PE-mediated blood pressure and that some ion channel activities cause an increase in renal vascular tension [9, 11].

Some studies examining maternal renal artery Doppler indices, such as Sohn and Fendel [17], showed maternal renal artery blood flow velocity in normal and hypertensive pregnancies, and also found an increase in resistance indices compared to normotensive ones as in fetuses.

RI, PI, and S/D values indicate impedance in the vascular bed, the best indicators of resistance in the vascular bed. In our study the finding that only PI was the meaningful indices. However, at the same time, RI and S/D indices are also important in terms of their correlation with arterial pressure. Since PI indicates changes in the total velocity waveform, some studies have described PI as a more relevant index for renal Doppler velocity measurement, but RI and S/D are measured based on two points on the maximum velocity curve [18].

Interstingly, contrary to our results, some studies show reduced renal artery resistance in fetuses of mothers with PE. Like Kaya *et al*. [19], they showed that the renal artery PIs, RIs and S/D ratios were significantly lower in fetuses of mothers with PE ($p < 0.001$ and $p = 0.013$, respectively). In another similar study, Afsari *et al*. [20] reported that renal artery S/D ratio, RI and PI were significantly decreased in the PE group compared to the control group ($p < 0.001$). Ma'ayeh *et al*. [21] showed that renal artery RIs and S/D ratios were significantly lower in the PE group ($p = 0.003$), but they did not show a statistically significant difference in PI. The explanation may highlight these discrepancies, that pregnant women diagnosed with PE had abnormal AF index and fetal growth excluded from these studies, and all participants with PE had normal AF index and fetal weight.

However, many previous studies have shown that patients with PE have a higher incidence of oligohydramnios, and in one study, this was associated with reprogrammed AQP1 (aquaporin 1) expression through a DNA methylation-mediated epigenetic mechanism [22].

In a study conducted with pregnant women with intrauterine growth restriction and oligohydramnios, renal artery Doppler indexes were found to be higher [23], and in another similar study examining fetal renal blood flow in hypoxemia, high renal artery PI due to renal hypoperfusion was shown [24].

Part of the discussion about decreased renal artery resistance may be explained by Platt *et al*. [25], who stated that Doppler indices are affected by the region of the disorder within the kidney, not the degree of renal dysfunction.

It seems that more research is needed to say the end point in the changes caused by PE in the fetal renal vascular bed with Doppler examination measurements.

The strengths of this study are that the Doppler studies were performed by a fetal medicine specialist and the gestational age of the control group was similar.

Limitations

Our study had some limitations. Pregnant women with PE were not differentiated according to mild or severe PE. Peak systolic velocities and renal volume were not studied in this study. In addition, the number of patients was small and the participant's maternal renal artery blood flow rate were not examined.

CONCLUSION

This study suggests that PE increases the resistance of renal arteries in fetuses of mothers with PE, which may contribute critically to kidney disease later in life. A future study investigating renal artery Doppler values for fetuses after delivery may provide important implications for understanding renal vascular blood flow changes in pregnancy complicated by PE.

Authors' Contribution

Study Conception: HAŞ, KA, ÇNE, VM, SG, NB; Study Design: HAŞ, KA, ÇNE, VM, SG, NB; Supervision: HAŞ, KA, ÇNE, VM, SG, NB; Funding: HAŞ, KA, VM; Materials: HAŞ, ÇNE, SG; Data Collection and/or Processing: HAŞ, ÇNE, VM, NB; Statistical Analysis and/or Data Interpretation: HAŞ, VM, NB; Literature Review: HAŞ, KA, VM, NB; Manuscript Preparation: HAŞ, KA, ÇNE, SG and Critical Review: HAŞ, ÇNE, VM.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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