

Doppler Sonography of Uterine Arteries in Pregnancy as a Marker of Preeclampsia

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ABSTRACT

Introduction: Preeclampsia is the cause of increased morbidity in mothers, and mortality and morbidity of both mothers and fetuses and newborns. The pathological process is already complete when the symptoms occur, and nothing concrete can be done to stop the process. Early identification of women at risk of developing preeclampsia is a key goal of antenatal care. Alongside chemical tests, Doppler sonography of the uterine arteries plays a major role in the prediction of preeclampsia.

Aims: To establish the probability of resistance to blood flow in the uterine arteries and the existence of notching in the control and test groups.

Materials and methods: The study comprised 60 subjects in the second trimester of pregnancy who were going for check-ups during their pregnancy or had been hospitalized at the Maternity Clinic of Sarajevo UCC. All the subjects were divided into two groups, a control and a test group, in relation to the presence of pathological blood flow in the uterine arteries. As well as ultrasound results, the patients also provided an exhaustive history about their previous pregnancies, if any, and any relevant laboratory results.

Results: A statistically significant difference was found in the average values of systolic and diastolic pressure during pregnancy between the control and the test group ($p = 0.001$). From an analysis of the resistance to blood flow in the uterine arteries in the control and test groups, we concluded that the flow on the side with the placenta and on the side without the placenta were physiological over five measurements in the control group of subjects. In the test group the largest number of cases of pathological flow were recorded, and there was also notching. Of the 21 subjects with a diagnosis of preeclampsia, there was notching in 10.

Conclusion: Doppler sonography in the second trimester of pregnancy is a good prognostic marker for early discovery of preeclampsia.

Keywords: Doppler sonography, Notch, Preeclampsia.

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INTRODUCTION

Preeclampsia is defined as hypertension after the 20th week of gestation, with one or more of the following symptoms: proteinuria, organ dysfunction (including kidney, liver, hematological or neurological complications), and the presence of fetal growth restriction. It is the cause of increased morbidity in mothers, and mortality and morbidity of both mothers and fetuses, and newborns.¹ Preeclampsia occurs in about 7–10% of pregnancies. The etiology of preeclampsia has still not been completely explained. One of the theories accepted today is that physiological changes to the spiral arteries in the uterus fail to take place in pregnant women with preeclampsia. Anatomically speaking, one uterine artery branches into eight arcuate arteries, which branch into eight radial arteries. Two hundred spiral arteries branch out from the radial arteries. Spiral arteries adapt to pregnancy in physiological conditions, and this adaptation develops during the first and second trimesters.¹ The process of creating normal uteroplacental circulation begins with the process of implantation, when the trophoblast invades the endometrium with the terminal capillary branches of the spiral arteries. There are two separate waves of migration of endovascular trophoblasts into the spiral arteries. The first wave begins during the 2nd month of pregnancy and lasts about 10 weeks. In the first wave of invasion, there are changes to the spiral arteries up to the border between the basal layer of the decidua and the myometrium. The second wave begins between the 14th week and 16th week of pregnancy and lasts for 4–6 weeks. This wave involves the myometrial segment of the spiral arteries, right up to the distal segments of the radial arteries.²

On the basis of this knowledge, Doppler measurements of the uterine blood flow may be used as a screening test and

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increased risk of the development of gestosis and uteroplacental insufficiency may be predicted.² The ultrasound analysis of the blood flow shows reduced resistance of blood flow in the spiral arteries, related to the destruction of the muscle layer of those blood vessels, caused by the invasion of the trophoblasts.³ If this

process is restricted due to the failure of the trophoblast invasion, the uteroplacental circulation remains in a state of high resistance and low flow. On color Doppler, this is reflected in a constant increase in resistance and the appearance of the ultrasound sign of notching. In Doppler sonography notching is defined as a reduction in the speed of blood flow after the systole, below the value of the minimum speed of blood flow at the end of the diastole. The basic problem of this method is that notching is often very difficult to see. The explanation of the phenomenon of notching is also based on the theory of increased resistance in the uterine arteries, where resistance occurs as a result of the incomplete physiological changes in the spiral arteries, which retain their muscle layer, which has the possibility of contraction, and this is directly reflected in the values of blood flow immediately after the systole. Notching cannot be seen in the spiral arteries but is noticed in the uterine arteries in the early diastolic phase of the coronary cycle as the result of the cumulative effect of increased resistance in all or the larger spiral arteries.⁴ The usefulness of color Doppler of the uterine arteries for screening for markers gradually increases in the second trimester.⁴ The reduction in blood flow in the uteroplacental circulation leads to disturbances in other levels of the fetoplacental and fetal circulation. These processes may also be observed, confirmed, and quantified in a noninvasive way using color Doppler ultrasonography.⁵ So far many diagnostic tests have been described that are able to predict potential groups of pregnant women at risk for developing preeclampsia, with varying sensitivity and precision.^{6,7} The great potential of ultrasonography and the advances in Doppler techniques give Doppler sonography a special place in the diagnostics of preeclampsia in the second trimester of pregnancy and analysis of the blood vessels responsible for the occurrence of this pathological condition, and in this way the outcome of pregnancy is improved, with the adoption of timely prophylactic measures.^{8,9} The aim of this research was to determine values of pathological blood flow in the uterine arteries in the second trimester of pregnancy.

MATERIALS AND METHODS

This clinical, retrospective–prospective study was conducted on 60 subjects in the second trimester of pregnancy who were having check-ups during their pregnancy or had been hospitalized at the Maternity Clinic of Sarajevo UCC. All the subjects were divided into two equal groups: the control group (30 subjects) and the test group (30 subjects). The inclusion criteria for the control group were the following: second trimester of pregnancy (after the 20th week of gestation) and physiological results of Doppler sonography of the uterine arteries: physiological values on the side with the placenta (RI = 0.39–0.52) and physiological values on the side without the placenta (RI = 0.37–0.61). The inclusion criteria for the control group were the following: second trimester of pregnancy (after the 20th week of gestation) and pathological results of Doppler sonography of the uterine arteries: pathological values on the side of the placenta (RI \geq 0.53) and physiological values on the side without the placenta (RI \geq 0.62), and verification of the sign of notching. Exclusion criteria for the research were history of hypertension before the 20th week of gestation and information about essential hypertension, chronic cardiovascular and kidney diseases, diagnosis of diabetes mellitus, abortions or premature births, pregnancy with diagnosed epilepsy, or experience of epileptic attacks during the research. At the beginning of the research, on the basis of the results of Doppler sonography of the uterine arteries, the subjects

were included in the research and allocated to one of the two comparative groups that were analyzed during this study. As well as ultrasound results, the patients also gave an exhaustive history about their previous pregnancies, if any, their body mass index (BMI) was analyzed, along with their blood pressure, and they provided any relevant laboratory results. All ultrasound examinations and measurements were conducted using a GE VOLUSON 730 ultrasound machine. Gestational age was verified by confirming the last menstruation date and by first ultrasound examination. During the first examination, an anomaly scan was performed for each pregnant woman as a standard procedure. The most often cause of hospitalization was clinical signs of preeclampsia.

The study was conducted on the basis of the fundamental principles of the Helsinki Declaration (latest revision, October 2013) on the rights of patients included in biomedical research. During the study, the identity and all personal details of the patients were permanently protected, according to the instructions on protection of patients' identity. In order to protect patients' data, each patient individually signed consent to participation in the research and received an identification number that served for statistical processing of data.

The database was created in the Microsoft Office Excel 2013 program, and the data were entered into it from the paper documentation. After verification of the integrity of the data, statistical analysis was performed using the IBM SPSS Statistics v. 20.0 for Windows program. Testing the normality of distribution of continuous numerical variables was performed by studying the histograms and quantile diagrams, and formal testing using the Kolmogorov–Smirnov test. Analysis of category variables was undertaken using the Pearson's χ^2 test or the Fisher's exact test of probability. If the distribution of continuous variables was symmetrical, the arithmetic mean and standard deviation were used to show the mean values and measures of dispersion, and for comparison of those variables parametric tests were used (Student's *t* test). The influence of the analyzed variables is shown through linear regression analysis, and the sensitivity and specificity of each variable is presented as a predictor of disease. The threshold of statistical significance was set at the conventional level of $\alpha = 0.05$.

RESULTS

The study included 60 pregnant women, who were divided into two groups: control ($n = 30$) and test ($n = 30$). There was no statistically significant difference in the age of pregnant women in the control and test groups ($p = 0.449$). There was no significant difference in the parity of pregnant women in the control and study groups ($\chi^2 = 0.287$; $p = 0.395$). In the control group, there were 18 (47.5%) primiparas and 12 (54.5%) multiparas, while in the test group there were 20 (52.6%) primiparas and 10 (45.5%) multiparas. Table 1 shows the flow on the side with the placenta in five measurements in each group. In the control group, it was found that the flows were physiological throughout the research (first measurement 0.46 ± 0.04 ; second measurement 0.44 ± 0.04 ; third measurement 0.41 ± 0.04 ; fourth measurement 0.38 ± 0.03 ; fifth measurement 0.37 ± 0.03). In the test group in the largest number pathological processes were recorded, followed by physiological processes, and there was also notching present. During all the measurements notching was found in two subjects on the side with the placenta. Twenty-one subjects had pathological flow during the first measurement, and 19 subjects during the remaining measurements.

Table 1: Analysis of flow on the side with the placenta in the test group

On the side with the placenta		Physiological flow	Pathological flow	Pathological flow—notching
First measurement	Control group	$n = 30; 0.46 \pm 0.04$		
	Test group	$n = 7; 0.41 \pm 0.04$	$n = 21; 0.62 \pm 0.04$	$n = 2$
Second measurement	Control group	$n = 30; 0.44 \pm 0.04$		
	Test group	$n = 9; 0.44 \pm 0.05$	$n = 19; 0.63 \pm 0.04$	$n = 2$
Third measurement	Control group	$n = 30; 0.41 \pm 0.04$		
	Test group	$n = 9; 0.43 \pm 0.05$	$n = 19; 0.63 \pm 0.05$	$n = 2$
Fourth measurement	Control group	$n = 30; 0.38 \pm 0.03$		
	Test group	$n = 9; 0.40 \pm 0.04$	$n = 19; 0.64 \pm 0.05$	$n = 2$
Fifth measurement	Control group	$n = 30; 0.37 \pm 0.03$		
	Test group	$n = 9; 0.39 \pm 0.04$	$n = 19; 0.61 \pm 0.16$	$n = 2$

Table 2: Analysis of flow on the side without the placenta in the test group

On the side without the placenta		Physiological flow	Pathological flow	Pathological flow—notching
First measurement	Control group	$n = 30; 0.53 \pm 0.06$		
	Test group	$n = 5; 0.53 \pm 0.09$	$n = 18; 0.68 \pm 0.04$	$n = 7$
Second measurement	Control group	$n = 30; 0.51 \pm 0.06$		
	Test group	$n = 8; 0.54 \pm 0.07$	$n = 17; 0.68 \pm 0.04$	$n = 5$
Third measurement	Control group	$n = 30; 0.46 \pm 0.06$		
	Test group	$n = 9; 0.52 \pm 0.06$	$n = 16; 0.69 \pm 0.04$	$n = 5$
Fourth measurement	Control group	$n = 30; 0.43 \pm 0.05$		
	Test group	$n = 8; 0.49 \pm 0.71$	$n = 17; 0.65 \pm 0.08$	$n = 2$
Fifth measurement	Control group	$n = 30; 0.41 \pm 0.04$		
	Test group	$n = 12; 0.49 \pm 0.06$	$n = 12; 0.68 \pm 0.03$	$n = 6$

Table 2 shows the flow on the side without the placenta in five measurements in each group. In the control group, it was found that the flows were physiological throughout the entire research (first measurement 0.53 ± 0.06 ; second measurement 0.51 ± 0.06 ; third measurement 0.46 ± 0.06 ; fourth measurement 0.43 ± 0.05 ; fifth measurement 0.41 ± 0.04). In the test group in the largest number pathological processes were recorded, then physiological processes, and there was also notching present. Eighteen subjects had pathological flow on the first measurement, 17 on the second and fourth measurements, and 16 on the third measurement. At the end of the research, 12 subjects had pathological flow. Notching was present in seven subjects during the first measurement, and five subjects had notching during the second and third measurements, two during the fourth measurement, and six subjects had notching at the end of the research.

Of the total number of subjects in the test group who did not have preeclampsia ($n = 9$), during the analysis of blood flow, no notching was recorded in eight, and notching was found in only one (Fig. 1). Of the 21 subjects with the diagnosis of preeclampsia, no notching was found in 11, but in 10 notching was present, and, using the Chi-square test, a statistically significant difference was established in the frequency of notching in relation to pregnancy with or without preeclampsia ($\chi^2 = 3.875; p = 0.045$) (Table 3).

By a detailed statistical analysis of the presence of notching in subjects in the test group with diagnosed preeclampsia, it was found that the sensitivity of notching was 47.62% and specificity 88.89% (Fig. 2). The prevalence of the disease in subjects with notching in their blood flow was 70%. The positive predictive value of notching as a marker for diagnosis of preeclampsia in the second

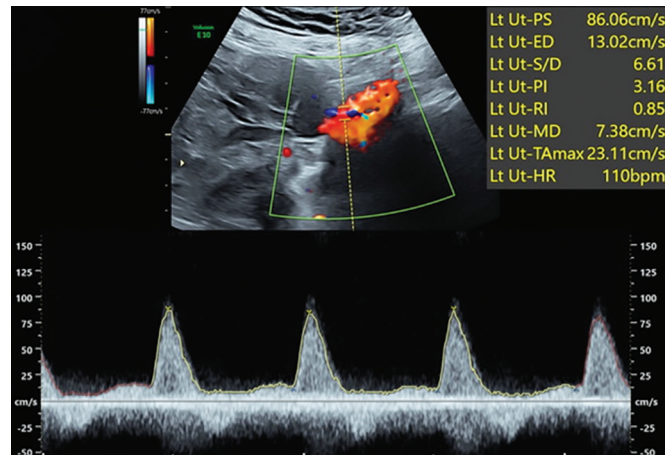


Fig. 1: Doppler of increased flow resistance

trimester is 90.91%, and the negative predictive value is 42.11% (Table 4). The mean BMI of the control subjects at the beginning of the study was $24.05 \pm 3.45 \text{ kg/m}^2$, and in test group $26.68 \pm 3.96 \text{ kg/m}^2$. At the end of the study, the mean BMI of the control subjects was $27.44 \pm 3.84 \text{ kg/m}^2$, and in test group $27.44 \pm 4.02 \text{ kg/m}^2$. By the ANOVA test, a statistically significant difference in BMI values was found between the control and the test group at the beginning of the study ($F = 7.539; p = 0.008$) and at the end of the study ($F = 20.888; p = 0.001$). The control group subjects had normal BMI values at the beginning of the study and high BMI at the end of the study. The subjects of the test group were overweight at the



Table 3: Frequency of pathological flow and notching in patients with and without preeclampsia

		Notching			Total
		No	Yes		
Preeclampsia	No	Number	8	1	9
		%	42.1	9.1	30.0
	Yes	Number	11	10	21
		%	57.9	90.9	70.0
Total	Number	19	11	30	
	%	100.0	100.0	100.0	

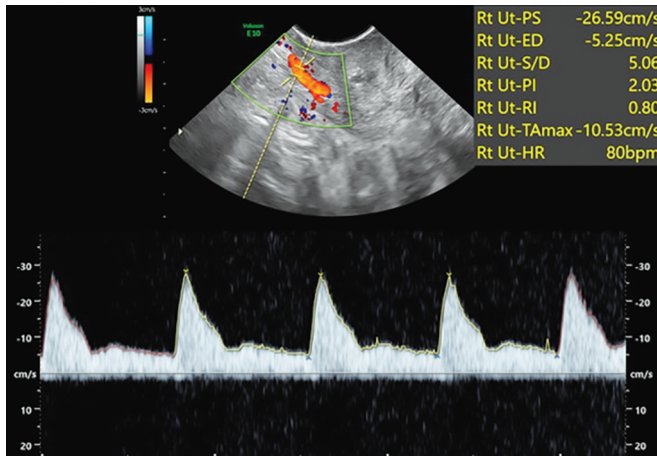


Fig. 2: Doppler with notch

Table 4: Specificity and sensitivity of notching as a marker for early diagnosis of preeclampsia

Statistic	Value (%)	95% CI
Sensitivity	47.62	25.71–70.22%
Specificity	88.89	51.75–99.72%
Disease prevalence	70.00	50.60–85.27%
Positive predictive value	90.91	59.89–98.53%
Negative predictive value	42.11	31.28–53.75%

beginning, and at the end of the study, BMI values were classified as obese pregnant women.

There was statistically significant difference in the average values of systolic pressure during pregnancy compared to the study groups ($F = 64.561; p = 0.001$). The control group subjects had an average systolic pressure value of 111.32 ± 8.28 mm Hg, and the test group subjects had a statistically significantly higher value of 131.90 ± 11.32 mm Hg. There was a statistically significant difference in the average values of diastolic pressure during pregnancy between two groups ($F = 64.685; p = 0.001$). The control group subjects had an average diastolic pressure value of 71.73 ± 4.37 mm Hg, and the test group subjects had a statistically significantly higher value of 84.03 ± 7.14 mm Hg. Analyzing the risk factors for preeclampsia in the study group, it was found that the prevalence of smoking as a risk factor was present in 23.3% in the test group. Preeclampsia in a previous pregnancy was diagnosed in one patient in the test group. Some of the subjects in the test group were treated by antihypertensive therapy and average blood pressure values were lower than expected due to the effect of the therapy used by pregnant women.

By linear regression it was shown that systolic and diastolic pressure are dependent parameters that are indicators of the presence of preeclampsia, while notching was isolated as an independent parameter of the presence of preeclampsia ($B = 0.348; t = 2.221; p = 0.037$) (Table 5).

Of the total number of subjects in the test group, six pregnant women had pathological flow both on the side with the placenta and the side without the placenta, and five of them developed preeclampsia. In 17 subjects pathological flow was established on only one side, and in 10 preeclampsia had developed. The combination of pathological flow on one side and notching on the other was found in six subjects, and in five preeclampsia had developed. One patient had bilateral notching and developed preeclampsia.

In the test group, there were three pregnant women with twin pregnancy and two of them developed preeclampsia. In the control group, there were two pregnant women with twin pregnancy and finally without preeclampsia (Fig. 3).

DISCUSSION

Hypertension in pregnancy is responsible for more than 60,000 maternal deaths around the world each year, and is a complication of 5% of all pregnancies. Pregnancy complicated by preeclampsia leads to increased maternal and perinatal morbidity and mortality.¹⁰ Preeclampsia is a complex illness that occurs in the second half of pregnancy, and it is estimated that it affects almost 4% of pregnancies in the United States. Almost 9% of maternal deaths in the United States are directly ascribed to preeclampsia and eclampsia, and it is the leading cause of premature birth and low birth weight in newborns. Early discovery, using general or high-risk screening methods, may reduce the consequences for health, especially in infants.¹¹ Rough figures on the incidence of preeclampsia between 2002 and 2010 in the regions of the eastern Mediterranean (EMRO) and the western Pacific (WPRO) (WHO regions) were 1.2–4.2%.¹² As was already pointed out in the introduction to this paper, the basic pathomorphological changes to the placenta during preeclampsia occur because of the inadequate migration of trophoblasts and the lack of physiological transformation of the spiral arteries. In contrast to a normal placenta, in preeclampsia the muscular, elastic layer of the spiral arteries remains intact, and as a result their lumen remains narrow throughout the pregnancy, and the walls are sensitive to vasoconstrictive substances.¹³ The spiral arteries are 60% narrower in a pregnant woman with preeclampsia, and the blood flow slows down due to the increased number of curves.¹⁴ The first report of screening for preeclampsia using color Doppler in the second trimester was published by Steel et al.¹⁴ in 1990, on a sample of 1,014 pregnant women at an average gestation of 18 weeks. Of the total number, pathological flow was found in 118 women, where 13% of the pregnant women developed preeclampsia. Although Doppler had been used experimentally in predicting intrauterine growth restriction since the mid-1980s, this was the first study to assess the use of Doppler in predicting preeclampsia. Then in 1994, North et al.¹⁵ identified 27% of subjects in their research who had developed preeclampsia, on the basis of pathological flow values above the 90 percentile, and 83% of them had intrauterine growth restriction and preeclampsia. In 2000, Albaiges et al.¹⁶ conducted research including subjects in the 23rd week of pregnancy in order to analyze color Doppler of the uterine arteries and the presence of notching as a predictive test for preeclampsia. In their results, they report a rate of detection of 90% of patients who developed

Table 5: Linear regression variables that affect the occurrence of preeclampsia

Group	Model		β in	t	Sig.	Partial correlation	Collinearity statistics
							Tolerance
Tested	1	Parity	-0.057	-0.311	0.758	-0.060	0.973
		BMI initial	-0.134	-0.746	0.462	-0.142	1.000
		BMI final	-0.090	-0.498	0.622	-0.095	1.000
		Systolic pressure	0.596	4.059	0.000	0.616	0.948
		Diastolic pressure	0.569	3.809	0.001	0.591	0.958
		Notching	0.266	1.436	0.163	0.266	0.892
	2	BMI initial	-0.131	-0.666	0.511	-0.129	0.862
		BMI final	-0.081	-0.425	0.674	-0.083	0.935
		Systolic pressure	0.663	4.473	0.000	0.659	0.875
		Diastolic pressure	0.584	3.859	0.001	0.603	0.945
	3	Notching	0.314	1.604	0.121	0.300	0.807
		Systolic pressure	0.664	4.201	0.000	0.651	0.831
		Diastolic pressure	0.586	3.721	0.001	0.605	0.922
	4	Notching	0.324	1.558	0.132	0.303	0.758
		Notching	0.348	2.221	0.037	0.428	0.736

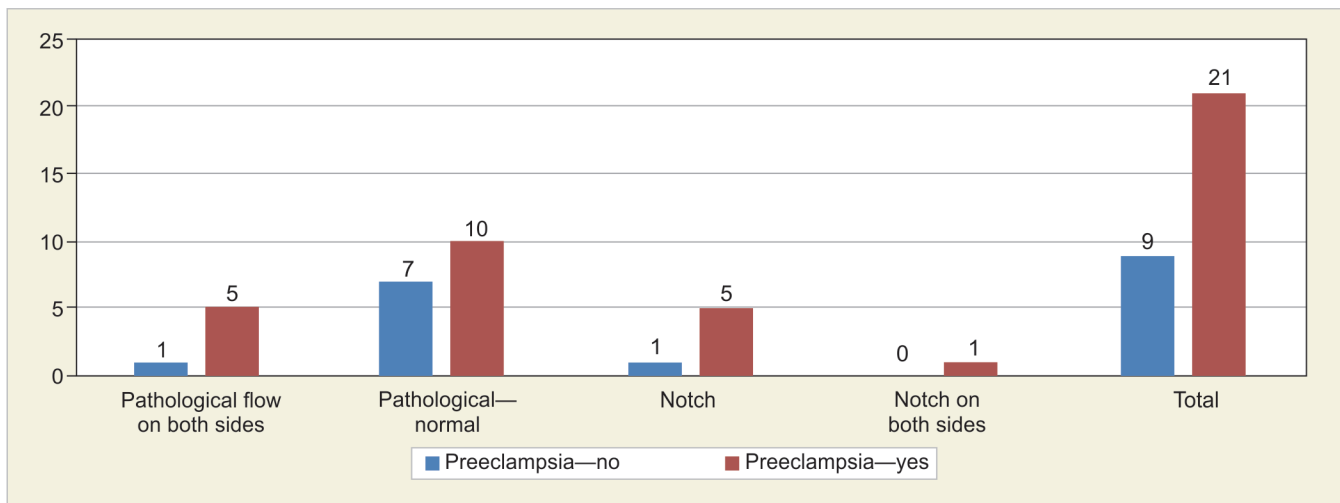


Fig. 3: Relation between Doppler sonography findings and preeclampsia

preeclampsia and 70% of children with intrauterine development. Moreover, 83% fetal deaths and 50% placental disorders were also identified. Further, they explained that the groups with the highest risk were those with severe pathological flow and the presence of notching, who had 40% risk of developing preeclampsia and 45% risk of intrauterine growth restriction. The relative risk of fetal death or undesirable pregnancy outcome before the 34th week in this group was from 50 to 100. In 2008, Yu et al.¹⁷ published the results of the largest screening study using Doppler of the uterine arteries in the second trimester of pregnancy in patients with low risk. In this research, 36% of the pregnant women had pathological values of blood flow in the uterine arteries, and 22% of them developed preeclampsia, with values of pathological flow higher than the 95th percentile. Although the incidence of preeclampsia was higher in nulliparous than in multiparous women (2.6% compared to 1.4%), Doppler of the uterine arteries was equally effective in screening for preeclampsia in both groups.

In our research, by analysis of the flow on the side with the placenta over five measurements in each of the groups tested, we

arrived at the following data: In the control group, it was found that the flows were physiological throughout the entire research (first measurement 0.46 ± 0.04 ; second measurement 0.44 ± 0.04 ; third measurement 0.41 ± 0.04 ; fourth measurement 0.38 ± 0.03 ; fifth measurement 0.37 ± 0.03). In the test group in the largest number pathological processes were recorded, then physiological results, and there was also notching present. In this research, of the total number of subjects in the test group, 19 subjects had pathological flow on the side with the placenta. Of the total number of subjects with pathological flow on the side with the placenta, in 13 preeclampsia developed, while in 6 preeclampsia did not develop. The average value of the pathological flow on the side with the placenta was 0.64 ± 0.04 . The average value of the pathological flow in subjects in the test group who developed preeclampsia was 0.64 ± 0.04 , and in subjects who did not develop preeclampsia, it was 0.61 ± 0.02 . No statistically significant difference was found in the average values of the pathological flow on the side with the placenta between subjects who developed preeclampsia and those who did not ($p = 0.137$). In all the measurements, notching

was found in two subjects on the side with the placenta. Twenty-one subjects had pathological flow during the first measurement, and 19 subjects during the remaining measurements. In analysis of sensitivity and specificity, the study by Bower et al.¹⁸ gave the best results. They had a positive predictive value of 68% for the development of preeclampsia, if notching was noticed during the analysis of blood flow in the uterine arteries. These results have not been confirmed by more recent studies. Conde-Agudelo et al.¹⁹ undertook a prospective study and found average sensitivity for early discovery of preeclampsia of 58%, and specificity of 73%, but even these values did not completely satisfy the criteria for acceptance of the Doppler technique as the only and most reliable diagnostic method in the early discovery of preeclampsia. A meta-analysis conducted in 2008 confirmed that it was better to perform color Doppler of the uterine arteries in the second trimester than in the first, and that it reaches its maximum usefulness in identification of serious early-onset preeclampsia. In women at low risk, higher resistance index (RI) in the uterine arteries in the second trimester had sensitivity of 78% and specificity of 95% for discovery of serious preeclampsia (a positive probability ratio of 15.6 and a negative one of 0.23).²⁰ Plasencia et al.,²¹ in their cohort study of 3,107 women at high and low risk for development of preeclampsia, analyzed color Doppler of the uterine arteries in two time periods. The first was between 11 and 13 + 6 weeks of pregnancy and the second between 21 weeks and 24 weeks of pregnancy. Abnormal flow in the uterine arteries was detected in 94% of patients who developed early preeclampsia, and in 74% of those who developed late preeclampsia. A total of 37% of pregnant women who had abnormal values on Doppler sonography in the first and second trimesters did not develop preeclampsia. The combination of Doppler and the mother's positive history increased the rate of detection of early preeclampsia to 90.9% and 100%, with a false-positive rate of 5 and 10%, respectively. Prajapati et al.²² also asserted that Doppler of the uterine arteries in the second trimester of pregnancy is a useful method for identification of preeclampsia. In their research, in which 200 pregnant women took part (at 22 – 24 + 6 weeks of pregnancy), they found that pathological flow was found statistically significantly more in patients with preeclampsia, which correlates with the results of our research. The mean value of pathological flow was significantly higher in subjects with a negative pregnancy outcome than the mean value in subjects who had a normal pregnancy outcome, with $p < 0.000$. The results are also in correlation with those of Jamal et al.²³ In the research by Pongrojapaw et al.,²⁴ Doppler screening of the uterine arteries was conducted as part of regular examinations during the middle trimester, between 20 weeks and 24 weeks, in women at high risk, at the Maternal and Foetal Medicine Unit of the University Hospital of Thammasat, in the period from 2008 to 2009. A total of 330 women took part in the research. Of the total number, 27 (8.18%) developed preeclampsia, and 16 (4.84%) had babies with low birth weight. The sensitivity of pathological flow in the uterine arteries and the presence of notching as a test for preeclampsia was 59.25%, and specificity was 66.67%.

CONCLUSION

Using Doppler sonography, especially in the period when physiological changes to the spiral arteries take place, is a relatively quick, pain-free and cheap way to determine resistance to blood flow in the uterine arteries, and to raise suspicion of preeclampsia already in the second trimester. In line with our results, women

with pathological blood flow values in their uterine arteries may be categorized in the group of pregnant women with risky pregnancies, and therefore supervision should be increased of these women and their babies to prevent later manifestations and complications from hypertensive disease.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms.

REFERENCES

1. Di Lorenzo G, Ceccarello M, Cecotti V, et al. First trimester maternal serum PIGF, free β -hCG, PAPP-A, PP-13, uterine artery Doppler and maternal history for the prediction of preeclampsia. *Placenta* 2012;33(6):495–501. DOI: 10.1016/j.placenta.2012.03.003.
2. Hafner T, Kurjak A, Kupešić S. Dopplerska mjerenja uteroplacentnog krvotoka. In: Kurjak A, ed. *Ultrazvuk u ginekologiji i porodništvu*. Zagreb: Art studio Azinović; 2000. pp. 383–385.
3. Kurjak A, Kupesic S, Hafner T, et al. Conflicting data on intervillous circulation in early pregnancy. *J Perinat Med* 1997;25(3):225–236. DOI: 10.1515/jpme.1997.25.3.225.
4. Woschitz MC, Idris T, Csapo B, et al. Uterine artery Doppler in women with history of previous preeclampsia and women with chronic hypertension: re-evaluation of a prognostic value in a high-risk population. *Gynecol Obstet (Sunnyvale)* 2014;4:206.
5. Srikanth S, Debnath J, Ravikumar R, et al. Doppler indices of the umbilical and fetal middle cerebral artery at 18–40 weeks of normal gestation: a pilot study. *Med J Armed Forces India* 2017;73(3):232–241. DOI: 10.1016/j.mjafi.2016.12.008.
6. Bibbins-Domingo K, Grossman DC, Curry SJ, et al. Screening for preeclampsia: US preventive services task force recommendation statement. *JAMA* 2017;317(16):1661–1667. DOI: 10.1001/jama.2017.3439.
7. Kandasamy Y, Watson D, Rudd D. Biomarker of early glomerular injury in pre-eclampsia. *Hypertens Pregnancy* 2015;34(4):391–399. DOI: 10.3109/10641955.2015.1065883.
8. Fareeha A, Hidayat U, Mashkoo A. Predictor of pre-eclampsia with uterine artery Doppler. *Pak Armed Forces Med J* 2016;66(6):886–890.
9. Sharma S, Singh S, Gujral U, et al. Uterine artery notching on color Doppler ultrasound and roll over test in prediction of pregnancy induced hypertension. *J Obstet Gynaecol India* 2011;61(6):649–651. DOI: 10.1007/s13224-011-0110-z.
10. Tranquilli AL, Dekker G, Magee L, et al. The classification, diagnosis and management of the hypertensive disorders of pregnancy: a revised statement from the ISSHP. *Pregnancy Hypertens* 2014;4(2):97–104. DOI: 10.1016/j.preghy.2014.02.001.
11. Henderson JT, Thompson JH, Burda BU, et al. Screening for Preeclampsia: A Systematic Evidence Review for the U.S. Preventive Services Task Force. Rockville (MD): Agency for Healthcare Research and Quality (US); 2017. (Evidence Synthesis, No. 148), available from: <https://www.ncbi.nlm.nih.gov/sites/books/NBK447462/>.
12. Abalos E, Cuesta C, Grosso AL, et al. Global and regional estimates of preeclampsia and eclampsia: a systematic review. *Eur J Obstet Gynecol Reprod Biol* 2013;170(1):1–7. DOI: 10.1016/j.ejogrb.2013.05.005.
13. Kattah AG, Garovic VD. The management of hypertension in pregnancy. *Adv Chronic Kidney Dis* 2013;20(3):229–239. DOI: 10.1053/j.ackd.2013.01.014.
14. Steel SA, Pearce JM, McParland P, et al. Early Doppler ultrasound screening in prediction of hypertensive disorders of pregnancy. *Lancet* 1990;335(8705):1548–1551. DOI: 10.1016/0140-6736(90)91376-L.
15. North RA, Ferrier C, Long D, et al. Uterine artery Doppler flow velocity waveforms in the second trimester for the prediction of preeclampsia and fetal growth retardation. *Obstet Gynecol* 1994;83(3):378–386.
16. Albaiges G, Missfelder-Lobos H, Lees C, et al. One-stage screening for pregnancy complications by color Doppler assessment of the uterine

- arteries at 23 weeks' gestation. *Obstet Gynecol* 2000;96(4):559–564. DOI: 10.1016/S0029-7844(00)00946-7.
17. Yu CK, Khouri O, Onwudiwe N, et al. Prediction of pre-eclampsia by uterine artery Doppler imaging: relationship to gestational age at delivery and small-for-gestational age. *Ultrasound Obstet Gynecol* 2008;31(3):310–313. DOI: 10.1002/uog.5252.
 18. Bower S, Schuchter K, Campbell S. Doppler ultrasound screening as part of routine antenatal scanning: prediction of preeclampsia and intrauterine growth retardation. *Br J Obstet Gynecol* 2000;100(11):989–994. DOI: 10.1111/j.1471-0528.1993.tb15139.x.
 19. Conde-Agudelo A, Lede R, Belizan J. Evaluation methods used in the prediction of hypertensive disorders of pregnancy. *Obstet Gynecol Surv* 2008;49(3):210–222. DOI: 10.1097/00006254-199403000-00027.
 20. Kane SC, Da Silva Costa F, Brennecke SP. New directions in the prediction of pre-eclampsia. *Aust N Z J Obstet Gynaecol* 2014;54(2):101–107. DOI: 10.1111/ajo.12151.
 21. Plasencia W, Maiz N, Poon L, et al. Uterine artery Doppler at 11 + 0 to 13 + 6 weeks and 21 + 0 to 24 + 6 weeks in the prediction of pre-eclampsia. *Ultrasound Obstet Gynecol* 2008;32(2):138–146. DOI: 10.1002/uog.5402.
 22. Prajapati SR, Maitra N. Prediction of pre-eclampsia by a combination of maternal history, uterine artery Doppler, and mean arterial pressure (a prospective study of 200 cases). *J Obstet Gynaecol India* 2013;63(1):32–36. DOI: 10.1007/s13224-012-0239-4.
 23. Jamal A, Abbasalizadeh F, Vafaei H, et al. Multicenter screening for adverse pregnancy outcomes by uterine artery Doppler in the second and third trimester of pregnancy. *Med Ultrason* 2013;15(2):95–100. DOI: 10.11152/mu.2013.2066.152.aj1fa2.
 24. Pongroj paw D, Chanthasenanont A, Nanthakomon T. Second trimester uterine artery Doppler screening in prediction of adverse pregnancy outcome in high risk women. *J Med Assoc Thai* 2010;93(Suppl 7):S127–S130.