Original Paper

The Role of Uterine Artery Doppler in the Second and Third Trimesters for Prediction of Preeclampsia and Fetal Growth Restriction Developed as a Consequence of Placental-Mediated Diseases

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ABSTRACT: Placenta-mediated pregnancy disorders represent a disease that includes preeclampsia (PE) and the birth of small for gestational age (SGA) children, these conditions increase the risk of mortality and morbidity both maternal and fetal/neonatal, in the short and long-term. Methods: The prospective study included 106 patients in whom ultrasound Doppler scans of uterine artery (UtA) were performed in the 2nd trimester between 20.0-23.6 weeks of gestation and the 3rd trimester between 28.0-32.6 weeks of gestation. Results: In the second trimester, the average of the UtA-PI percentiles was statistically significant ($p < 0.05$) in correlation with PE and SGA, as in the third trimester. Statistically significant ($p < 0.05$) was also the correlation of UtA-PI >95 percentile with the development of PE and SGA. On the other hand, the present notch, in the two trimesters studied, analyzed as a single index, did not present a statistically significant association ($p > 0.05$). Conclusions: The results of our study showed that UtA-PI Doppler is the best predictor of preeclampsia considering the association of intrauterine growth restriction, as most studies have found.

KEYWORDS: Doppler ultrasonography, UtA, PE, SGA

Introduction

Placenta-mediated pregnancy disorders represent a disease that includes preeclampsia and fetal growth restriction [1,2].

Considering that these conditions increase the risk of mortality and morbidity both maternal and fetal/neonatal, in the short and long term, early prediction of these disorders is necessary.

Since two decades ago, Doppler ultrasound analysis of the uterine artery, as a non-invasive routine procedure, in the second and third trimesters of pregnancy has been proposed as a predictive test for adverse pregnancy outcomes in high-risk pregnancies [3].

Doppler of the uterine artery is closely related to placental function and therefore placental dysfunction, even the subclinical one, could be detected quite early [4].

The presence of a placental development abnormality, characteristic of preeclampsia and intrauterine growth restriction induces an insufficient uteroplacental blood flow, due to the lack of transformation of the arteries into arterial vessels with low resistance.

This is a consequence of the fact that the trophoblastic invasion of the decidual portion of the spiral arteries should occur by the twelfth week, followed by the trophoblastic invasion of the myometrial portion of the spiral arteries, which ends by 18-19 weeks, but it can extend up to 24 weeks of pregnancy [5].

Insufficient trophoblast invasion after 24 weeks of pregnancy is manifested by low diastolic velocities and the presence of an early and persistent protodiastolic notch after 24 weeks, so that the uterine artery remains the most correct indirect indicator of the utero-placental vascular bed.

The increase in blood flow resistance in the uterine arteries is associated with the onset of preeclampsia and intrauterine growth restriction,

as studies from the last three decades have shown [6,7].

The purpose of this study was to show the importance of using uterine artery Doppler in the routine prenatal consultation of pregnant women, both in the second trimester, but also in the third trimester, by correlating abnormal uterine artery Doppler values with adverse pregnancy outcomes, represented by preeclampsia and small for gestational age.

Materials and Methods

This prospective study, which included 106 patients, was carried out in the Clinical Hospital "Filantropia" Craiova in the Obstetrics and Gynecology Department, between January 2018-May 2022.

The patients included in the study were divided into a group that developed placental-mediated disease (76 patients with PE and SGA) and a control group consisting of 30 patients who had a normal pregnancy.

Ultrasound Doppler scans of uterine artery (UtA) were performed in the 2nd trimester between 20.0-23.6 weeks of gestation and the 3rd trimester between 28.0-32.6 weeks of gestation.

With the acceptance of participation in the study, the patients benefited from a detailed anamnesis and a complete clinical examination.

Only singleton pregnant women were included in the study.

Preeclampsia was defined as the onset of hypertension and proteinuria after 20 weeks of gestation. To assess SGA, we used estimated fetal weight (EFW) below the 10th percentile.

All patients received detailed information about the study and signed an informed consent.

The study was carried out in accordance with the Declaration of Helsinki regarding patients' rights, the study receiving the approval of the Ethics Committee of the University of Medicine and Pharmacy of Craiova.

Statistical Analyses

The statistical analysis was performed in the Department of Biostatistics, University of Medicine and Pharmacy of Craiova.

We used a Student's T-test and an ANOVA analysis, as well as the Fisher exact test of parameters for a comparison of differences between study groups.

Data were presented as mean±standard deviation (SD).

The result was significant at $p < .05$ considered as an acceptable level of statistical significance.

Results

A prospective study was conducted for 106 patients with single pregnancy, in the second trimester (20.0-23.6 weeks of gestation) and the third trimester (28.0-32.6 weeks of gestation).

Maternal age in the two studied groups was approximately the same, 28.5±6.25 years in the control group and 28.4±6.2 years in the group with PE/SGA.

Table 1. Risk factors in the studied groups.

Group	Nulliparity	Previous PE	Previous SGA	Essential hypertension	Previous stillbirth	Gestational diabetes
Control group (n=30)						
Yes	11	3	2	1	2	1
No	19	27	28	29	28	29
Report	37	10	7	3	7	3
PE/SGA group (n=76)						
Yes	41	16	9	6	7	6
No	35	60	67	70	69	70
Report	54	21	12	8	9	8
	*The chi-square statistic is 2.5702. The p-value is .108894. The result is **not significant** at p< .05.*	*The chi-square statistic is 1.7861. The p-value is .181405. The result is **not significant** at p< .05.*	*The chi-square statistic is 0.6195. The p-value is .431245. The result is **not significant** at p < .05.*	*The chi-square statistic is 20.8352. The p-value is < .00001. The result is **significant** at p < .05.*	*The chi-square statistic is 0.1791. The p-value is .672106. The result is **not significant** at p < .05.*	*The chi-square statistic is 0.7256. The p-value is .394309. The result is **not significant** at p< .05.*

In the second trimester, between 20.0-23.6 weeks of gestation, calculating the mean values of the two uterine arteries in percentiles, we noticed lower values of the mean blood flow impedance in the control group, 25.3 percentiles, compared to 53.1 percentiles in the group with complications.

Also, mean values of PI in the two uterine arteries were lower in the control group, 0.9 and 0.8, compared to the group with complications, 1.1 in both arteries, right and left (Table 2).

These changes in the velocity of the uterine arteries were statistically significant, so the Doppler measurement of the uterine arteries is recommended to detect the risk of complications.

Table 2. Statistical correlation of mean Doppler UtA in the second trimester in the two groups.

	Left UtA-RI a	Left UtA-PI	Right UtA-RI	Right UtA-PI	Mean UtA-PI (percentiles)
Mean UtA	0.6	1.0	0.6	1.0	45.8
Control group					
Mean	0.5	0.9	0.5	0.8	25.3
SD	0.1	0.3	0.1	0.2	26.8
Maximum	0.7	1.8	0.7	1.4	92.0
Minimum	0.4	0.4	0.3	0.4	0.5
PE/SGA group					
Mean	0.6	1.1	0.6	1.1	53.1
SD	0.1	0.4	0.1	0.3	38.2
Maximum	1.2	2.3	1.1	1.7	99.0
Minimum	0.4	0.4	0.4	0.7	3.0
p<0.001	**p=0.000**	**p=0.007**	**p=0.001**	**p=0.000**	**p=0.000**

We wanted to see what is the role of abnormal UtA-PI, i.e. values >95 percentile, on the induction of SGA or PE.

In the second trimester, we met only 13 cases with the pulsatility index >95 percentile in the two groups (Figure 1).
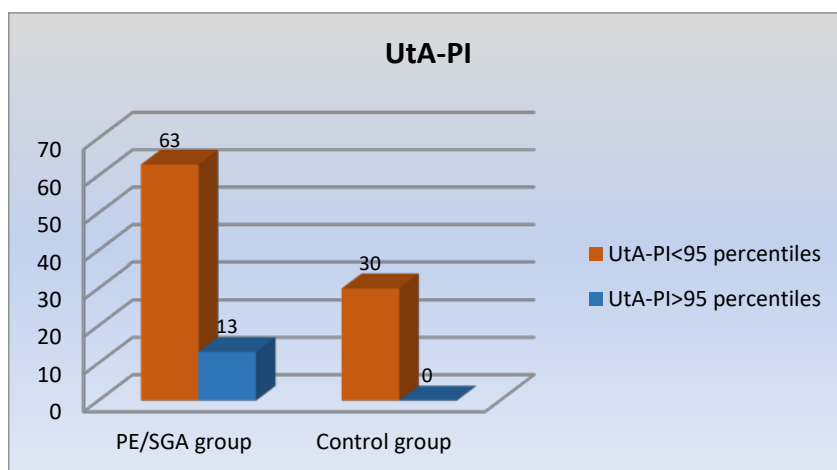

Figure 1. UtA-PI in the two study groups in the second trimester.

We found that the mean value of UtA-PI<95 percentiles was 44.73±36.03 SD in the group that developed PE and/or SGA, compared to 22.86±26.49 SD in the control group (Table 3).

Table 3. Statistical significance of UtA-PI>95 percentiles in the second trimester.

	PE/SGA group (Media±SD)	Control group (Media±SD)
UtA-PI<95 percentiles	44.73±36.03	22.86±26.49
UtA-PI>95 percentiles	97.30±1.37	0
The Fisher exact test statistic value is 0.0177. The result is significant at p <.05.		

But also, the statistical correlation of the involvement of UtA-PI>95 percentile in predicting the risk of installation of PE and/or SGA was statistically significant, p<0.05 (Table 4).

Table 4. Statistical correlation of UtA-P with the development of PE and SGA in the second trimester.

	Pregnancy Normal development	PE	SGA
UtA-PI <95 percentiles	30	19	44
UtA-PI >95 percentiles	0	12	1
The Fisher exact test statistic value is 0. The result is significant at p <.05.			

Like UtA-PI, notch incidence decreases after 24 weeks of pregnancy and remains stable.

The diastolic notch present after this gestational age is a manifestation of the abnormal uterine vascular tension and the increase in uterine artery impedance.

Table 5. The statistical significance of UtA Notch in the two groups in the second trimester.

Lot	Right UtA Notch	Left UtA Notch
Control group		
No	25	26
Yes	5	4
Report		
PE/SGA group		
No	55	60
Yes	21	16
Report		
	*The Fisher exact test statistic value is 0.3186. The result is **NOT** significant at p < .05.*	*The Fisher exact test statistic value is 0.4221. The result is **NOT** significant at p < .05.*

As noted, (Table 5), the number of cases in the control group was lower than in the group with complications.

But considering that the measurements were performed at gestational ages below 24 weeks, these measurements were not statistically significant in any group (p>0.05), we only created a risk group, which required more intense monitoring.

This, because up to 22-24 weeks of pregnancy, the presence of a notch is not permanent, it may disappear after this gestational age.

We also analyzed the same parameters in the third trimester to see if abnormal uterine artery Doppler maintains its ability to predict adverse late pregnancy outcomes.

Table 6. The statistical correlation of the mean Doppler UtA in the third trimester in the two groups.

	Right UtA-PI	Right UtA-RI	Left UtA-PI	Left UtA-RI	Mean UtA-PI (percentiles)
Mean UtA-PI	0.9	0.6	0.9	0.6	62.9
Control group					
Mean	0.8	0.5	0.7	0.5	43.9
SD	0.2	0.1	0.3	0.1	29.6
Maximum	1.4	0.7	1.5	0.7	98.0
Minimum	0.6	0.4	0.5	0.4	8.0
PE/SGA group					
Mean	1.0	0.6	1.0	0.6	71.3
SD	0.2	0.1	0.4	0.1	28.3
Maximum	1.4	0.8	1.9	0.9	99.0
Minimum	0.5	0.3	0.4	0.4	4.0
p<0.05	p=0.000	p=0.000	p=0.000	p=0.000	p=0.000

So, the UtA Doppler evaluation can be useful in the third trimester as well, for predicting adverse pregnancy outcomes.

We performed the statistical analysis of UtA in the two groups studied, considering that the abnormal values refer to the Pulsatility Index >1.23 and the presence of notch and we found a significant statistical correlation, p<0.05 (Table 7).

Table 7. Statistical correlation between abnormal vs. normal UtA in the third trimester.

UtA Doppler	PE/SGA group	Control group
Normal	52	30
Abnormal	24	0
*The Fisher exact test statistic value is 0.0002. The result is **significant** at p < .05.*		

A statistical correlation between the presence/absence of a notch on the right UtA, did not show a significant statistical difference between this parameter and the installation of PE or SGA, even if the notch was present in 19 cases in the group with complications, compared to 3 cases in the control group.

Table 8. Statistical correlation of cases with a notch on the right UtA.

Right UtA notch	PE/SGA group	Control group
Notch (-)	57	27
Notch (+)	19	3
*The Fisher exact test statistic value is 0.1157. The result is **NOT** significant at p < .05.*		

Even at the level of the left UTA, we did not find a significant statistical correlation between the presence/absence of a notch on the right UTA, between this parameter and the installation of PE or SGA, even if the notch was present in 16 cases in the group with complications, compared to 4 cases in the control group.

Discussion

The studies carried out in the last decades have confirmed the increase in blood flow resistance in the uterine arteries in patients who developed preeclampsia or SGA, Doppler ultrasonography of the uterine arteries being the most reliable indicator of the bed of the spiral artery [6,8,9].

For a good pregnancy evolution, a perfect vascular adaptation between the maternal and fetal circulation is vital.

Doppler screening of the uterine artery is used in clinical practice due to its easy access, its non-invasive appearance and last but not least due to the possibility of selecting a population at risk.

This selection of a risk group can help clinicians for the purpose of more frequent monitoring, all of which being beneficial for both the mother and the fetus.

Although uterine artery Doppler is used for screening mainly in the second trimester of pregnancy, a number of studies have shown that uterine artery Doppler can also be useful in the third trimester to predict a perinatal complication [10,11].

So that in accordance with this, our objective was to compare the follow-up of the Doppler role of the uterine artery in the two trimesters.

In our study, in the second trimester, the mean PI values in the two uterine arteries were lower in the control group, compared to the group with complications.

But these changes in the velocity of the uterine arteries were statistically significant, so the Doppler measurement of the uterine arteries is recommended to detect the risk of complications.

In the third trimester, a high statistical significance is maintained between the analyzed parameters, so the examination of the uterine arteries can be used also in the third trimester, for suspected late-onset small-for-gestational-age fetuses and late-onset preeclampsia, as other studies have shown [12,13].

But the recommendation is that the uterine artery Doppler in the third trimester should be used in combination with other tests for a correct clinical decision [14].

Cnossen et al. [15] showed in a systematic review and bivariable meta-analysis, that the pulsatility index and bilateral notch represent the most indicated Doppler indices for detecting the mentioned complications, even if previous studies were hesitant with the prediction of preeclampsia and growth intrauterine restriction by using uterine artery Doppler [16,17].

An abnormal Doppler at the level of both uterine arteries, UtA-Pi >95 percentile or a uni/bilateral notch in the second trimester represents an increased risk of developing severe adverse outcomes, including preeclampsia and SGA.

It seems that pregnant women with a bilateral notch would have a higher risk of increased maternal and fetal morbidity, compared to those with a unilateral notch [9,18].

In our study, we analyzed the pulsatility index of the uterine artery and the presence of the notch, both as individual indicators and taken together.

We found that analyzed together, the Pulsatility Index and the presence of uni/bilateral notch presented a strong statistical significance ($p<0.05$) in both trimesters studied, while the notch analyzed as an individual indicator did not present any statistical significance ($p>0.05$) in none of the two trimesters of pregnancy studied.

This makes us note that the presence of a notch as a single indicator does not have a significant association, although most preeclamptic women present a uni/bilateral notch.

Even if UtA-PI remains the strongest predictor for placenta-mediated diseases both in the second and third trimesters, a series of studies consider that the uterine artery notch is not an index to be neglected [19].

Conclusions

The results of our study showed that PI Doppler of the uterine artery is the best predictor of preeclampsia and considering the association also for intrauterine growth restriction, as found by most studies.

Conflict of interests

None to declare

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