

Doppler Uterine Artery Ultrasound in the Second Trimester of Pregnancy to Predict Adverse Pregnancy Outcomes

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ABSTRACT: Purpose. To determine in uterine artery (UtA) the mean pulsatility index (PI), systolic/diastolic (S/D) ratio and the presence/absence of notch in the second trimester of pregnancy, with normal or abnormal pregnancy outcome. Material and Methods. We performed an analysis of 135 cases with high risk pregnancy in Obstetrics and Gynecology Department of The Municipal Hospital Filantropia, Craiova, between October 2016 and May 2020. The ultrasound evaluation in the second trimester was performed during the second trimester morphology scan, or after this, but up to 24 weeks of pregnancy. Results. The study showed only in the case of early preeclampsia (PE) a statistical significance for mean PI-UtA percentiles in the second trimester. In the other studied categories of pregnancy outcome, even we did not have a statistical significance, we found a specificity of 75% and positive predictive value of 88.89% in late PE. The presence of notch in the second trimester was statistically significant (p value <0.05) in the case of premature birth (PB) and early PE. A positive predictive value of 77.50% we found only in case of late PE. Conclusions. Our results show that routine Doppler screening of the uterine arteries during the second trimester did not make an accurate prediction of fetal growth restriction, preeclampsia or preterm birth. However, we believe that the present study results prove that this screening may select a population with increased risk of adverse outcome, which would give them the opportunity to benefit from an early intervention.

KEYWORDS: Pregnancy, high risk, Doppler.

Introduction

With the use of the Doppler technique, which is a non-invasive method of indirect assessment of uteroplacental circulation, a potential screening has been reached for the early detection of a possible preeclampsia or severe fetal growth restriction.

The normal course of pregnancy is characterized by increased diastolic blood flow velocity and diastolic notch loss in the second trimester of pregnancy, around the gestational age of 22 weeks. Pregnancy with persistent notch and increased blood flow resistance may have a high risk of premature birth, preeclampsia, and intrauterine growth restriction [1,2].

The trophoblastic invasion of the spiral arteries, which begins in early pregnancy and ends in the second trimester of pregnancy, is a necessary physiological phenomenon, because these arteries are thus transformed into larger vessels that have a lower resistance by losing the musculoskeletal structure [3].

When this trophoblastic invasion does not occur, there is a status of increased vascular resistance and implicitly a low blood flow in the utero-placental circulation, with the possibility of preeclampsia or fetal growth restriction [4,5].

The purpose of this study was to determine mean pulsatility index (PI), systolic/diastolic (S/D) ratio and the presence/absence of notch in the second trimester of pregnancy, with normal or abnormal pregnancy outcome. In this study, we have investigated and the predictive value of uterine artery Doppler for the identification of adverse pregnancy outcomes, specially preterm delivery, preeclampsia (PE) and small for gestational age (SGA).

Materials and Methods

This prospective study included a group of 135 patients, studied between October 2016 and May 2020, in the Obstetrics and Gynecology Clinic of the Craiova Municipal Hospital "Filantropia".

Patients were recruited from pregnant women with risk factors for the high-risk pregnancy category, based on inclusion and exclusion

criteria. The ultrasound evaluation in the second trimester was performed during the second trimester morphology scan, or after this event, up to 24 weeks of pregnancy. The patients signed a written informed consent regarding their participation in the study, and the protocol was approved by the Ethics Committee of the University of Medicine and Pharmacology of Craiova.

Doppler velocimetry of the uterine artery was routinely performed for women with high-risk pregnancies, and the uterine artery was identified transabdominally in the lower quadrant of the abdomen, 1cm from the level of the apparent intersection of the uterine and iliac vessels. Doppler parameters were automatically calculated by at least three consecutive values. All ultrasonographic parameters from high-risk pregnancies were statistically analyzed and correlated with the subsequent evolution of pregnancy in the third trimester.

The statistical assessment was carried out in part in Excel (Microsoft, USA) and in part in Matlab (Mathworks, USA). Several statistic descriptors were computed on incidence tables: count, sensitivity, specificity, positive predictive value, and negative predictive value. Since all available data was categorical for statistical significance we used the Chi-square test.

Whenever the requirements for the Chi-square test were not fulfilled Fisher's exact test was used. A p value less than 0.05 was considered statistically significant for all tests performed.

Results

The Doppler ultrasonographic parameters analyzed were mean pulsatility index, S/D ratio of the two uterine arteries and the presence/absence of notch, in correlation with the evolution of pregnancy in the third trimester and their predictive role.

Pregnant patients were assigned according to the complication that occurred in the third trimester of pregnancy, as follows:

- 33 pregnant women with PE
- 31 pregnant women with SGA
- 14 pregnant women with SGA associated with PE
- 26 low-risk pregnant women, considered as the control group

45 pregnant women selected from all these categories of pregnant women with complications, gave birth prematurely (Figure 1).

The common element of these cases was the inclusion in the high-risk pregnancy group, according to the specialized classifications.

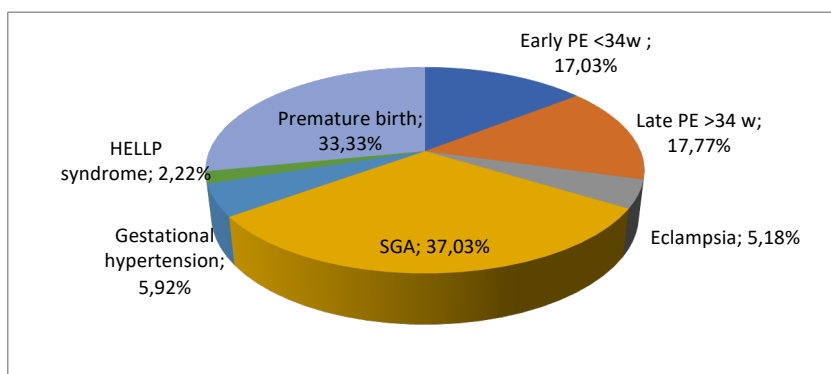


Figure 1. Adverse pregnancy outcome in high risk pregnancy.

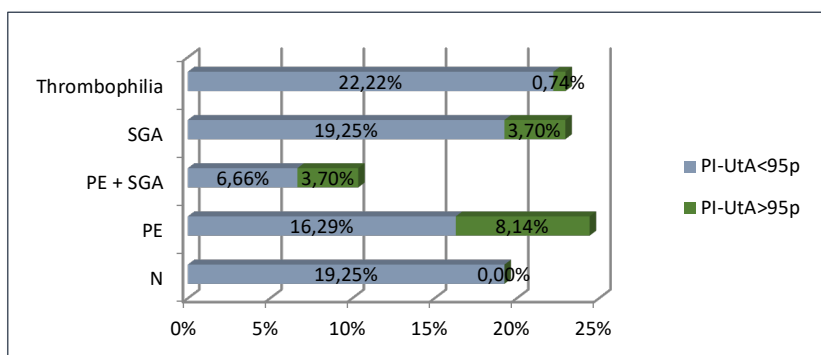


Figure 2. Mean PI-UtA (percentiles) in the second trimester.

The pulsatility index (PI) is currently the most commonly used index for evaluating UtA Doppler waveforms. The highest percentage of abnormalities of the pulsatility index (PI-UtA > 95 percentiles) was found in cases with preeclampsia (8.14%), followed by cases with SGA and PE associated with SGA, 3.70% each (Figure 2).

There was a statistical correlation of PI-UtA mean in the second trimester of the entire study group with adverse pregnancy outcome (Fisher's Exact test $p < 0.001$). Thus, PI-UtA correlates statistically significant with adverse pregnancy outcome. The study showed only in the case of early PE a statistical significance (Fisher's Test $p = 0.0255$) for the presence of mean PI-UtA > 95 percentiles in the second trimester. In the late PE category, although we did not have a statistical significance (Fisher's Test $p = 0.0949$), we found

a specificity of 75% and a positive predictive value (PPV) of 88.89%. In the rest of the studied categories, the values obtained were not statistically significant: in the premature birth category we had Fisher's Test p-value of 0.1290 and SGA cases presented Fisher's Test p-value of 0.4516. We also had no predictive significance in the presence of mean PI-UtA > 95 percentiles (Table 1).

Systolic/diastolic ratio of flow velocities was measured as a peripheral resistance index. In pregnancy with normal evolution, the UtA-S/D ratio remained constant between 1.8 to 1.9.

Therefore, we considered as abnormal values, the values > 1.8 of the UtA-S/D ratio. We found the abnormal values in all the studied categories, the highest incidence being found in cases with PE, 9.62% and in cases with SGA, 8.14% (Figure 3).

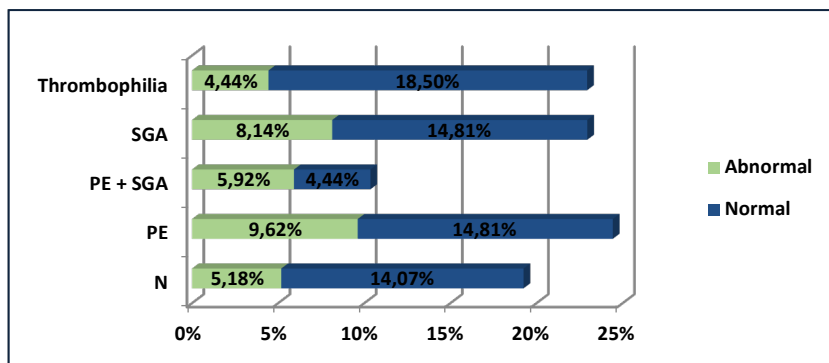


Figure 3. S/D right UtA/S/D left UtA ratio in the second trimester.

The statistical correlation of S/D-UtA ratio of all the cases in the second trimester with the respective pathology, we found that the statistical chi-square is 7,388, the p-value is .116752. The result is not significant at $p < .05$. Such as, in our study, S/D-UtA ratio in the second trimester, did not have a statistical significance (chi-square statistic $p > 0.05$) for adverse outcome of pregnancy (Table 1).

However, abnormal S/D ratio had a relatively good specificity (70%) in case of premature

birth and a negative predictive value (NPV) in case of early and late PE of 81.11% and 85.56% respectively. But, the relatively low positive predictive values limit the predictive utility of this test.

Notching noted in Doppler ultrasound at 18-24 weeks was significantly associated with adverse pregnancy outcome. The highest incidence of diastolic notch was present in cases that developed PE in the third trimester, 12.59% of cases with uni/bilateral notch (Figure 4).

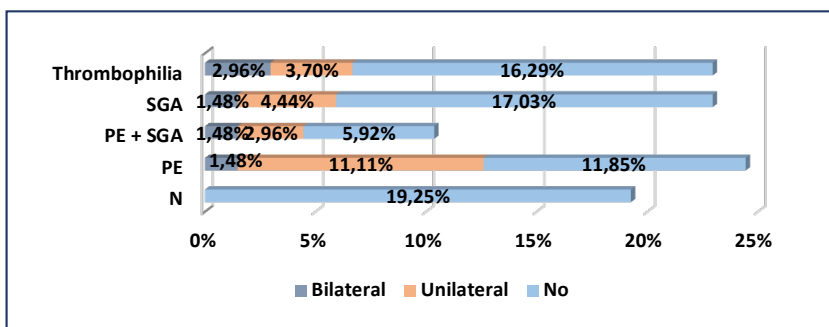


Figure 4. Presence/absence Notch UtA in the second trimester.

A statistical correlation of diastolic notch with the respective pathology was identified in all cases (Fisher's Exact test $p < 0.001$).

The presence of diastolic notch in the second trimester was statistically significant for premature birth and early PE (chi-square testing, $p < 0.01$, respectively chi-square testing $p < 0.001$), and statistically nonsignificant for late PE and SGA (chi-square statistics $p = 0.351$ respectively chi-square testing $p = 0.261$).

In the case of premature birth we also had a good specificity (77.78%) and a negative predictive value of 73.68%.

In the case of late PE and SGA we had a relatively lower specificity, of 62.50% and 64.71% respectively, and a positive predictive value of 77.50%, we only met in the case of late PE.

Relatively low positive predictive values limit the predictive utility of this test (Table 1).

Table 1. Uterine artery Doppler sonography predicting adverse outcome of pregnancy.

Outcome/Indices UtA	Number	Sensitivity	Specificity	Positive predictive value	Negative predictive value
PREMATURE BIRTH					
Abnormal S/D ratio	18	40.00%	70.00%	40.00%	70.00%
<i>The chi-square statistic is 0.6593. The p-value is .416793. Not significant at $p < .05$.</i>					
mean PI>95 percentiles	13	27.78%	21.21%	16.13%	65.00%
<i>Fisher's Exact Test for Count Data p-value=0.1290. Not significant at $p < .05$.</i>					
Notch	20	44.44%	77.78%	50.00%	73.68%
<i>The chi-square statistic is 7.1053. The p-value is .007686. Significant at $p < .05$.</i>					
EARLY PE					
Abnormal S/D ratio	10	37.04%	67.59%	22.22%	81.11%
<i>The chi-square statistic is 0.2083. The p-value is .648077. Not significant at $p < .05$.</i>					
mean PI>95 percentiles	4	76.47%	43.75%	59.09%	63.64%
<i>Fisher's Exact Test for Count Data p-value=0.0255. Significant at $p < .05$.</i>					
Notch	23	21.30%	37.04%	57.50%	10.53%
<i>The chi-square statistic is 17.9852. The p-value is .000022. Significant at $p < .05$.</i>					
LATE PE					
Abnormal S/D ratio	11	45.83%	69.37%	24.44%	85.56%
<i>The chi-square statistic is 2.0524. The p-value is .15197. Not significant at $p < .05$.</i>					
mean PI>95 percentiles	7	80.00%	75.00%	88.89%	60.00%
<i>Fisher's Exact Test for Count Data p-value=0.0949. Not significant at $p < .05$.</i>					
Notch	31	27.93%	62.50%	77.50%	15.79%
<i>The chi-square statistic is 0.8672. The p-value is .351744. Not significant at $p < .05$.</i>					
SGA					
Abnormal S/D ratio	19	38.00%	69.41%	42.22%	65.56%
<i>The chi-square statistic is 0.7782. The p-value is .377681. Not significant at $p < .05$.</i>					
mean PI>95 percentiles	5	92.86%	0.00%	43.33%	0.00%
<i>Fisher's Exact Test for Count Data p-value=0.4516. Not significant at $p < .05$.</i>					
Notch	18	26.19%	64.71%	55.00%	34.74%
<i>The chi-square statistic is 1.2613. The p-value is .261399. Not significant at $p < .05$.</i>					

The results indicated that second-trimester uterine Doppler artery can detect a number of significant adverse pregnancy outcomes.

In our study we found in the second trimester a significant association between abnormal Doppler uterine artery, referring to the presence of diastolic notch and mean PI > 95 percentiles, and early PE.

In the case of premature birth only the presence of diastolic notch had a statistically significance.

We found no significant association between abnormal uterine Doppler artery in the second trimester and the incidence of late PE and SGA in the study group patients.

Discussion

The failure of the trophoblastic invasion of the uterine spiral arteries, prevents the adaptation of the involved arteries and implicitly reduces the blood flow to the placenta.

In these conditions, the uteroplacental circulation remains in a high degree of resistance and low blood flow.

This process can be detected by Doppler studies of the uterine artery.

However, the clinical utility of uterine artery Doppler flow in predicting adverse pregnancy outcomes with reference to the general population remains largely unknown [6,7].

In a first-trimester study, it was found that in women with abnormal Doppler, the likelihood

ratio (LR) for the development of preeclampsia is higher (about 5), compared to LR of 0.5 in those with normal Doppler [8].

In our study, abnormal Doppler values of the uterine artery, referring to mean PI, S/D ratio and diastolic notch presence, were associated with PE, SGA and NP.

We found that abnormal uterine Doppler arteries in the second trimester had a high predictive value only for late PE, according to the 2019 study by Thakur et al. [9], with a high sensitivity and specificity, of 80% and 75% respectively in the case of PI-UtA.

But early PE showed a good statistically significance for mean PI>95 percentiles and diastolic notch, as shown in other studies [10,11].

However, low positive predictive values (<50%) may limit the predictive utility of tests for other categories of adverse pregnancy outcome.

In a large retrospective cohort study, PI of the uterine artery was able to predict 25 to 77% of growth-restricted babies born at different gestational ages [12], as in our study where PPV was 43.33%, but insufficient to establish the clinical utility of the test.

Another observational study that used both Doppler studies on the uterine artery and biochemical markers at 19 to 24 weeks of pregnancy reported detection rates between 100 and 42% for newborns small for gestational age born premature (<32 weeks), between 32-37 weeks, or over 37 weeks of gestation [13].

According to the data from our study, it appears that routine Doppler screening of the uterine artery in the second trimester for the prediction of SGA without PE does not show clinical utility.

This is in contradiction with the Lesmes study [14] which included 63,975 women with singleton pregnancies who delivered 3702 SGA newborn and where PI-UtA at 19-24 weeks showed an increase.

But the screening used was a combined study for SGA, along with maternal factors, fetal biometrics and PI-UtA, and the conclusion was that this type of screening was weaker in the second trimester than in the third trimester of pregnancy.

Premature birth is also influenced by the presence of complications that appeared in the third trimester and that were studied, referring to preeclampsia and SGA.

The incidence of premature birth in our study was 33.33%, with a statistical significance only

in the presence of a diastolic notch, the results being in relative accordance with other studies in the literature [15,16], but these studies also show a statistical significance of PI-UtA.

However, these studies show that the predictive ability is quite low for premature birth, as we found in our study.

In our study, it appears that uterine Doppler artery alone for predicting adverse pregnancy outcomes had a limited role, rather than selecting cases at risk for complications.

Conclusions

Our results show that routine Doppler screening of the uterine arteries during the second trimester did not accurately predict the development of SGA or preterm birth, adequately, necessary to be considered clinically useful, except being PE.

But, we believe that the data obtained by us, can select a population with increased risk of adverse outcome, which would represent an opportunity to screen when intervention might be possible.

Conflict of interests

None to declare.

Reference

1. Toal M, Keating S, Machin G, Dodd J, Adamson SL, Windrim RC, Kingdom JC. Determinants of adverse perinatal outcome in high-risk women with abnormal uterine artery Doppler images. *Am J Obstet Gynecol*, 2008, 198:330.e1-330.e7.
2. Sciscione AC, Hayes EJ Society for Maternal-Fetal M. Uterine artery Doppler flow studies in obstetric practice. *Am J Obstet Gynecol*, 2009, 201(2):121-126.
3. Verma D, Gupta S. Prediction of adverse pregnancy outcomes using uterine artery Doppler imaging at 22-24 weeks of pregnancy: A North Indian experience. *Turk J Obstet Gynecol*, 2016, 13(2):80-84.
4. Bahado-Singh RO, Jodicke C. Uterine artery Doppler and first trimester screening. *Clin Obstet Gynecol*, 2010, 53(4):879-887.
5. Bower S, Vyas S, Campbell S, Nicolaidis KH. Colour Doppler imaging of the uterine artery in pregnancy: normal ranges of impedance to blood flow, mean velocity and volume of flow. *Ultrasound Obstet Gynecol*, 1992, 2(4):261-265.
6. Novac MV, Niculescu M, Manolea MM, Dijmarescu AL, Iliescu DG, Novac MB, Rotaru LT, Stoenescu MF, Tabacu MC, Tudorache S, Busuioc CJ, Gheonea IA. Placental findings in pregnancies complicated with IUGR-histopathological and immunohistochemical analysis. *Rom J Morphol Embryol*, 2018, 59(3):715-720.

7. Parry S, Sciscione A, Haas DM, Grobman WA, Iams JD, Mercer BM, Silver RM, Simhan HN, Wapner RJ, Wing DA, Elovitz MA, Schubert FP, Peaceman A, Esplin MS, Caritis S, Nageotte MP, Carper BA, Saade GR, Reddy UM, Parker CB; Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-be. Role of early second-trimester uterine artery Doppler screening to predict small-for-gestational-age babies in nulliparous women. *Am J Obstet Gynecol*, 2017, 217(5):594.e1-594.e10.
8. Papageorgiou AT, Yu CK, Nicolaides KH. The role of uterine artery Doppler in predicting adverse pregnancy outcome. *Best Pract Res. Clin Obstet Gynaecol*, 2004, 18(3):383-396.
9. Thakur M, Mehra R. Role of second trimester uterine artery doppler for the prediction of preeclampsia in high risk pregnancy. *Int J Reprod Contracept Obstet Gynecol*, 2019, 8(3):906-911.
10. Espinoza J, Kusanovic JP, Bahado-Singh R, Gervasi MT, Romero R, Lee W, Vaisbuch E, Mazaki-Tovi S, Mittal P, Gotsch F, Erez O, Gomez R, Yeo L, Hassan SS. Should bilateral uterine artery notching be used in the risk assessment for preeclampsia, small-for-gestational-age, and gestational hypertension? *J Ultrasound Med*, 2010, 29(7):1103-1115.
11. Lakshmy SR, Praveenkumar M, Shobana U, Thasleem Z. Uterine artery Doppler: Changing Concepts in Prediction and Prevention of PE and FGR. *J. Fetal Med*, 5:93-105.
12. Familiari A, Bhide A, Morlando M, Scala C, Khalil A, Thilaganathan B. Mid-pregnancy fetal biometry, uterine artery Doppler indices and maternal demographic characteristics: role in prediction of small-for-gestational-age birth. *Acta Obstet Gynecol Scand*, 2016, 95(2):238-244.
13. Poon LC, Lesmes C, Gallo DM, Akolekar R, Nicolaides KH. Prediction of small-for-gestational-age neonates: screening by biophysical and biochemical markers at 19-24 weeks. *Ultrasound Obstet Gynecol*, 2015, 46(4):437-445.
14. Lesmes C, Gallo DM, Saiid Y, Poon LC, Nicolaides KH. Prediction of small-for-gestational-age neonates: screening by uterine artery Doppler and mean arterial pressure at 19-24 weeks. *Ultrasound Obstet Gynecol*, 2015, 46(3):332-340.
15. van Zijl MD, Koullali B, Mol BWJ, Snijders RJ, Kazemier BM, Pajkrt E. The predictive capacity of uterine artery Doppler for preterm birth-A cohort study. *Acta Obstet Gynecol Scand*, 2020, 99(4):494-502.
16. Afrakhteh M, Moeini A, Taheri MS, Haghightkha HR, Fakhri M, Masoom N. Uterine Doppler velocimetry of the uterine arteries in the second and third trimesters for the prediction of gestational outcome. *Rev. Bras. Ginecol. Obstet*, 2014, 36(1), 35-39.

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