Original Paper

The Ability of Doppler Uterine Artery Ultrasound to Predict Premature Birth

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ABSTRACT: Objective. Demonstration of the predictive capacity of Doppler Uterine Artery (UtA) on preterm birth (PB) by serial measurement at various ages of pregnancy. Methods. The prospective study included a group of 116 pregnant women, of whom 85 gave birth prematurely and 31 pregnant women gave birth at term, constituting the control group. UtA Doppler measurement was performed by the abdominal approach. Quantitative wave evaluations were performed by the pulsatility index (PI), the systole/diastole ratio (S/D), as well as the qualitative analysis of the flow rate waveform (notch). UtA Doppler evaluation was performed in 3 pregnancy periods: 18.0-22.6 weeks, 28.0-31.6 weeks, and 32.0-35.6 weeks. Results. Only at the third examination, at 32.0-35.6 weeks of gestation, was there a statistically significant difference between the S/D-UtA ratio and PI-UtA correlated with the risk of premature birth ($p<0.05$). Although there was an association between UtA Doppler and late preterm birth, the predictive ability was low. Also, UtA Doppler was not statistically significant for preterm birth before 32 weeks of gestation. Conclusions. Although we did not find a statistical association between second-trimester UtA Doppler and preterm birth, we do suggest a closer look at women with abnormal UtA Doppler in the second trimester. We believe that, according to the results obtained, UtA Doppler can predict especially iatrogenic premature birth depending on the prediction of the most severe complications, severe preeclampsia, and SGA.

KEYWORDS: *UtA Doppler, premature birth, prediction.*

Introduction

Despite concerns about preventing premature birth, it is currently considered a global epidemic, leading to the birth of approximately 15 million premature babies worldwide [1], and is estimated to account for approximately 11% of all births worldwide [2].

Studies over the years have tried to establish an association between premature birth and a wide range of risk factors such as socioeconomic factors, medical factors, obstetrics and fetuses, finding some common points, but premature birth continues to occur in a proportion of about two-thirds without presenting any risk factor [3].

The remodeling of the over 100 spiral arteries at the decidual and myometrial levels is a guarantee of complete placentation and the normal evolution of pregnancy.

Absence or incomplete reconversion of the spiral arteries can lead to preeclampsia and intrauterine growth restriction (IUGR) [4].

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However, subsequent studies have shown that late spontaneous abortion and preterm labor can be influenced by these abnormal remodeling of the spiral arteries, all of which constitute the "Great Obstetrical Syndromes" [5].

In women with this syndrome associated with the failure of the physiological transformation of the spiral arteries, there is an abnormal resistance of UtA, measured by Doppler ultrasound in the middle of the trimester [6].

This aspect could be predictive for preeclampsia and IUGR, but also iatrogenic PB [7].

However, the results of the studies were contradictory in the association between spontaneous PB and UtA resistance [8,9].

Materials and Methods

This prospective study that took place in the Obstetrics and Gynecology Clinic of the Municipal Clinical Hospital Philanthropy Craiova, between January 2019 and January 2022, included a group of 116 pregnant women, of which 85 gave birth prematurely and 31 pregnant women gave birth at term, and which constituted the control group.

We studied women with a singleton gestation, scanned for routine fetal abnormalities between 18 and 22 weeks of gestation, and who had risk factors for PB.

A detailed interview was conducted at the first monitoring visit to obtain demographic, clinical, and medical history data.

UtA Doppler measurement was performed at the intersection with the external iliac artery through an abdominal approach.

Quantitative wave evaluations were performed by the pulsatility index (PI), the S/D ratio, as well as the qualitative analysis of the notch.

UtA evaluation was performed in 3 pregnancy periods: 18.0-22.6 weeks, 28.0-31.6 weeks, and 32.0-35.6 weeks.

The study was approved by the Ethics Committee of the University of Medicine and Pharmacy of Craiova, and a written informed consent was obtained from each patient or their caretakers.

Statistical Analyses

The sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios (LR+and LR-) were calculated with their 95% Confidence Intervals, of each parameter of the evaluated UtA.

We used the median and range (Minimum and Maximum) for nonparametric data and the mean and standard deviation for parametric data.

A $p<0.05$ indicated statistical significance.

Results

The mean age of the study groups was similar, 28.5±4.6 years in the term birth group and 28.6±5.6 years in the premature birth group with birth between 28.0-34.0 weeks of gestation.

Only in premature birth groups with births between 34.1-36.6 weeks of gestation, the mean age was higher 30.4±4.1 years, but we did not find a significant statistical significance, P=0.106.

Maternal BMI was approximately the same in all groups, 24kg/m2, BMI index not representing a significant statistical difference regarding premature birth, P=0.246.

The number of nulliparous, 25 cases (46.15%) was higher in the group with premature birth produced between 28.0-34.0 weeks of gestation, similar to the number of nulliparous pregnant women in the group with premature birth at 34.1-36.6 weeks (42.37%).

Also, the number of previous preterm birth was higher in the group with premature birth produced between 28.0-34.0 weeks of gestation, 13 cases (50%), it was 22 cases (37.29%) in the 34.1-36.6 gestational weeks group, and only 8 cases (25.80%) in the group that gave birth at term.

GA at delivery was 38.4±0.8 weeks of gestation at term group birth, 33.1±0.5 weeks of gestation at a premature birth group with birth between 28.0-34.0 weeks of gestation, and 35.5±0.7 weeks of gestation in a group with premature birth produced between 34.1-36.6 weeks of gestation.

This parameter was the only one where we found a significant difference, $P<0.001$, but this is indubitable, all these data are presented in Table 1.

During the Doppler examination of the uterine arteries, we evaluated the following parameters: S/D ratio, pulsatility index, and the presence/absence of notch, uni/bilateral.

The S/D ratio was considered as peripheral resistance index.

In a pregnancy with normal evolution, this ratio is considered to remain at constant values of 1.08-1.09.

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Table 1. Demographic characteristics of the study population.

Parameter	Term birth group	Premature birth group		p-value
	>37 weeks	28.0-34.0 weeks	34.1-36.6 weeks	
Maternal age (y, Median±SD)	28.5±4.6	28.6±5.6	30.4±4.1	P=0.106 ANOVA SS 97.17 MS 48.58 F 2.28 F Crit 3.07
Maternal BMI (kg/m2, Median±SD)	24.9±3.0	24.2±1.7	25.3±3.1	P=0.246 ANOVA SS 22.37 MS 11.18 F 1.419 F crit 3.07
Nulliparous (n, %)	23 (74.19%)	12 (46.15%)	25 (42.37%)	
GA at delivery (weeks, Median±SD)	38.4±0.8	33.1±0.5	35.5±0.7	P<0.001 ANOVA SS 404.82 MS 202.41 F 462.76 F crit 3.07
Previous preterm birth (n, %)	8 (25.80%)	13 (50%)	22 (37.29%)	

In this regard, we considered that values >1.8 represent abnormal values, trying to see if this ratio can be involved in the occurrence of pregnancy complications that could cause premature iatrogenic birth (Figures 1,2).

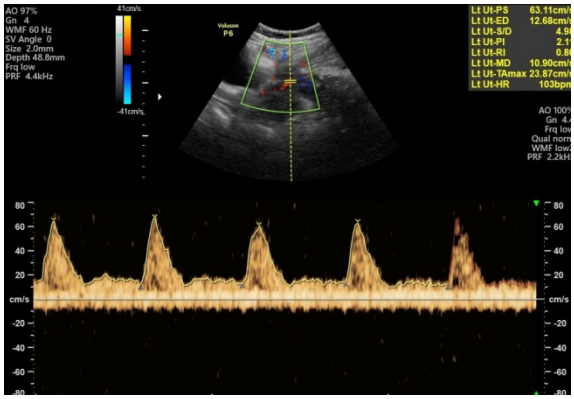

Figure 1. 20.4 weeks of gestation; Lt UtA: S/D 4.9; PI 2.1; RI 0.8; notch.

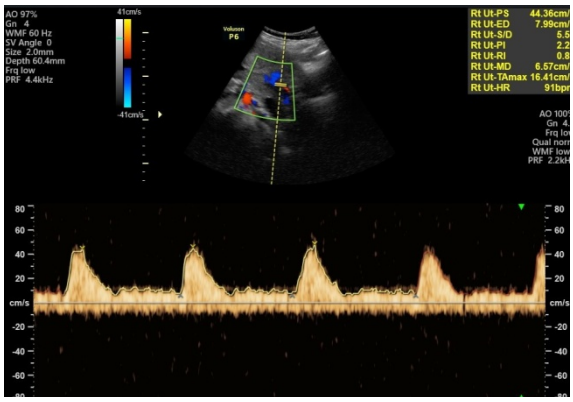

Figure 2. 25.3 weeks of gestation; Rt UtA: S/D 3.8; PI 1.6; RI 0.7.

On the first examination, at 18.0-22.6 weeks of gestation, we noticed that there was no statistically significant difference between the S/D ratio and the risk of preterm birth (p>0.05), so this ratio is a weak predictor of preterm birth (Table 2).

Table 2. Correlation of the UtA-S/D ratio on Doppler velocimetry with PB at 18.0-22.6 weeks of gestation.

	Rt UtA S/D	Lt UtA S/D	S/D Rt UtA/Lt UtA
Median PB	2.38	2.68	0.97
SD PB	0.72	1.60	0.23
Median Control	2.58	2.63	1.05
SD Control	0.64	0.80	0.39
p-value	0.17	0.84	0.27

At the second assessment, at 28.0-31.6 weeks of gestation, there was no statistically significant difference between the S/D ratio and the risk of preterm birth (p>0.05), so this ratio is a weak predictor of preterm birth, at this age of a pregnancy (Table 3).

Table 3. Correlation of the UtA-S/D ratio on Doppler velocimetry with PB at 28.0-31.6 weeks of gestation.

	Rt UtA S/D	Lt UtA S/D	S/D Rt UtA/Lt UtA
Median PB	2.31	2.19	1.08
SD PB	1.32	0.43	0.76
Median Control	2.30	2.27	1.04
SD Control	0.63	0.55	0.29
p-value	0.97	0.48	0.68

On the third examination, at 32.0-36.6 weeks gestation, there was a statistically significant difference between the S/D ratio and the risk of preterm birth ($p<0.05$), so this ratio as a predictor of spontaneous preterm birth at this age of pregnancy could be significant (Table 4).

Table 4. Correlation of the UtA-S/D ratio Doppler with PB at 32.0-35.6 weeks of gestation.

	Rt UtA S/D	Lt UtA S/D	S/D Rt UtA/Lt UtA
Median PB	2.34	1.87	1.04
SD PB	3.88	0.62	0.15
Median Control	2.00	2.20	0.93
SD Control	0.24	0.38	0.17
p-value	0.41	0.00	0.00

Resistance to blood flow in the uteroplacental circulation is transmitted upstream to the uterine arteries and can be measured as a pulsatility index (PI) or an increased resistance index (IR).

We analyzed the PI values at the three Doppler examinations, at different gestational ages and performed the statistical analysis.

At the first visit, at 18.0-22.6 weeks of gestation, we found values of over 95 percentiles in 6.89% of cases that gave birth prematurely and in 0.86% of cases that gave birth at term.

At this gestational age, there was no statistically significant difference between UtA-PI and the risk of preterm birth ($p>0.05$), so this ratio could not be a predictor of preterm birth at this gestational age in our study (Table 5).

Table 5. Correlation of the UtA-PI Doppler with PB at 18.0-22.6 weeks of gestation.

	Rt UtA-PI	Lt UtA-PI	mean PI	Percentiles
Median PB	1.06	1.14	1.10	42.47
SD PB	0.66	0.68	0.63	34.22
Median Control	1.05	1.06	1.05	39.32
SD Control	0.31	0.40	0.27	29.09
p-value	0.91	0.45	0.58	0.63

At 28.0-31.6 weeks of gestation, there was no statistically significant difference between UtA-PI and the risk of preterm birth, $p>0.05$ (Table 6).

Table 6. Correlation of the UtA-PI Doppler with PB at 28.0-31.6 weeks of gestation.

	Rt UtA-PI	Lt UtA-PI	mean PI	Percentiles
Median PB	0.95	0.87	0.91	53.62
SD PB	0.42	0.25	0.30	32.28
Median Control	0.87	0.87	0.87	54.45
SD Control	0.30	0.29	0.24	31.71
p-value	0.29	0.92	0.48	0.90

At the next examination, from 32.0-35.6 weeks of gestation, there is a statistically significant difference between UtA-PI and the risk of preterm birth ($p<0.05$), so this parameter may be a predictor of preterm birth at this age of gestation (Table 7).

Table 7. Correlation of the UtA-PI Doppler with PB at 32.0-35.6 weeks of gestation.

	Rt UtA-PI	Lt UtA-PI	mean PI	Percentiles
Median PB	0.71	0.68	0.69	35.21
SD PB	0.28	0.27	0.27	26.90
Median Control	0.84	0.87	0.84	70.90
SD Control	0.18	0.21	0.14	20.44
p-value	0.01	0.00	0.00	0.00

In our study, in pregnancies that gave birth prematurely, we had at a gestational age of 18.0-22.6 weeks, 18 pregnancies with a present notches, 9 notches on left UtA and 9 notches on right UtA, 3 of them being bilaterally located, but this the situation can be considered normal at this gestational age.

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At 28.0-31.6 weeks of gestation, the number of cases with a notch decreased to 13 cases, 6 with a notch on the left UtA and 9 with a notch on the right UtA, no bilateral case.

At 32.0-35.6 weeks of gestation, we had only 5 cases, 3 with a notch on the left UtA and 2 with a notch on the right UtA. Due to the small number of cases, we could not make a significant statistic.

We calculated, depending on the normal or abnormal appearance of the Doppler velocimetry, the accuracy of the prediction of this parameter.

We considered several changes in Doppler waveforms that could be considered abnormal: protodiastolic notch persistence, unilateral or bilateral after 23 weeks of pregnancy or S/D>3 after 30 weeks of gestation, or an increased pulsatility index (PI>95 percentiles).

Table 8. Predictive accuracy of UtA Doppler.

Parameter	Sn (IC 95%)	Sp (IC 95%)	PPV (IC 95%)	NPV (IC 95%)	LR+ (IC 95%)	LR- (IC 95%)
UtA (18.0-22.6 wk)	90%	28%%	11%	97%	1.26	0.35
UtA (28.0-31.6 wk)	75%	27%	11%	90%	1.03	0.93
UtA (32.0-35.6 wk)	73%	27%	9%	90%	0.99	1.02

Table 8 shows the relationship between abnormal UtA Doppler and premature birth for different gestational ages.

Negative predictive values are constantly high at all three gestational ages studied.

A test result was associated with 90% sensitivity, 28% specificity, 11% positive predictive value, and 97% negative predictive value in estimating preterm birth at the assessment at 18.0-22.6 gestational weeks.

At 28.0-31.6 gestational weeks the test result was associated with 75% sensitivity, 27% specificity, 11% positive predictive value, and 90% negative predictive value.

Finally, at 32.0-35.6 gestational weeks, the test result was associated with 73% sensitivity, 27% specificity, 9% positive predictive value, and 90% negative predictive value in predicting birth before 37 weeks of gestation.

Considering the low positive predictive value (9-11%), we can estimate that this will be the percentage that will characterize pregnant women who will give birth prematurely in the presence of an abnormal Doppler of UtA.

The negative predictive value of 90-97% shows that in the conditions in which we have a normal Doppler on the uterine arteries, the probability that a pregnant woman at risk will give birth at term and not prematurely is high.

Discussion

Although important progress has been made recently in the prevention of premature birth, premature birth remains responsible for the death of approximately 1 million children under the age of 5 in 2015 [10,11].

It was found that it would be possible to predict some unfavorable events during pregnancy, by evaluating the uterine artery Doppler.

But regarding the best time during pregnancy to evaluate the uterine artery Doppler for the prediction of adverse pregnancy outcomes, the results of the studies are divergent.

While some authors noted that uterine artery Doppler in the second and third trimesters of pregnancy can predict adverse pregnancy outcomes [12,13], other authors argued that uterine artery Doppler performed in all trimesters of pregnancy is relevant [14,15].

In this study, we evaluated the utility of UtA Doppler measurement in 3 periods of pregnancy, both in the second and third trimesters, at 18.0-22.6, 28.0-31.6 and at 32.0-35.6 weeks of gestation to predict premature birth.

We did not notice any significant statistical difference before 32 weeks, only in premature births after 32 weeks we found a significant statistical difference, $p<0.05$.

Maternal characteristics were also not associated with the risk of premature birth.

A study conducted in 2004 [16] regarding the involvement of uterine artery resistance in the second trimester of pregnancy in the generation of premature birth, did not report a significant statistical correlation.

But other studies show that in premature birth there are increased values of UtA-PI in premature births before 33 weeks, but the prognostic significance only by this parameter or in combination with other markers, could not be proven [9,17].

In our study, we found a significant statistical difference only in cases with premature birth after 32 weeks, when we found a significant difference in the mean uterine artery S/D and UtA-PI.

It seems that UtA-PI in the third trimester can be used as a unique marker for predicting pregnancy complications, including premature birth, especially iatrogenic.

Along with the high values of UtA-PI, persistent notch in the second trimester, can be used as markers for monitoring pregnant women who may develop many pregnancy complications, such as PE, IUGR or SGA and PB [18,19].

We used this marker to monitor all pregnancies, but we had too few cases with a notch to perform a significant statistical analysis.

A deterioration of the placental function could be the basis of the increased values of UtA-PI in premature birth, as histopathological findings also showed [20].

We found the predictive capacity of UtA-PI quite limited, even if the sensitivity was between 73 and 90%, and the negative predictive value was over 90%, but the positive likelihood ratio of only 1.26 does not justify screening for low-risk cases.

These results are in line with other studies that showed that compared to maternal characteristics, obstetric history and maternal and fetal complications from the current pregnancy, the UtA-PI Doppler does not excel in a better prediction, even if it is considered that the UtA-PI Doppler would represent an efficient marker for predicting premature birth [9,21].

However, measurement of the UtA Doppler is a non-invasive, relatively fast and inexpensive ultrasound method, which can be performed during the routine scan of fetal anomalies in the second trimester.

The identification of a high-risk pregnancy thus requires a strict monitoring of the cases, determining a possible reduction of maternal and fetal complications, by involving some preventive measures.

Conclusion

Based on our results, we consider that Doppler screening of the uterine artery in the second and third trimesters is mandatory, both for the prediction of PE, IUGR or SGA, which can cause iatrogenic preterm birth, but also for the prediction of spontaneous preterm birth, even if not with such great accuracy. UtA-PI can only be used alone, in the third trimester, or associated with other clinical and paraclinical markers in the last two trimesters.

Conflict of interests

None to declare.

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