Jurnal Medical Aradean (Arad Medical Journal)
Vol. XX, issue 3, 2017, pp. 17-26

UTERINE ARTERY DOPPLER FLOW INDICES FROM 11 TO 14 WEEKS GESTATIONAL AGE

V. Daşcău[1], Gh. Furău[1], C. Furău[1], Cristina Onel[1], Casiana Stănescu[2], Liliana Tătaru[1], Cristina Ghib-Para[3], Cristina Popescu[4], Maria Puschita[5]

[1]Department of Obstetrics and Gynecalogy, „Vasile Goldiş" Western University, Arad, Romania
[2]Department of Anatomy, „Vasile Goldiş" Western University, Arad, Romania
[3]Department of Haematology, „Vasile Goldiş" Western University, Arad, Romania
[4]Department of Life Sciences, „Vasile Goldiş" Western University, Arad, Romania
[5]Department of Internal Medicine, „Vasile Goldiş" Western University, Arad, Romania

ABSTRACT. Uterine artery Doppler flow screening studies during the 11th and 14th weeks of pregnancy have been shown to be important in the prediction and prevention of pregnancy complications preeclampsia and IUGR in pregnant women. Our study of the Doppler flow indices of the uterine arteries involves 216 patients examined in our clinic, with pregnancies ranging from 11 weeks + 0 days to 13 weeks + 6 days. There were 83 patients from 11 weeks + 0 days to 11 weeks + 6 days (38.43%), 61 from 12 weeks + 0 days to 12 weeks + 6 days (28.25%), and 72 from 13 weeks + 0 days to 13 weeks + 6 days (33.33%). The values of the Doppler indices were: PI 1.75±0.78, 1.89± 0.80, 1.75±0.80, and 1.57±0.70, RI 0.73±0.13, 0.75±0.13, 0.72±0.13, and 0.70±0.13, and PI/RI 2.31±0.71, 2.43±0.74, 2.32±0.70, and 2.16±0.65 for the entire group and for the three intervals respectively. There were 105 (48.61%), 37 (17.13%, with 21 cases or 55.76% on the right side), and 74 (34.26%) patients with bilateral, unilateral and absent uterine artery notching, respectively. The Doppler indices for the three aforementioned groups were: 2.11±0.77, 1.59±0.69, and 1.30±0.55 for the PI, 0.79±0.10, 0.71±0.13, and 0.65±0.14 for the RI, and 2.63±0.70, 2.18±0.64, and 1.92±0.50 for the PI/RI, respectively. The indices for the arteries with and without notching in all patients, as well as for the uterine arteries with and without notching in patients with unilateral notching, were 2.10±0.75, 1.27±0.53, 2.01±0.67, and 1.18±0.42 for the PI, 0.78±0.10, 0.65±0.13, 0.78±0.11, and 0.63±0.12 for the RI, and for the PI/RI, 2.62±0.70, 1.90±0.47, 2.54±0.67, and 1.82±0.41 respectively.The mean uterine artery PI, RI, and PI/RI decrease from 11 weeks + 0 days-11 weeks + 6 days to 13 weeks + 0 days-13 weeks + 6 days. They also decrease from pregnant patients with bilateral uterine artery notching to those without notching. The frequency of uterine artery notching decreases with increasing gestational age. Our results are similar to those in literature.
KEYWORDS: pregnancy, gestational age, uterine artery notching, Doppler indices, pulsatility index, resistivity index, preeclampsia, IUGR

INTRODUCTION

Pre-eclampsia (PE) remains one of the leading causes of maternal, intrauterine and perinatal mortality and morbidity (about 10-15% of all maternal deaths). The first trimester is considered to be the preferred gestational period for PE screening and for the most accurate prediction of patients at high risk for PE as the prophylactic use of low-dose aspirin beginning in early pregnancy (prior to 16 weeks) is able to reduce the prevalence of PE by as much as 50% (85% in case of early PE) and significantly decrease rates of perinatal disease and death (Alves et al., 2013). No single efficient screening procedure for predicting PE has been adopted in clinical practice, but uterine artery Doppler is the most widely studied clinical test available for this particular purpose, becoming a very useful method for the indirect assessment of uteroplacental circulation in early pregnancy (11–14 weeks). If combined with other elements and factors like examination of maternal history, mean arterial pressure (MAP) and certain biochemical markers (pregnancy-associated plasma protein A or PAPP-A and placenta growth factor or PIGF), uterine artery Doppler can be an adjunct screening tool for predicting PE and intrauterine growth restriction (IUGR) as abnormal uterine artery Doppler results have been proven to be strongly correlated with several types of adverse maternal and perinatal outcomes (Alves et al., 2013; Peixoto et al., 2016).

Early identification of pregnant patients at risk of developing PE and IUGR is more likely to facilitate targeted antenatal surveillance and possibly an efficient early intervention (Poon et al., 2012; Khalil et al., 2013; Roberge et al., 2013).

In clinical setting, reference ranges for UtA Doppler ultrasound during pregnancy are recommended and used for the appropriate analysis of impedance to blood flow. The pulsatility index (PI) has been advocated as the best Doppler index in several studies (Ferreira et al., 2016). In

some studies, transvaginal approach was used at 11–14 weeks of gestation, while transabdominal ultrasound was used from 15 weeks onwards. The PI was significantly higher in both trimesters using transvaginal approach (Peixoto et al., 2016; Scandiuzzi et al., 2016; Ghulmiyyah et al., 2012; Velauthar et al., 2014).

First and second trimester uterine artery Doppler blood flow assessments have been shown to have a high predictive value for clinical outcome (Akbaş et al., 2014). A rather wide range of specificity and sensitivity values for subsequent pregnancy complications were found in studies which have correlated Doppler velocimetry and clinical outcomes (Akbaş et al., 2014).

For a correct and clinically significant uterine artery PI measurement, the gestational age must be between 11+0 and 13+6weeks. The transabdominal route for ultrasound should be used to obtain a midsagittal section of the uterus and cervical canal; after the internal cervical os is identified, the transducer should be tilted gently from side to side in each paracervical region, using color flow mapping, to identify the uterine arteries (Poon et al., 2012; Khalil et al., 2013). Pulsed wave Doppler with the sampling gate set at 2 mm to cover the whole vessel and an angle of insonation <30◦ should be used to obtain flow velocity waveforms from the ascending branch of the uterine artery at the point closest to the internal os; when three similar consecutive waveforms are obtained, the PI should be measured and the mean PI of the left and right arteries calculated (Poon et al., 2012; Khalil et al., 2013).

MATERIALS AND METHODS

We assessed the uterine artery Doppler flow indices in 216 pregnant patients within the 11 weeks + 0 days and 13 weeks + 6 days gestational ages in our clinic by using a Sonoscape SSI-6000 and a General Electric Logiq e ultrasound devices. The Doppler flow was analyzed with a 2 mm window and an insonation angle of less than 30 degrees, according to existing guidelines. This study is an extension of previous ones, carried out by the same team of researchers on increasing number of patients, the previous results being cited as discussions.

RESULTS

There were 83 patients from 11 weeks + 0 days to 11 weeks + 6 days (38.43%), 61 from 12 weeks + 0 days to 12 weeks + 6 days (28.25%), and 72 from 13 weeks + 0 days to 13 weeks + 6 days (33.33%) gestational age in our group (figure 1).

Our research showed revealed that a number of 105 (48.61%), 37 (17.13%, with 21 cases or 55.76% on the right side), and 74 (34.26%) patients had bilateral, unilateral and absent uterine artery notching, respectively (figure 2).

The uterine arteries in the study group according to the presence (n=227, representing both uterine arteries in bilateral notch cases and the arteries with notching in unilateral notch patients) or absence (n=185, representing both uterine arteries in absent notch cases and the arteries without notching in unilateral notch patients) of notching were also assessed, as well as the indices for the uterine arteries with and without notching in the patients with unilateral notching (n=37). The values of the Doppler indices are shown in table 1 and figures 3-5.

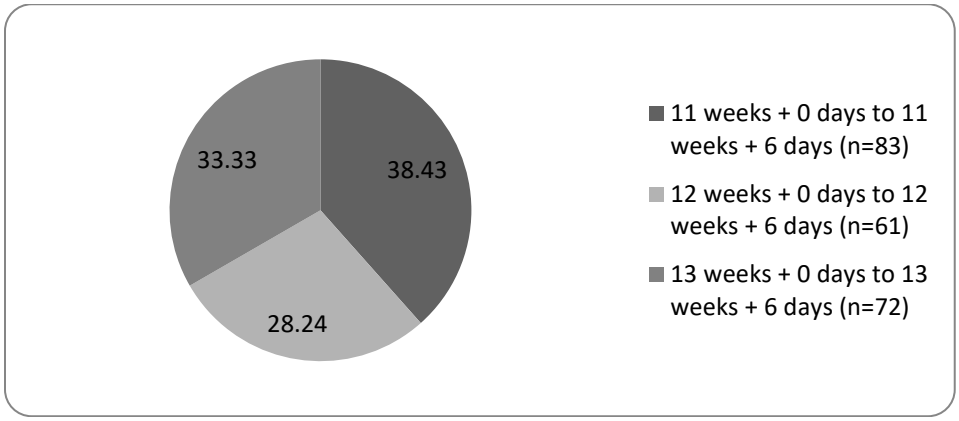

Figure 1: Age group distribution

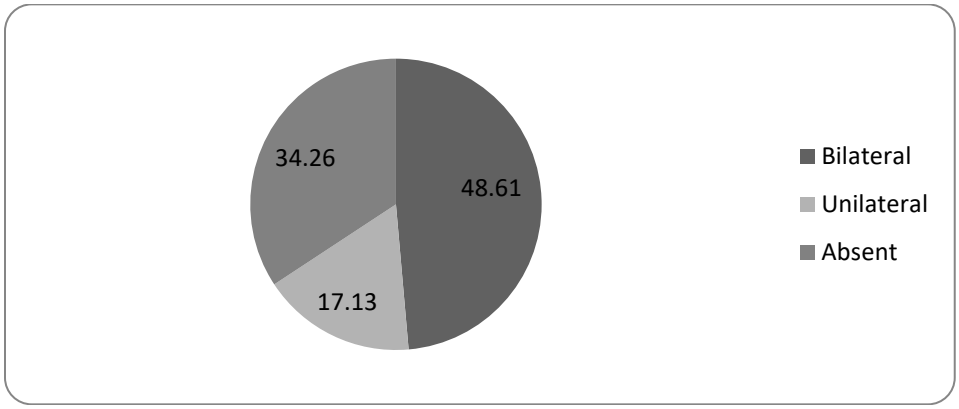

Figure 2: Notch type distribution

Jurnal Medical Aradean (Arad Medical Journal)
Vol. XX, issue 3, 2017, pp. 17-26

Table 1. Mean PI±SD, mean RI±SD, 5th and 95th percentiles

	PI				RI				PI/RI			
Group	Value	5th	95th	Range	Value	5th	95th	Range	Value	5th	95th	Range
All (216 patients)	1.75±0.78	0.74	3.24	0.46-4.33	0.73±0.13	0.49	0.91	0.36-1	2.31±0.71	1.22	3.71	1.14-5.35
11 weeks + 0 days to 11 weeks + 6 days (83 patients)	1.89±0.80	0.72	3.45	0.46-4.33	0.75±0.13	0.50	0.92	0.36-1	2.43±0.74	1.41	3.79	1.20-4.67
12 weeks + 0 days to 12 weeks + 6 days (61 patients)	1.75±0.80	0.76	3.52	0.55-4.29	0.72±0.13	0.51	0.92	0.40-0.96	2.32±0.70	1.49	3.88	1.34-4.71
13 weeks + 0 days to 13 weeks + 6 days (72 patients)	1.57±0.70	0.73	2.86	0.49-3.93	0.70±0.13	0.46	0.90	0.37-0.94	2.16±0.65	1.42	3.29	1.14-5.35
Bilateral uterine artery notching (105 patients)	2.11±0.77	1.11	3.58	0.72-4.33	0.79±0.10	0.61	0.93	0.46-1	2.63±0.70	1.76	3.96	1.41-5.35
Unilateral uterine artery notching (37 patients)	1.59±0.69	0.75	2.71	0.55-3.55	0.71±0.13	0.50	0.88	0.40-0.96	2.18±0.64	1.43	3.01	1.37-4.67
Absent uterine artery notching (74 patients)	1.30±0.55	0.55	2.38	0.46-2.82	0.65±0.14	0.41	0.87	0.36-1	1.92±0.50	1.32	2.83	1.14-4.29
Uterine artery with notch (n=247)	2.10±0.75	1.11	3.55	0.72-4.33	0.78±0.10	0.61	0.93	0.46-1	2.62±0.70	1.76	3.96	1.41-5.35
Uterine artery without notch (n=185)	1.27±0.53	0.58	2.35	0.46-2.82	0.65±0.13	0.41	0.86	0.36-1	1.90±0.47	1.32	2.76	1.14-4.29
Uterine artery with notch in unilateral notch patients (n=37)	2.01±0.67	1.22	3.16	0.91-3.55	0.78±0.11	0.58	0.91	0.52-0.96	2.54±0.67	1.80	3.78	1.67-4.67
Uterine artery without notch in unilateral notch patients (n=37)	1.18±0.42	0.63	2.04	0.55-2.09	0.63±0.12	0.44	0.81	0.40-0.84	1.82±0.41	1.41	2.52	1.37-2.62

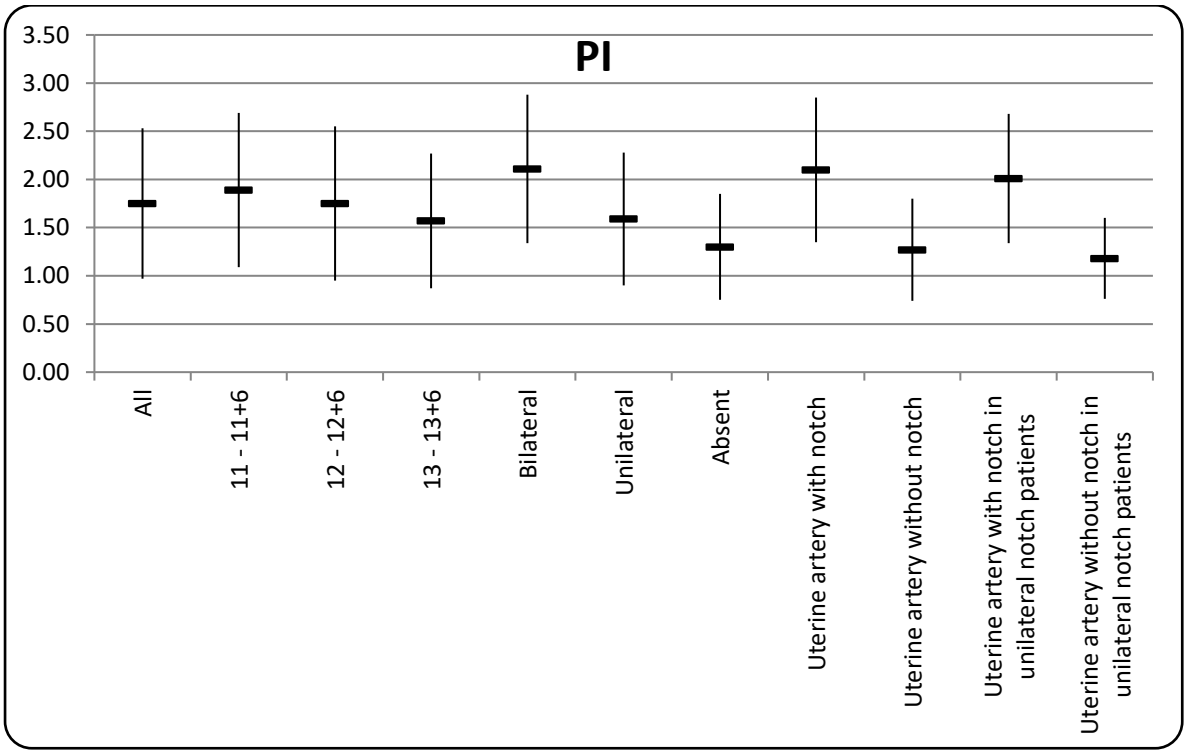

Figure 3. Mean PI±DS

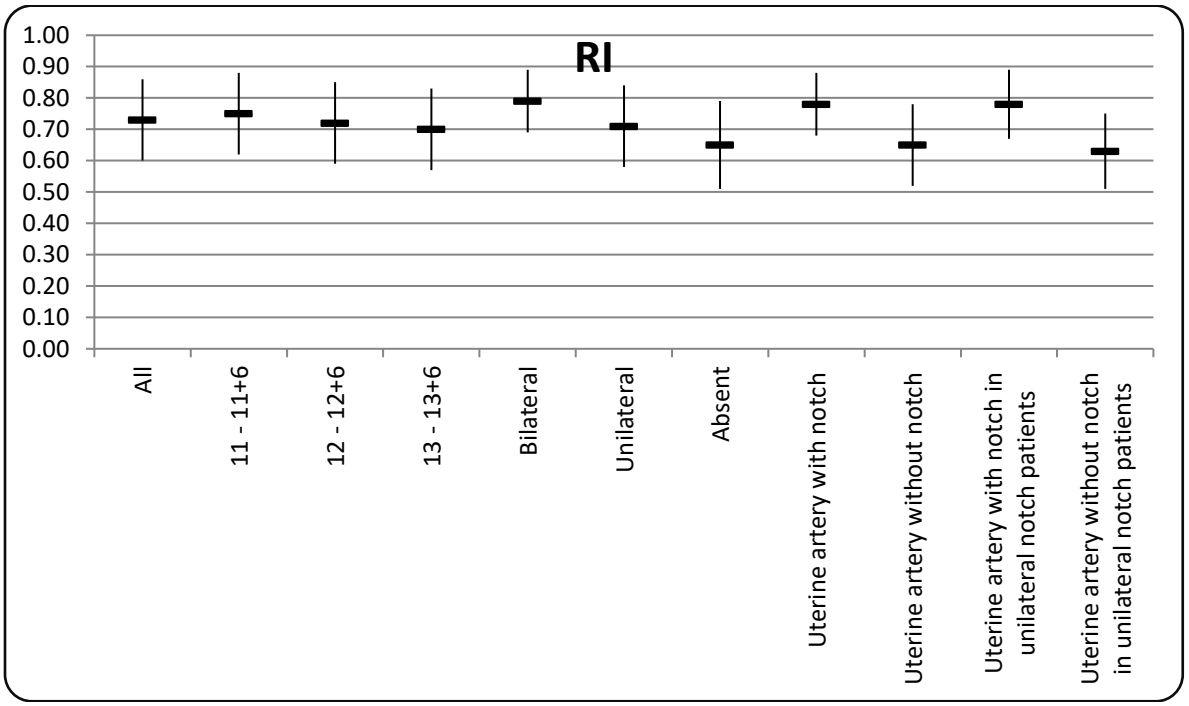

Figure 4. Mean RI±DS

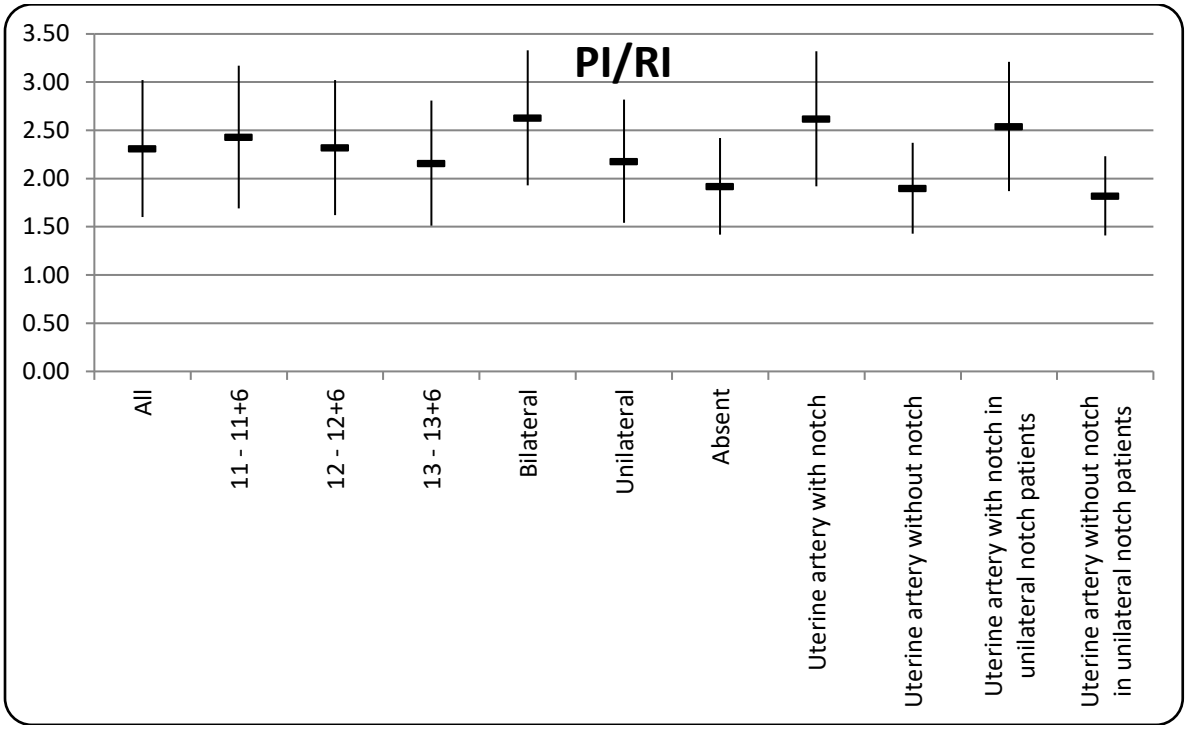

Figure 5. Mean PI/RI±DS

Table 2 and figure 6 present the frequency of different types of uterine artery notching among the three gestational age groups, while table 3 and figure 7 present the distribution of types of uterine artery notching among the three gestational age groups.

Table 2. Distribution of frequency of different types of uterine artery notching among the three gestational age groups

Notching	11 weeks + 0 days to 11 weeks + 6 days (n=83)	12 weeks + 0 days to 12 weeks + 6 days (n=61)	13 weeks + 0 days to 13 weeks + 6 days (n=72)
Bilateral	45 (54.22%)	30 (49.18%)	30 (41.67%)
Unilateral	17(20.48%)	9 (14.75%)	11 (15.28%)
Absent	21 (25.30%)	22 (36.07%)	31 (43.06%)

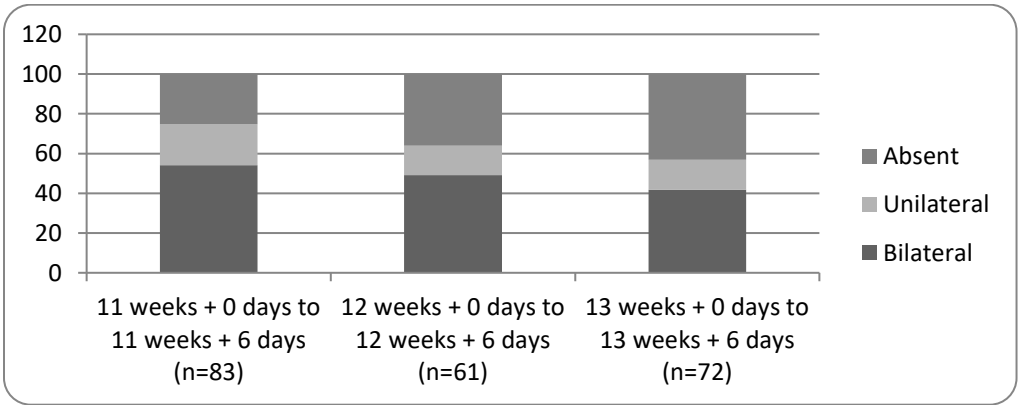

Figure 6. Distribution of frequency of different types of uterine artery notching among the three gestational age groups

Table 3. Distribution of types of uterine artery notching among the three gestational age groups

Notching	Bilateral (n=105)	Unilateral (n=37)	Absent (n=74)
11 weeks + 0 days to 11 weeks + 6 days (n=83)	45 (42.86%)	17 (45.95%)	21 (28.38%)
12 weeks + 0 days to 12 weeks + 6 days (n=61)	30 (28.57%)	9 (24.32%)	22 (29.73%)
13 weeks + 0 days to 13 weeks + 6 days (n=72)	30 (28.57%)	11 (29.73%)	31 (41.89%)

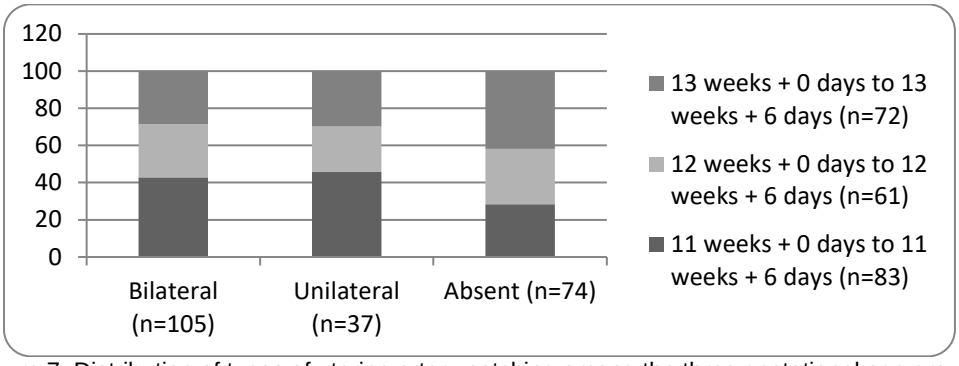

Figure 7. Distribution of types of uterine artery notching among the three gestational age groups

We used Student's t-test to compare the PI and RI among different groups, the results being shown in table 4 (NS=non significant) (table 4).

In the group we studied, uterine artery notching was:

-always absent in case of PI below the 4th percentile, RI below the 3.5 percentile, and PI/RI below the 4th percentile;

-always present in case of PI above the 90.5 percentile and PI/RI above the 99th percentile, while no such percentile could be established for the RI (there were two patients with an RI of 1 and absent notching.

The rates of FNR (false negative rate), defined as a present uterine artery notching, were

-5% for PI below the 4.6 percentile and 10% for PI below the 16.2 percentile

-5% for RI below the 4.6 percentile and 10% for RI below the 11.6 percentile

-10% for PI/RI below the 4.6 percentile.

As for the FPR (false positive rate), defined as an absent uterine artery notching, the situation was the following:

-4.5% for PI above the 89.8 percentile and 10.1% for PI above the 77.1 percentile

-10% for RI above the 93 percentile

-5% for PI/RI above the 95.4 percentile and 10% for PI/RI above the 86.1 percentile.

The frequencies of notching for different indices percentiles and quartiles are shown in table 5 and figures 8 and 9.

Percentile	<5%	<10%	>90%	>95%
PI	4.55%	2.33%	97.67%	100%
RI	4.55%	6.98%	90.91%	88.37%
PI/RI	9.09%	6.98%	95.45%	93.02%
Quartile	I	II	III	IV
PI	21.71%	50.39%	73.64%	89.15%
RI	23.26%	55.04%	72.09%	84.50%
PI/RI	20.93%	49.61%	76.74%	87.60%

Table 5: Frequency of uterine artery notching for different indices percentiles and quartiles

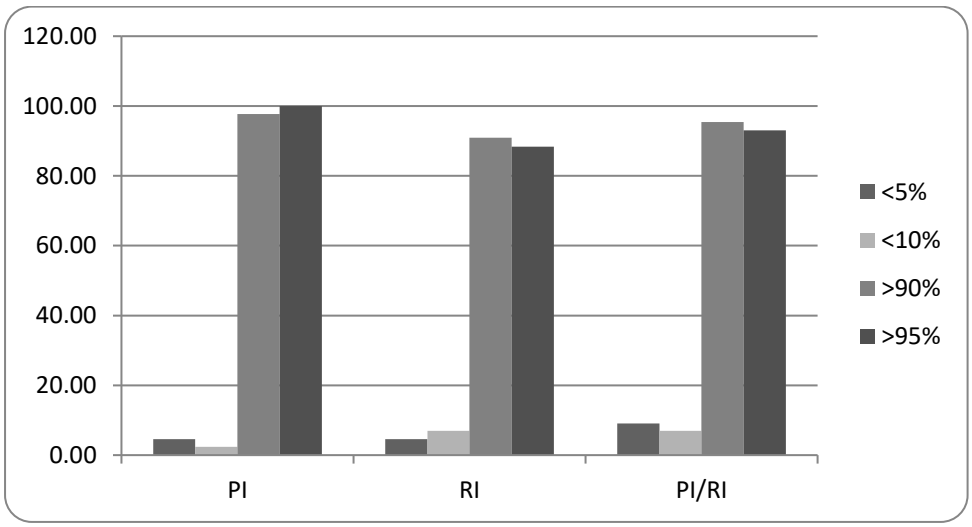

Figure 8. Frequency of uterine artery notching for different percentiles of Doppler flow indices

Jurnal Medical Aradean (Arad Medical Journal)
Vol. XX, issue 3, 2017, pp. 17-26

Table 4: Comparison of PI and RI

Comparison	p	Comparison	p	Comparison	p
PI Total vs Bilateral notch	<0.0005	RI Total vs Bilateral notch	<0.00005	PI/RI Total vs Bilateral notch	<0.0005
PI Total vs Unilateral notch	NS	RI Total vs Unilateral notch	NS	PI/RI Total vs Unilateral notch	NS
PI Total vs Absent Notch	<0.00001	RI Total vs Absent Notch	<0.00005	PI/RI Total vs Absent Notch	<0.00005
PI Bilateral notch vs Unilateral notch	<0.0005	RI Bilateral notch vs Unilateral notch	<0.0005	PI/RI Bilateral notch vs Unilateral notch	<0.001
PI Bilateral notch vs Absent Notch	<0.000000001	RI Bilateral notch vs Absent Notch	<0.000000001	PI/RI Bilateral notch vs Absent Notch	<0.000000001
PI Unilateral notch vs Absent Notch	<0.05	RI Unilateral notch vs Absent Notch	<0.05	PI/RI Unilateral notch vs Absent Notch	<0.05
PI Total vs 11 - 11+6	NS	RI Total vs 11 - 11+6	NS	PI/RI Total vs 11 - 11+6	NS
PI Total vs 12 - 12+6	NS	RI Total vs 12 - 12+6	NS	PI/RI Total vs 12 - 12+6	NS
PI Total vs 13 - 13+6	NS	RI Total vs 13 - 13+6	NS	PI/RI Total vs 13 - 13+6	NS
PI 11 - 11+6 vs 12 - 12+6	NS	RI 11 - 11+6 vs 12 - 12+6	NS	PI/RI 11 - 11+6 vs 12 - 12+6	NS
PI 11 - 11+6 vs 13 - 13+6	<0.01	RI 11 - 11+6 vs 13 - 13+6	<0.05	PI/RI 11 - 11+6 vs 13 - 13+6	<0,05
PI 12 - 12+6 vs 13 - 13+6	NS	RI 12 - 12+6 vs 13 - 13+6	NS	PI/RI 12 - 12+6 vs 13 - 13+6	NS
PI Present Notch vs Absent Notch	<0.000000001	RI Present Notch vs Absent Notch	<0.000000001	PI/RI Present Notch vs Absent Notch	<0.000000001
PI Present Notch vs Unilateral with Present Notch	NS	RI Present Notch vs Unilateral with Present Notch	NS	PI/RI Present Notch vs Unilateral with Present Notch	NS
PI Present Notch vs Unilateral with Absent Notch	<0.000000001	RI Present Notch vs Unilateral with Absent Notch	<0.000000001	PI/RI Present Notch vs Unilateral with Absent Notch	<0.000000001
PI Absent Notch vs Unilateral with Present Notch	<0.000000001	RI Absent Notch vs Unilateral with Present Notch	<0.00000005	PI/RI Absent Notch vs Unilateral with Present Notch	<0.000000001
PI Absent Notch vs Unilateral with Absent Notch	NS	RI Absent Notch vs Unilateral with Absent Notch	NS	PI/RI Absent Notch vs Unilateral with Absent Notch	NS
PI Unilateral with Present Notch vs Unilateral with Absent Notch	<0.00000005	RI Unilateral with Present Notch vs Unilateral with Absent Notch	<0.0000005	PI/RI Unilateral with Present Notch vs Unilateral with Absent Notch	<0.0000005

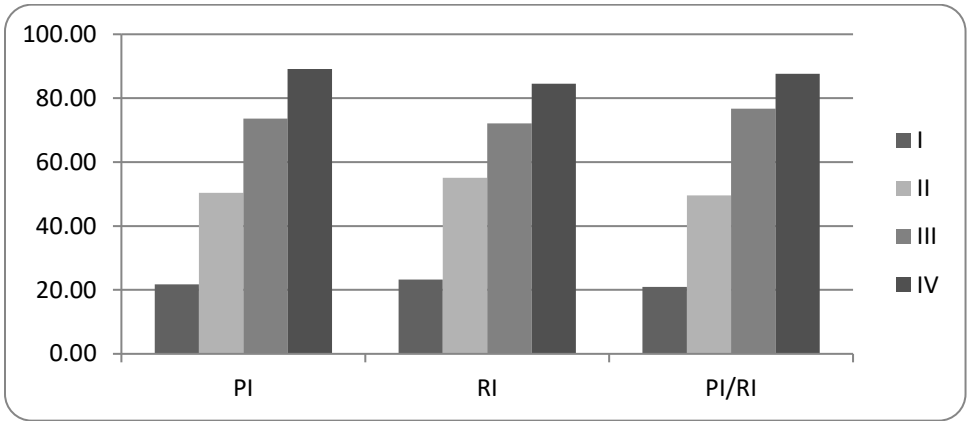

Figure 9. Frequency of uterine artery notching for different quartiles of Doppler flow indices

DISCUSSIONS

The frequency of bilateral uterine artery notching in our study is 48.61%. The frequency of both bilateral and unilateral uterine artery notching decrease with increasing gestational age.

The results in our study are similar to those in literature:

-mean PI 1.79, 1.68, 1.58, and 1.49 at 11, 12, 13 and 14, with the 95th percentile at 2.70, 2.53, 2.38, and 2.24 weeks respectively (Gómez et al., 2008);

-PI 1.96±0.6, 1.83±0.53, 1.71±0.47, and 1.58±0.41, with the 95th percentile at 3.13, 2.88, 2.63, and 2.38 at 11, 12, 13, and 14 weeks respectively (Gómez et al., 2006);

-PI 1.6±0.5, 1.5±0.6, 1.4±0.4, and 1.3±0.4 at 11, 12, 13, and 14 weeks respectively (Alves et al., 2013);

-RI 0.7±0.1, 0.7±0.1, 0.6±0.1, and 0.6±0.1 at 11, 12, 13, and 14 weeks respectively (Alves et al., 2013);

-PI 2.32 ± 0.79 and RI 0.83 ± 0.07 with notching, 1.61 ± 0.78 and 0.71 ± 0.16 without notching (da Costa et al., 2010);

-95th percentile of RI at 11-14 weeks at 0.85 (Melchiorre et al., 2009);

-the frequency of bilateral notching 48.6%, 47.9%, 30.6%, and 28.4% at 11, 12, 13, and 14 weeks respectively (Gómez et al., 2006);

-the frequency of bilateral notching 40.68%, 26.09%, and 33.33% and of unilateral notching 25.42%, 17.39%, and 16.67% at 11 weeks + 0 days to 11 weeks + 6 days, 12 weeks + 0 days to 12 weeks + 6, and 13 weeks + 0 days to 13 weeks + 6 days, respectively (Dascau et al., 2016);

-the frequency of bilateral notching 50%, 39.53%, and 33.96% and of unilateral notching 22.22%, 18.60%, and 16.98% at 11 weeks + 0 days to 11 weeks + 6 days, 12 weeks + 0 days to 12 weeks + 6, and 13 weeks + 0 days to 13 weeks + 6 days, respectively (Dascau et al., 2016);

-the PI 1.69±0.75, 1.79± 0.78, 1.57±0.68, and 1.61±0.75 and the RI 0.72±0.14, 0.73±0.14, 0.70±0.13, and 0.71±0.14 at 11 weeks + 0 days to 13 weeks + 6 days, 11 weeks + 0 days to 11 weeks + 0 days to 13 weeks + 6 days, 11 weeks + 6 days, 12 weeks + 0 days to 12 weeks + 6, and 13 weeks + 0 days to 13 weeks + 6 days, respectively (Dascau et al., 2016);

-the PI 1.75±0.79, 1.88± 0.81, 1.71±0.81, and 1.58±0.72 and the RI 0.72±0.14, 0.75±0.14, 0.71±0.14, and 0.70±0.14 at 11 weeks + 0 days to 13 weeks + 6 days, 11 weeks + 0 days to 11 weeks + 0 days to 13 weeks + 6 days, 12 weeks + 0 days to 12 weeks + 6, and 13 weeks + 0 days to 13 weeks + 6 days, respectively (Dascau et al., 2016);

-the PI 1.75±0.79, 1.90± 0.82, 1.72±0.81, and 1.58±0.71 and the RI 0.72±0.14, 0.75±0.14, 0.72±0.13, and 0.70±0.13 at 11 weeks + 0 days to 13 weeks + 6 days, 11 weeks + 0 days to 11 weeks + 0 days to 13 weeks + 6 days, 12 weeks + 0 days to 12 weeks + 6, and 13 weeks + 0 days to 13 weeks + 6 days, respectively (Daşcău et al., 2017).

CONCLUSIONS

The mean uterine artery PI and RI and the frequency of bilateral and unilateral uterine artery notching decrease from 11 weeks + 0 days-11 weeks + 6 days to 13 weeks + 0 days-13 weeks + 6 days (statistically not significant) and also from pregnant patients with bilateral uterine artery notching to those without notching (statistically not significant).

Our aim is to screen, as much as possible, all pregnant patients between 11 and 14 weeks of pregnancy who are referring to our clinic by uterine artery Doppler ultrasound in order to discover bilateral notching as soon as possible for specific prophylactic treatment, according to existing guidelines and recommendations, to be started.

REFERENCES

Akbaş M, Şen C, Calay Z. Correlation between First and Second Trimester Uterine Artery Doppler Velocimetry and Placental Bed Histopathology Int Sch Res Notices. 2014 Jul 13;2014

Alves JA, Silva BY, de Sousa PC, Maia SB, Costa Fida S. Reference range of uterine artery Doppler parameters between the 11th and 14th pregnancy weeks in a population sample from Northeast Brazil. Rev Bras Ginecol Obstet. 2013 Aug;35(8):357-62.

Antonio Gadelha da Costa; Patricia Spara; Thiago de Oliveira Costa; William Ramos Tejo Neto Uterine arteries resistance and pulsatility indices at the first and second trimesters of normal pregnancies Radiol Bras. 2010 Mai/Jun;43(3):161–165

Dascau V, Gh. Furau, C. Furau, C. Onel, C. Stănescu, L. Tătaru, C. Ghib-Para, M. Puschita Uterine Artery Doppler Flow Indices in Pregnant Women During The 11 Weeks + 0 Days ind 13 Weeks + 6 Days Gestational Ages: A Study Of 118 Patients J Med Ar 2016; 19 (1), 37-41

Dascau V, Gh. Furau, C. Furau, C. Onel, C. Stănescu, L. Tătaru, C. Ghib-Para, C. Popescu , L. Pilat., M. Puschita Uterine Artery Doppler Flow Indices in Pregnant Women During The 11 Weeks + 0 Days ind 13 Weeks + 6 Days Gestational Ages: A Study Of 168 Patients; MAEDICA – a Journal of Clinical Medicine 2017 a; 12(1): 36-41

Daşcău Voicu, Furău Gheorghe, Furău Cristian, Onel Cristina, Stănescu Casiana, Tătaru Liliana, Popescu Cristina, Puşchiţa Maria Uterine Artery Doppler Flow Indices in Pregnant Women During the 11 Weeks + 0 Days and 13 Weeks + 6 Days Gestational Ages: a Study of 201 Patients; Proceedings 5th Congress of the Romanian Society of Ultrasound in Obstetrics and Gynecology, 2017 b, 213-218

Ferreira AE, Mauad Filho F, Abreu PS, Mauad FM, Araujo JuniorE, Martins WP. The reproducibility of first and second trimester uterine artery pulsatility index by transvaginal and transabdominal ultrasound. Ultrasound Obstet Gynecol 2015; 46: 546-52. [CrossRef]J Turk Ger Gynecol Assoc 2016; 17: 16-20

Ghulmiyyah L, Sibai B. Maternal mortality from pre-eclampsia/eclampsia. Semin Perinatol 2012;36:56-9.

Gomez O, F. Figueras, J. M. Martinez, M. Del Rio, M. Palacio, E. Eixarch, B. Puerto, O. Coll, V. Cararach and J. A. Vanrell Sequential changes in uterine artery blood flow pattern between the first and second trimesters of gestation in relation to pregnancy outcome Ultrasound Obstet Gynecol 2006; 28: 802–808

Gómez O, F. Figueras, S. Fernández, M. Bennasar, J. M. Martínez, B. Puerto, E. Gratacós Reference ranges for uterine artery mean pulsatility index at 11–41 weeks of gestation Ultrasound Obst Gyn Volume 32, Issue 2, August 2008, 128–132

Khalil A., NicolaideS KH How to record uterine artery Doppler in the first trimester *Ultrasound Obstet Gynecol* 2013; 42: 478–479

Melchiorre K, K. Leslie, F. Prefumo, A. Bhide and B. Thilaganathan First-trimester uterine artery Doppler indices in the prediction of small-for-gestational age pregnancy and intrauterine growth restriction Ultrasound Obstet Gynecol 2009; 33: 524–529

Peixoto AB, Da Cunha Caldas TM, Tonni G, De Almeida Morelli P, Santos LD, Martins WP, Araujo Júnior E. Reference range for uterine artery Doppler pulsatility index using transvaginal ultrasound at 20-24w6d of gestation in a low-risk Brazilian population. J Turk Ger Gynecol Assoc. 2016 Jan 12;17(1):16-20.

Poon LC, Syngelaki A, Akolekar R, Lai J, Nicolaides KH. Combined screening for preeclampsia and small for gestational age at 11–13weeks. *Fetal Diagn Ther* 2012 [Epub ahead of print].

Roberge S, Nicolaides KH, Demers S, Villa P, Bujold E. Prevention of perinatal death and adverse perinatal outcome using lowdose aspirin: a meta-analysis. Ultrasound Obstet Gynecol. 2013;41(5):491-9.

Scandiuzzi RM, de Campos Prado CA, Araujo Júnior E, Duarte G, Quintana SM, da Silva Costa F, Tonni G, de Carvalho Cavalli R, Marcolin AC Maternal uterine artery Doppler in the first and second trimesters as screening method for hypertensive disorders and adverse perinatal outcomes in low-risk pregnancies Obstet Gynecol Sci 2016;59(5):347-356

Velauthar L, Plana MN, Kalidindi M, Zamora J, Thilaga-nathan B, Illanes SE, et al. First-trimester uterine artery Doppler and adverse pregnancy outcome: a meta-analysis involving 55,974 women. Ultrasound Obstet Gynecol 2014;43:500-7.