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UTERINE ARTERY DOPPLER FLOW INDICES FROM 21 TO 24 WEEKS GESTATIONAL AGE

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ABSTRACT. Uterine artery Doppler flow studies during the 21th and 24th weeks of pregnancy are important in the prediction of preeclampsia and IUGR in pregnant women and also in the prevention thereof. Our study of the Doppler flow indices of the uterine arteries involves 150 patients examined in our clinic, with pregnancies ranging from 21 weeks + 0 days to 23 weeks + 6 days. There were 41 patients from 21 weeks + 0 days to 21 weeks + 6 days (27.33%), 54 from 22 weeks + 0 days to 22 weeks + 6 days (36%), and 55 from 23 weeks + 0 days to 23 weeks + 6 days (36.67%). The values of the Doppler indices were: PI 1.06±0.45, 1.09±0.42, 1.06±0.56, and 1.05±0.32, RI 0.58±0.11, 0.59±0.11, 0.57±0.12, and 0.59±0.09, and PI/RI 1.77±0.38, 1.78±0.35, 1.77±0.48, and 1.76±0.26for the entire group and for the three intervals respectively. There were 21 (14%), 22 (14.67%, with 13 cases or 59.09% on the left side), and 107 (71.33%) patients with bilateral, unilateral and absent uterine artery notching, respectively. The Doppler indices for the three aforementioned groups were: 1.53±0.69, 1.12±0.42, and 0.96±0.32 for the PI, 0.68±0.11, 0.60±0.11, and 0.56±0.10for the RI, and 2.17±0.61, 1.81±0.33, and 1.68±0.25 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 1.43±0.64, 0.96±0.31, 1.25±0.49, and 1.00±0.28 for the PI, 0.66±0.12, 0.56±0.10, 0.63±0.12, and 0.58±0.08 for the RI, and 2.08±0.56, 1.68±0.25, 1.90±0.39, and 1.71±0.23for the PI/RI respectively. The mean uterine artery PI, RI, and PI/RI decrease from 21 weeks + 0 days-21 weeks + 6 days to 23 weeks + 0 days-23 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. Our results are similar to those in literature.
KEYWORDS: pregnancy, gestational age, uterine artery notching, Doppler indices, pulsatility index, resistivity index, preeclampsia, IUGR

INTRODUCTION

Doppler ultrasound, as a non-invasive imaging method for the examination of the uteroplacental circulation, could be used as a screening test for several pregnancy associated diseases and complications, including preeclampsia and IUGR (Campbell et al., 1983). Elevated blood flow resistance indices of the uterine arteries at 20 and 24 weeks of gestation occur more commonly in women who develop pre-eclampsia occur more commonly in women who develop pre-eclampsia,but the association reveals only low positive predictive values (Valensise et al., 1998). Conflicting results published to date perhaps reflect differences in the selected populations, the anatomical sites of measurement, the indices used to describe an abnormal waveform, as well as the outcome measures for prediction (Valensise et al., 1998; Chappell et al., 1998). Doppler indices have been analyzed only in a cross-sectional way without considering the longitudinal fall in resistance that is to be observed in normal pregnances (Arduini et al., 1994).

Several studies have assessed the uterine artery Doppler flow indices at gestational ages of 21-24 weeks or close to this period:

-172 women at high risk for hypertensive disorders of pregnancy or intrauterine growth restriction; the impedance to flow in the uterine arteries at 21–24 weeks of gestation was measured, an abnormal result by a resistance index of more than 0.68 being defined (Zimmermann et al., 1997);

- the average resistance index from the left and right uterine and arcuate arteries in 925 pregnancies at 16–24 weeks gestation was calculated; a resistance index above the 95th centile meanta 10-fold increase in risk for a severe adverse outcome, defined by fetal death, placental abruption, intrauterine growth restriction or pre-eclampsia (Bewley et al., 1991);

- a study of 2058 pregnancies at 18–22 weeks revealed a resistance index above the 95th centile or the presence of an early diastolic notch in either of the two uterine arteries in 16% of the pregnancies; this study showed that abnormal Doppler results provide a better prediction of the more severe types of pregnancy complications (Bower et al., 1993);

- an abnormal result (mean resistance index of more than 0.58) was found in 9.6% of patients in a group of 272 primigravidas at 22 weeks of gestation (Valensise et al., 1993);

- the examination of the uterine arteries at 19–24 weeks of gestation in 457 nulliparous women found an increased impedance, meaning a resistance index greater than 0.57 in 11% of cases (North et al., 1994);

-334 patients considered to be at medium risk for the development of pregnancy-induced hypertension, examined at 20 weeks of gestation 10. a mean resistance index above the 90th centile and the presence of bilateral diastolic notches, was found in 4.2% of cases (Chan et al., 1995);

-946 unselected women examined at 19–21 weeks of gestation 12; 12.4% had bilateral notches and an odds ratio for developing pre-eclampsia of 12.8, and 52.6 for pre-eclampsia requiring delivery before 37 weeks; normal uterine artery Doppler studies revealed an odds ratio for developing pre-eclampsia of 0.11 and 0.3 for intrauterine growth restriction (birth weight below the 5th centile for gestation), it was 0.3; women with normal uterine artery Doppler studies at 20 weeks constitute a group that have a low risk of developing obstetric complications related to uteroplacental insufficiency, while patients with bilateral notches have an increased risk of the subsequent development of such complications; as a result, Doppler studies of the uterine arteries at the time of the routine 20-week anomaly scan may be of use in determining the type and level of antenatal care that is offered to women (Kurdi et al., 1998);

Frusca et al. - 419 nulliparous women examined at 20 weeks of gestation; those with increased mean resistance index (greater than 0.58) had the uterine arteries reexamined by color Doppler at 24 weeks, with persistently high resistance observed in 8.6% of the patients; in the group with increased resistance at 20 weeks and normal results at 24 weeks, the prevalence of pregnancy complications was not increased compared to those with normal impedance at 20 weeks (Frusca et al., 1997);

-1233 unselected women examined by continuous wave Doppler at 20 weeks of gestation, those with increased impedance (resistance index greater than the 95th centile or early diastolic notch in either of the uterine arteries) being reexamined at 24 weeks; a persistently increased impedance was observed in 8.9% of the patients in this group (Harrington et al., 1996);

-1757 singleton pregnancies attending for routine ultrasound examination at 23 weeks were also examined by uterine artery Doppler, with an increased impedance observed in 7.3% of patients, including 5.1% with mean pulsatility index of above 1.45 and 4.4% with bilateral uterine artery notches; the results of this study suggest that a one-stage color Doppler screening program at 23 weeks identifies most women who subsequently develop the serious complications of impaired placentation associated with delivery before 34 weeks and the screening results are similar if the high-risk group is defined either as those with increased PI or those with bilateral notche (Albaiges et al., 2000);

-2600 unselected women were randomized to Doppler and non-Doppler groups; the Doppler studies were performed at 19–22 weeks and then again at 32 weeks for those classified as being at low risk, and monthly Doppler studies in those considered at high risk.; an abnormal result was defined by the presence of an abnormal waveform bilaterally at the uterine arteries; there was a high frequency of pregnancy complications in women with abnormal uterine artery waveforms and abnormal waveforms were an indicator of subsequent fetal compromise, but no improvement in neonatal outcome was revealed by routine Doppler screening (Davies et al., 1992).

MATERIALS AND METHODS

We assessed the uterine artery Doppler flow indices in 150 pregnant patients within the 21 weeks + 0 days and 23 weeks + 6 days gestational ages in our clinic during the 2014-2016 period (both in and outpatients) 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.

RESULTS

Among the 150 pregnant women in the group we studied, there were 41 patients from 21 weeks + 0 days to 21 weeks + 6 days (27.33%), 54 from 22 weeks + 0 days to 22 weeks + 6 days (36%), and 55 from 23 weeks + 0 days to 23 weeks + 6 days (36.67%) gestational age (figure 1).

Our study revealed that 21 (14%), 22 (14.67%, with 13 cases or 59.09% on the left side), and 107 (71.33%) patients had bilateral, unilateral and absent uterine artery notching, respectively (figure 2).

We also assessed the uterine arteries in the study group according to the presence (n=64) or absence (n=236) of notching, as well as the indices for the uterine arteries with and without notching in the patients with unilateral notching (n=22). The values of the Doppler indices are shown in tables 1-3 and figures 3-5.

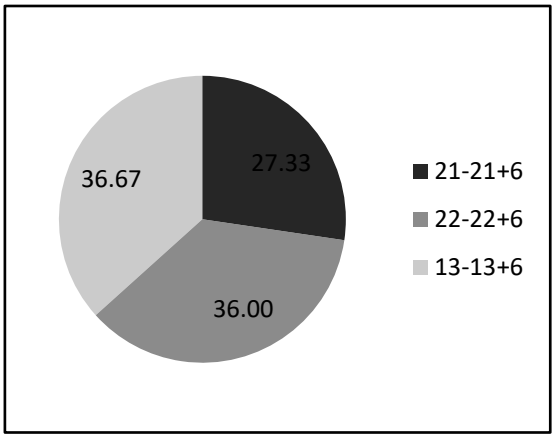

Figure 1: Age group distribution

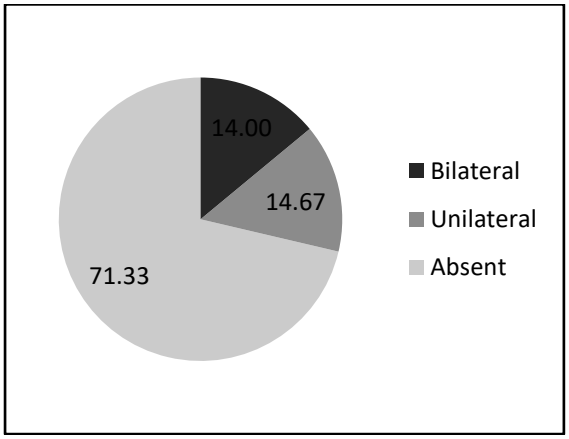

Figure 2: Notch type distribution

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

	PI			
Group	Value	5th	95th	Range
All (150 patients)	1.06±0.45	0.61	1.92	0.34-3.88
21 weeks + 0 days to 21 weeks + 6 days (41 patients)	1.09±0.42	0.61	1.82	0.50-2.92
22 weeks + 0 days to 22 weeks + 6 days (54 patients)	1.06±0.56	0.54	2.08	0.34-3.88
23 weeks + 0 days to 23 weeks + 6 days (55 patients)	1.05±0.32	0.69	1.70	0.57-2.11
Bilateral uterine artery notching (21 patients)	1.53±0.69	0.89	2.92	0.69-3.88
Unilateral uterine artery notching (22 patients)	1.12±0.42	0.63	1.94	0.48-2.44
Absent uterine artery notching (107 patients)	0.96±0.32	0.59	1.57	0.34-2.23
Uterine artery with notch (n=64)	1.43±0.64	0.76	2.44	0.61-3.88
Uterine artery without notch (n=236)	0.96±0.31	0.59	1.57	0.34-2.23
Uterine artery with notch in unilateral notch patients (n=22)	1.25±0.49	0.76	1.97	0.61-2.44
Uterine artery without notch in unilateral notch patients (n=22)	1.00±0.28	0.63	1.50	0.48-1.75

Table 2. Mean RI±SD, 5th and 95th percentiles

	RI			
Group	Value	5th	95th	Range
All (150 patients)	0.58±0.11	0.43	0.80	0.28-0.89
21 weeks + 0 days to 21 weeks + 6 days (41 patients)	0.59±0.11	0.43	0.77	0.38-0.84
22 weeks + 0 days to 22 weeks + 6 days (54 patients)	0.57±0.12	0.40	0.82	0.28-0.89
23 weeks + 0 days to 23 weeks + 6 days (55 patients)	0.59±0.09	0.46	0.76	0.41-0.82
Bilateral uterine artery notching (21 patients)	0.68±0.11	0.49	0.84	0.45-0.89
Unilateral uterine artery notching (22 patients)	0.60±0.11	0.44	0.80	0.35-0.84
Absent uterine artery notching (107 patients)	0.56±0.10	0.43	0.75	0.28-0.83
Uterine artery with notch (n=64)	0.66±0.12	0.49	0.84	0.41-0.89
Uterine artery without notch (n=236)	0.56±0.10	0.43	0.74	0.28-0.83
Uterine artery with notch in unilateral notch patients (n=22)	0.63±0.12	0.49	0.80	0.41-0.84
Uterine artery without notch in unilateral notch patients (n=22)	0.58±0.08	0.48	0.71	0.35-0.74

Table 3. Mean PI/RI±SD, 5th and 95th percentiles

	PI/RI			
Group	Value	5th	95th	Range
All (150 patients)	1.77±0.38	1.39	2.40	1.21-4.41
21 weeks + 0 days to 21 weeks + 6 days (41 patients)	1.78±0.35	1.40	2.36	1.32-3.48
22 weeks + 0 days to 22 weeks + 6 days (54 patients)	1.77±0.48	1.35	2.51	1.21-4.41
23 weeks + 0 days to 23 weeks + 6 days (55 patients)	1.76±0.26	1.46	2.25	1.28-2.64
Bilateral uterine artery notching (21 patients)	2.17±0.61	1.53	3.48	1.47-4.41
Unilateral uterine artery notching (22 patients)	1.81±0.33	1.48	2.43	1.37-2.90
Absent uterine artery notching (107 patients)	1.68±0.25	1.37	2.14	1.21-2.72
Uterine artery with notch (n=64)	2.08±0.56	1.53	2.90	1.47-4.41
Uterine artery without notch (n=236)	1.68±0.25	1.37	2.14	1.21-2.72
Uterine artery with notch in unilateral notch patients (n=22)	1.90±0.39	1.54	2.63	1.49-2.90
Uterine artery without notch in unilateral notch patients (n=22)	1.71±0.23	1.43	2.11	1.37-2.36

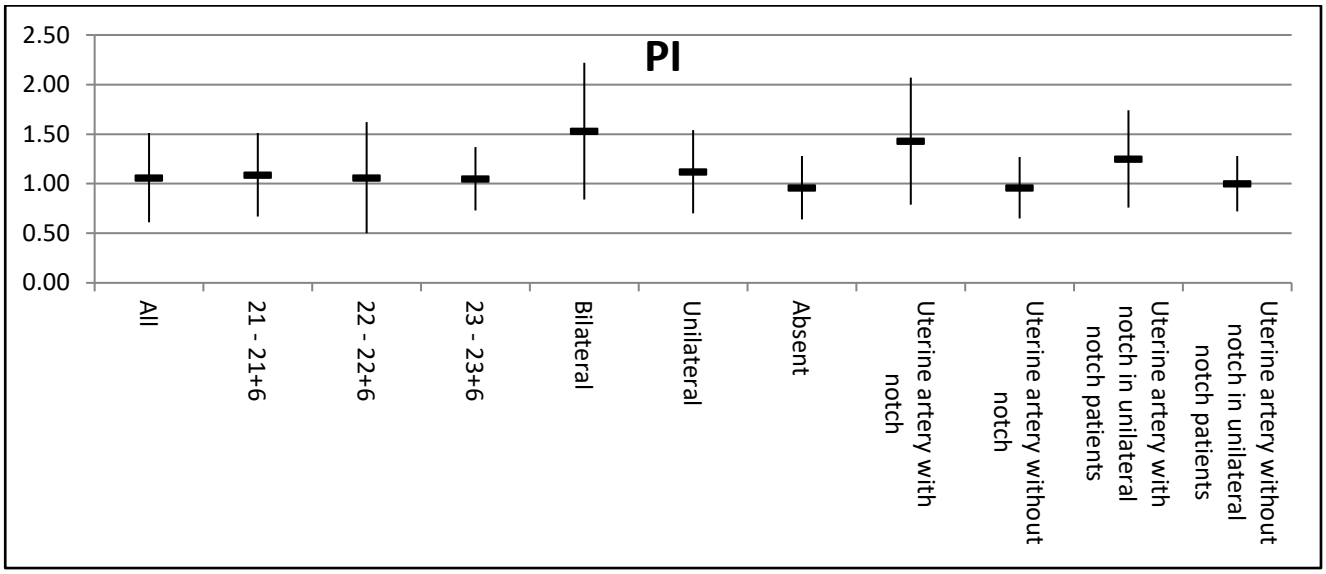

Figure 3. Mean PI±DS

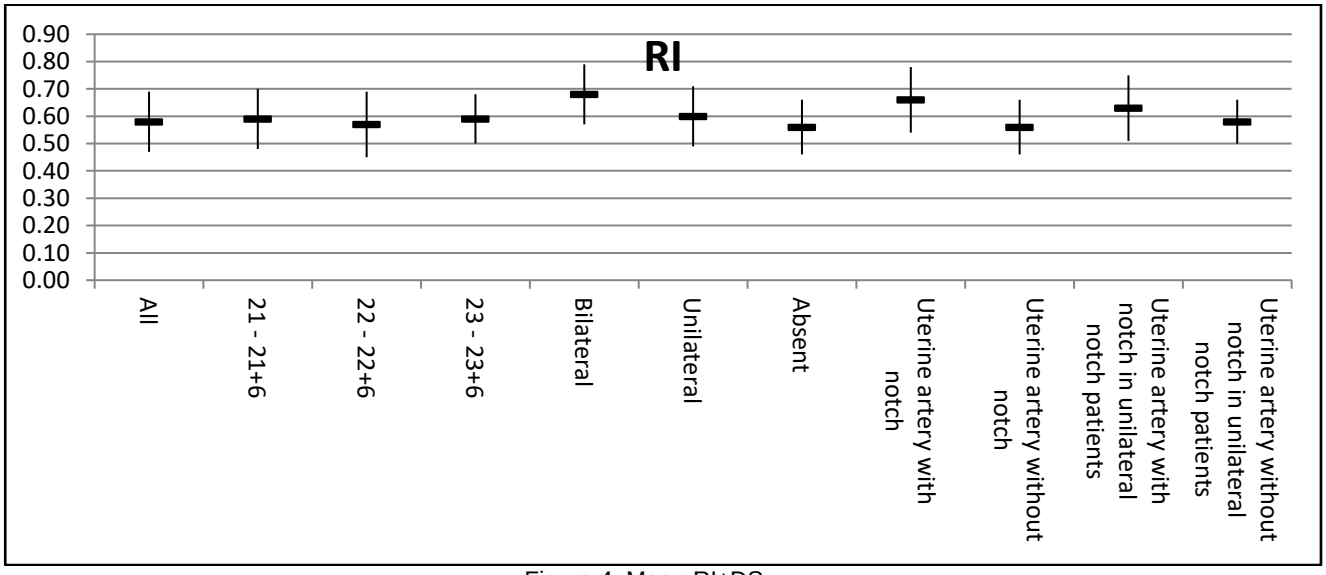

Figure 4. Mean RI±DS

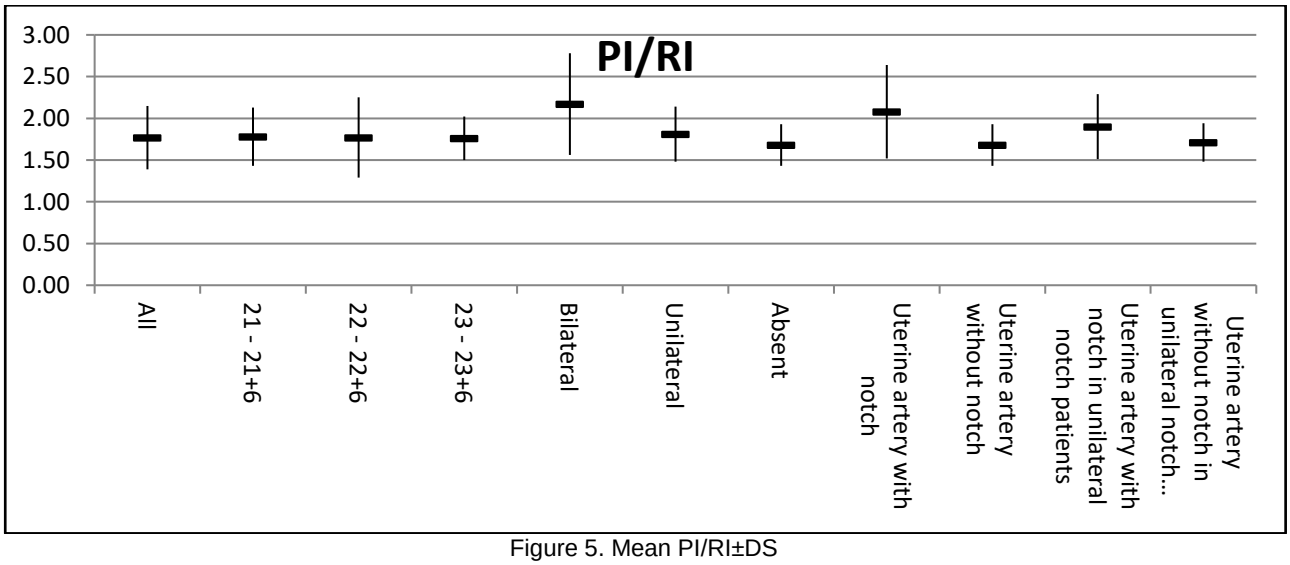

Figure 5. Mean PI/RI±DS

Table 4 and figure 6 present the frequency of different types of uterine artery notching among the three gestational age groups (a decrease in the frequency of both can be observed), while table 5 and figure 7 present the distribution of types of uterine artery notching among the three gestational age groups.

Table 4. Distribution of frequency of different types of uterine artery notching among the three gestational age groups

Notching	21 weeks + 0 days to 21 weeks + 6 days (n=41)	22 weeks + 0 days to 22 weeks + 6 days (n=54)	23 weeks + 0 days to 23 weeks + 6 days (n=55)
Bilateral (n=21)	5 (12.20%)	7 (12.96%)	9 (16.36%)
Unilateral (n=22)	5(12.20%)	7 (12.96%)	10 (18.18%)
Absent (n=107)	31 (75.60%)	40 (74.06%)	36 (65.46%)

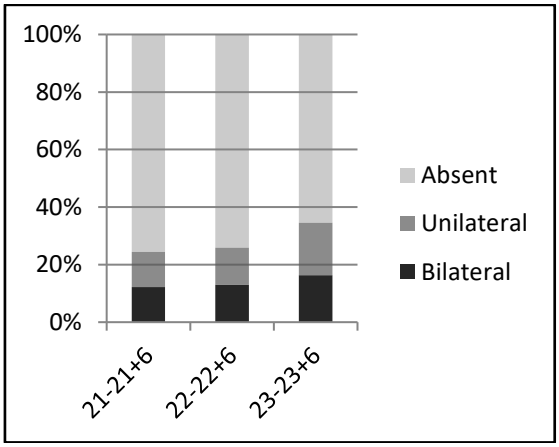

Figure 6. Distribution of frequency of different types of uterine artery notching among the three gestational age groups

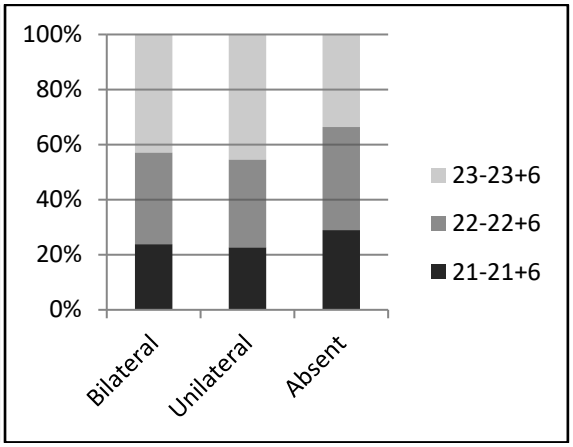

Figure 7. Distribution of types of uterine artery notching among the three gestational age groups

Table 5. Distribution of types of uterine artery notching among the three gestational age groups

Notching	Bilateral (n=21)	Unilateral (n=22)	Absent (n=107)
21 weeks + 0 days to 21 weeks + 6 days (n=41)	5 (23.81%)	5 (22.73%)	31 (28.97%)
22 weeks + 0 days to 22 weeks + 6 days (n=54)	7 (33.33%)	7 (31.82%)	40 (37.38%)
23 weeks + 0 days to 23 weeks + 6 days (n=55)	9 (42.86%)	10 (45.45%)	36 (33.65%)

We used Student's t-test to compare the PI and RI among different groups (all patients versus different gestational age groups and versus groups according to the presence or absence of notching, as well as different groups between them, and the indices of all uterine arteries with and without notching within the group), the results being shown in table 4 (NS=non significant) (table 6).

Table 6: Comparison of PI and RI

Comparison	p	Comparison	p	Comparison	p
PI Total vs Bilateral notch	<0.00000005	RI Total vs Bilateral notch	<0.0000001	PI/RI Total vs Bilateral notch	<0.00000005
PI Total vs Unilateral notch	NS	RI Total vs Unilateral notch	NS	PI/RI Total vs Unilateral notch	NS
PI Total vs Absent Notch	<0.01	RI Total vs Absent Notch	<0.05	PI/RI Total vs Absent Notch	<0.005
PI Bilateral notch vs Unilateral notch	<0.005	RI Bilateral notch vs Unilateral notch	<0.005	PI/RI Bilateral notch vs Unilateral notch	<0.001
PI Bilateral notch vs Absent Notch	<0.00000001	RI Bilateral notch vs Absent Notch	<0.00000001	PI/RI Bilateral notch vs Absent Notch	<0.00000001
PI Unilateral notch vs Absent Notch	<0.005	RI Unilateral notch vs Absent Notch	<0.05	PI/RI Unilateral notch vs Absent Notch	<0.005
PI Total vs 21 - 21+6	NS	RI Total vs 21 - 21+6	NS	PI/RI Total vs 21 - 21+6	NS
PI Total vs 22 - 22+6	NS	RI Total vs 22 - 22+6	NS	PI/RI Total vs 22 - 22+6	NS
PI Total vs 23 - 23+6	NS	RI Total vs 23 - 23+6	NS	PI/RI Total vs 23 - 23+6	NS
PI 21 - 21+6 vs 22 - 12+6	NS	RI 21 - 21+6 vs 22 - 12+6	NS	PI/RI 21 - 21+6 vs 22 - 12+6	NS
PI 21 - 21+6 vs 23 - 13+6	NS	RI 21 - 21+6 vs 23 - 13+6	NS	PI/RI 21 - 21+6 vs 23 - 13+6	NS
PI 22 - 22+6 vs 23 - 13+6	NS	RI 22 - 22+6 vs 23 - 13+6	NS	PI/RI 22 - 22+6 vs 23 - 13+6	NS
PI Present Notch vs Absent Notch	<0.00000001	RI Present Notch vs Absent Notch	<0.00000001	PI/RI Present Notch vs Absent Notch	<0.00000001
PI Present Notch vs Unilateral with	NS	RI Present Notch vs Unilateral with	NS	PI/RI Present Notch vs Unilateral with Present	NS

Present Notch		Present Notch		Notch	
PI Present Notch vs Unilateral with Absent Notch	<0.005	RI Present Notch vs Unilateral with Absent Notch	<0.005	PI/RI Present Notch vs Unilateral with Absent Notch	<0.005
PI Absent Notch vs Unilateral with Present Notch	<0.0001	RI Absent Notch vs Unilateral with Present Notch	<0.005	PI/RI Absent Notch vs Unilateral with Present Notch	<0.0005
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	<0.05	RI Unilateral with Present Notch vs Unilateral with Absent Notch	NS	PI/RI Unilateral with Present Notch vs Unilateral with Absent Notch	NS

In the group we studied, uterine artery notching was always absent in case of PI below the 14.7 percentile, RI below the 2.7 percentile, and PI/RI below the 11.3 percentile and always present in case of PI above the 98.7 percentile, RI above the 98.3 percentile, and PI/RI above the 98.7 percentile.

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

-5% for PI below the 20th percentile and 10% for PI below the 50th percentile

-5% for PI below the 20th percentile and 10.1% for RI below the 33rd percentile

-5% for PI below the 20th percentile and 10.3% for PI/RI below the 51.7 percentile.

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

-30% for PI above the 93.3 percentile

-16.67% for RI above the 98 percentile

-12.5% for PI/RI above the 97.3.

The frequencies of notching for different indices percentiles and quartiles are shown in table 7.

Table 7: Frequency of uterine artery notching for different indices percentiles and quartiles

Percentile	**<5%**	**<10%**	**>90%**	**>95%**
PI	6.67%	3.33%	66.67%	66.67%
RI	6.67%	6.67%	60%	66.67%
PI/RI	0%	0%	63.33%	66.67%
Quartile	**I**	**II**	**III**	**IV**
PI	6.67%	13.33%	16%	49.33%
RI	8%	12%	20%	45.33%
PI/RI	4%	14.67%	17.33%	49.33%

DISCUSSIONS

The mean uterine artery PI and RI vary and the frequency of bilateral and unilateral uterine artery notching vary from 21 weeks + 0 days-21 weeks + 6 days to 23 weeks + 0 days-23 weeks + 6 days. They also decrease from pregnant patients with bilateral uterine artery notching to those without notching.

The frequency of bilateral uterine artery notching in our study is 14%,

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

-mean PI 1.10±0.30, 1.05±0.27 (Gómez et al, 2006) and 1.05 and 1.00 at 21 and 22, respectively (Gómez et al, 2006), and 1.41 (Albaiges et al., 2003), 1.09 (Papageorghiou et al., 2002) and 0.96 (Gomez et al., 2008) at 23 weeks

-mean RI 0.67 at 23 weeks (Albaiges et al., 2003)

-5th percentile for the PI 0.71, 0.69, 0.66, and 0.64 and 95th percentile for the PI 1.54, 1.47, 1.41, and 1.35 at at 21, 22, 23, and 24 weeks, respectively (Gomez et al., 2008);

-mean PI 1.10, 1.06, 1.03 and 0.99 at 21, 22, 23, and 24 weeks, respectively (Borges Peixoto et al., 2016);

-5th percentile for the PI 0.56, 0.54, 0.52, and 0.49 and 95th percentile for the PI 1.62, 1.57, 1.51, and 1.46 at at 21, 22, 23, and 24 weeks, respectively (Borges Peixoto et al., 2016);

-PI values: 1.14±0.37, range 0.45-2.34, 5th and 95th percentiles at 0.53 and 1.75 (Maciel Scandiuzzi et al., 2016)

-RI values: 0.62±0.09, range 0.35-0.84, 5th and 95th percentiles at 0.47 and 0.77 (Maciel Scandiuzzi et al., 2016)

-the PI 1.06±0.40, 1.00± 0.33, 1.07±0.45, and 1.11±0.38 and the RI 0.58±0.11, 0.57±0.10, 0.58±0.12, and 0.59±0. at 21 weeks + 0 days to 23 weeks + 6 days, 21 weeks + 0 days to 21 weeks + 6 days, 22 weeks + 0 days to 22 weeks + 6, and 23 weeks + 0 days to 23 weeks + 6 days, respectively (Dascau et al, 2016 a);

-the PI 1.05±0.46, 1.01±0.36, 1.08±0.62, and 1.05±0.33 and the RI 0.58±0.11, 0.57±0.11, 0.57±0.13, and 0.59±0.09 at 21 weeks + 0 days to 23 weeks + 6 days, 21 weeks + 0 days to 21 weeks + 6 days, 22 weeks + 0 days to 22 weeks + 6, and 23 weeks + 0 days to 23 weeks + 6 days, respectively (Dascau et al, 2016 b);

CONCLUSIONS

The mean uterine artery PI and RI and the frequency of bilateral and unilateral uterine artery

notching decrease from 21 weeks + 0 days-21 weeks + 6 days to 23 weeks + 0 days-23 weeks + 6 days. They also decrease from pregnant patients with bilateral uterine artery notching to those without notching. In our study, the frequency of both bilateral and unilateral notching increase with increasing gestational age.

Our aim is to screen, as much as possible, all pregnant patients between 21 and 24 weeks of pregnancy who are referring to our clinic of pregnancy 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.

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