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Investigating Uterine Artery Doppler Indices in Normal Pregnancies

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ABSTRACT

Background & Objective: Clinical use of uterine artery (UtA) Doppler ultrasound imaging requires reference values, however despite the common use of UtA Doppler examination during pregnancy, to the best of our knowledge, there is no such range for Iranian pregnant women. Therefore, the present study was conducted aimed to investigate uterine artery Doppler indices in Iranian normal pregnancies.

Materials & Methods: This observational longitudinal study was conducted on 486 low-risk pregnant women. The amount of plausibility index (PI) and resistance index (RI), as well as the presence of diastolic notch was assessed in weeks 11 to 14, 17 to 24, and 27 to 32 through Doppler ultrasound.

Results: The bilateral notch for gestational age of 11 to 14 weeks was detected at about 6%, for gestational age of 17 to 24 weeks was 4.2% and for gestational age of 27 to 32 weeks was 3.6%. Reference intervals for mean uterine artery PI according to gestational ages showed a significant difference between different percentages ($p<0.001$). Also, there is a significant relationship between the mean uterine arteries PI/RI and the presence or absence of pregnancy complications (IUGR, premature birth, IUFD) among the participants.

Conclusion: The results of this research showed a significant relationship between PI and pregnancy complications, while this was not detected in RI and diastolic notch. These results are relatively consistent with the findings of researchers in other countries.

Keywords: Uterine Artery Doppler, Low-risk, Pregnancy, Ultrasound

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1. Introduction

Uterine artery (UtA) Doppler ultrasound is a valuable method for the indirect assessment of uteroplacental blood circulation **(1)**. It is considered a potential screening tool to predict preeclampsia (PE), fetal growth restriction (FGR), placental abruption, and stillbirth **(2, 3)**.

The UtA-PI value can be clinically useful for preeclampsia screening **(4)**, pregnancy-induced hypertension evaluation, and FGR detection, especially in the early stages of pregnancy **(5)**. UtA Doppler examination provides important information about the process of vascular development and transformation of spiral arteries into arterioles. Also, the position of the uteroplacental arteries, the underlying reflection is from the placenta **(6)**.

One of the challenges of modern obstetrics is to identify high-risk women in the early stages. Apart from the fact that high-risk women can be closely monitored for signs of PE or FGR, prevention of the disease is currently possible using low-dose aspirin **(7-9)**.

Use of low-dose aspirin significantly reduces the risk of very severe PE, especially when it started before 16 weeks of pregnancy. Direct assessment of trophoblast invasion in human pregnancy is not possible **(10)**. However, the use of Doppler imaging allows a non-invasive assessment of uteroplacental circulation by comparing systolic and diastolic waveforms **(11)**.

UtA Doppler shows the mother's vascular status by evaluating the plausibility index (PI), resistance index (RI), and the presence of an early diastolic notch. Persistence of early diastolic notch or abnormal velocities is associated with failure of trophoblast invasion. Doppler ultrasound is a valuable tool for management of high-risk pregnancies **(12, 13)**.

This screening test, which is performed as a supplement to routine ultrasound evaluations of pregnancy, does not include significant additional costs and it can identify a group of patients who will benefit the most from increased monitoring during pregnancy **(13)**.

Clinical use of UtA Doppler ultrasound imaging requires reference values, however despite the common use of UtA Doppler examination during pregnancy, to the best of our knowledge, there is no such range for Iranian pregnant women **(9)**. The PI is currently the most used index to evaluate UtA Doppler waveform patterns **(14)**. Therefore, the present study was conducted aimed to investigate uterine artery Doppler indices in Iranian normal pregnancies.

2. Materials and Methods

This observational longitudinal study was conducted on 486 low-risk pregnant women referring to the perinatal clinic of Yas Hospital Complex, affiliated to the Tehran University of Medical Sciences between January 2020 and December 2021.

The inclusion criteria were pregnant women whose gestational age was at 11 to 14 weeks based on crown-rump length (CRL). Exclusion criteria included smoking, alcohol consumption, substance (such as cannabis, cocaine, and others) abuse during pregnancy, positive medical or obstetrics history (such as chronic hypertension, antiphospholipid syndrome, thrombophilia, immunodeficiency virus infection, and sickle cell disease), positive drug history (including anti-hypertensive, anti-depressant, anti-epileptic, anti-inflammatory, anti-retroviral, anti-thyroid, beta-mimetic, lithium, steroid, thyroxine) and the presence of any fetal abnormalities.

All pregnant women were evaluated in terms of fetus chromosomal abnormality by measuring the thickness of the fetal nuchal translucency (NT), beta human chorionic gonadotropin (βHCG), and pregnancy-related plasma protein (PAPP-A) in 11 to 13+6 weeks and scan anomaly in 18 weeks of pregnancy. Furthermore, the amount of PI and RI, as well as the presence of diastolic notch were assessed in weeks 11 to 14, 17 to 24, and 27 to 32 using an ultrasound device (Philips, Affinity 50, USA), with a 6 MHz probe. A sagittal section of the uterus was obtained and the cervical canal and the internal opening of the cervix were identified. The transducer was gently tilted from one side to the other and color flow mapping was used to identify each uterine artery along each side of the cervix at the level of the internal opening of the cervix. A pulsed wave Doppler with 2 mm sampling gate was used to cover the whole vessel and it was made sure that the radiation angle was less than 30 degrees. PI and RI were measured when three consecutive similar waveforms were obtained. The presence or absence of a bilateral diastolic notch was investigated. A notch was defined as a persistent decrease in blood flow velocity in early diastole below the peak diastolic velocity. All ultrasound and Doppler studies were performed by an expert perinatologist. Finally, the correlation between Doppler ultrasound indices and pregnancy outcome incidence including PE, IUGR, premature birth, and intrauterine death (IUFD) was investigated.

Descriptive statistics including mean and standard deviation, as well as frequency and percentage, were used to describe the data. Data was analyzed using SPSS software (version 24). Independent T-test, Non-parametric Mann–Whitney U-test, and One-Way ANOVA were used to assess differences in means. Chi-square and Fisher's exact test were applied to evaluate differences in proportions. $P<0.05$ was considered as significant level.

3. Results

The mean age of the participants was 31.4 ± 5.9 years. The demographic and clinical characteristics of the participants are shown in Table 1. The bilateral notch for gestational age of 11 to 14 weeks was detected at 6%, for gestational age of 17 to 24 weeks was 4.2% and for gestational age of 27 to 32 weeks was 3.6% (Figure 1).

Table 1. Demographic characteristics and clinical history and pregnancy outcomes of the women included in the study

Variables	Mean± SD or Number (%)
Age (years)	31.4 ± 5.9
BMI (kg/m^2)	28.1 ± 4.4
Gravida	2.2 ± 1.1
Live child	1.2 ± 0.6
History of Diabetes mellitus	7 (1.4)
History of Insulin use	4 (0.8)

Variables	Mean± SD or Number (%)
History of Metformin use	4 (0.8)
History of Hypertension	3 (0.6)
History of Covid-19	6 (1.2)
History of Covid-19 vaccination	154 (32.1)
Small for Gestational Age	52 (10.7)
Intrauterine Fetal Death	3 (0.6)
Intrauterine Growth Restriction	16 (1.6)
Maternal complication of high blood pressure	20 (4.1)
Maternal complication of Diabetes Miletus	23 (4.7)
Maternal complication of blood transfusion	2 (0.4)
Gestational Age of delivery (week)	37.5 ± 3.4
Cesarean section	194 (39.9)
Newborn weight (gram)	3011.59 ± 554.05
Abnormal APGAR minute 1	3 (0.6)
Abnormal APGAR minute 5	1 (0.2)

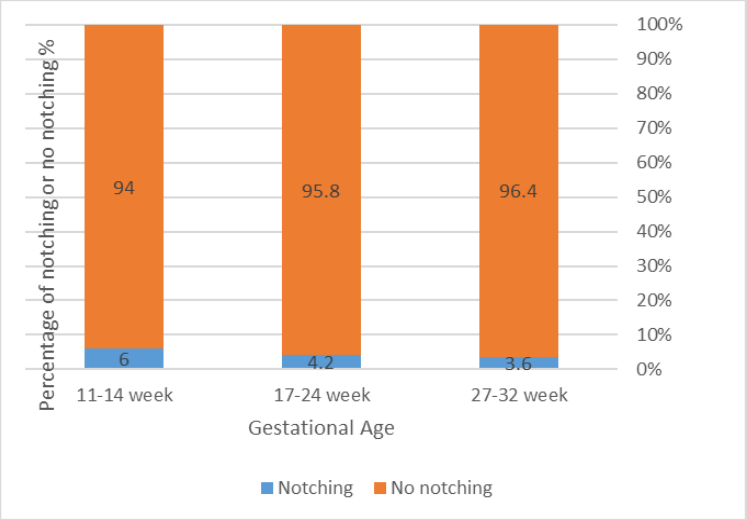


Figure1. Prevalence of bilateral notching in different gestational ages

Reference intervals for mean uterine artery PI according to gestational ages showed a significant difference between different percentages (P<0.001) (Table 2). The reference intervals for the average uterine artery PI and RI according to the gestational age of some different countries (in different continents of the world) were shown in Table 3.

Table 2. Reference intervals for mean uterine artery plausibility index and resistance index according to gestational ages

Variables	Abdominal UtA			
	GA (Weeks)	5th percentile	50th percentile	95th percentile
Bilateral plausibility index	**11-14**	1.15	1.44	1.94
	17-24	0.78	1.24	1.75
	27-32	0.67	0.99	1.10
P-value			<0.001	
	11-14	0.57	0.71	0.85
	17-24	0.58	0.76	0.89

Bilateral resistance index	**27-32**	0.43	0.57	0.71
P-value			0.132	

Table 3. Reference intervals for mean uterine artery pulsation index and resistance index according to gestational ages in different countries

Number	Authors	Country	Variables	Abdominal UtA			
				GA (Weeks)	5th percentile	50th percentile	95th percentile
1	Casmod Y, et al. (2016) (1)	South Africa	Bilateral PI	11-14	1.1	1.7	2.7
				15-24	0.7	1.0	1.5
				25-34	0.6	0.8	1.2
			Bilateral RI	11-14	0.51	0.68	0.82
				15-24	0.48	0.69	0.81
				25-34	0.37	0.55	0.69
2	Gómez O, et al. (2008) (15)	Spain	Bilateral PI	11-14	0.99	1.49	2.24
				19-22	0.69	1.00	1.47
				32-34	0.50	0.70	0.99
			Bilateral RI	11-14	0.48	0.65	0.76
				19-22	0.45	0.63	0.74
				32-34	0.36	0.57	0.66
3	Liao AW, et al. (2009) (16)	Brazil	Bilateral PI	11-14	1.38	1.69	1.03
				20-25	2.14	2.48	1.57
				30-34	2.01	2.11	1.34
			Bilateral RI	11-14	1.11	1.23	0.78
				20-25	1.03	1.11	0.72
				30-34	0.89	0.98	0.67
4	Clark AR, et al. (2018) (17)	Thailand	Bilateral PI	11-13	1.08	1.04	0.98
				18-24	0.81	0.92	0.95
				28-34	0.94	0.97	0.88
			Bilateral RI	11-14	0.91	0.99	0.85
				17-24	0.88	0.95	0.83
				27-32	0.76	0.86	0.72
5	Attia AM, et al. (2019) (18)	Egypt	Bilateral PI	11-14	2.17	2.35	2.26
				17-24	1.85	1.92	1.88
				27-32	0.95	1.03	0.97
			Bilateral RI	11-14	0.84	0.91	0.88
				17-24	0.75	0.78	0.75
				27-32	0.65	0.71	0.66
6	Guedes-Martinis l, et al. (2015) (5)	Portugal	Bilateral PI	11-14	0.95	0.98	0.96
				17-24	0.78	0.74	0.74
				27-32	0.44	0.43	0.39
			Bilateral	11-14	0.96	1.01	0.99

Number	Authors	Country	Variables	Abdominal UtA			
				GA (Weeks)	5th percentile	50th percentile	95th percentile
			RI	17-24	0.85	0.86	0.85
				27-32	0.68	0.72	0.65

Also, the PI in SGA fetuses at gestational ages of 11-14 weeks (P=0.001), 24-17 weeks (P=0.009) and 32-27 weeks (P<0.001) were significantly higher than normal fetuses. Also, the PI in IUGR fetuses at gestational ages of 14-11 weeks (P=0.002) and 32-27 weeks (P=0.047) were significantly higher than normal fetuses. The relationship between the mean uterine arteries PI/RI and pregnancy complications are shown in Tables 4-6.

Table 4. Bilateral abdominal mean uterine artery plausibility index and resistance index in different gestational age according to the presence or absence of SGA

Variables	GA (Weeks)	Abdominal UtA		P-value
		With SGA	Without SGA	
Bilateral Mean plausibility index	11-14	1.53±0.14	1.35±0.19	0.001
	17-24	1.24±0.08	1.17±0.19	0.009
	27-32	1.06±0.03	0.92±0.14	<0.001
Bilateral Mean resistance index	11-14	0.65±0.154	0.69±0.721	0.230
	17-24	0.59±0.102	0.62±0.124	0.109
	27-32	0.55±0.127	0.56±0.168	0.711

Table 5. Bilateral abdominal mean uterine artery plausibility index and resistance index in different gestational age according to the presence or absence of IUGR

Variables	GA (Weeks)	Abdominal UtA		P-value
		With IUGR	Without IUGR	
Bilateral Mean plausibility index	11-14	1.68±0.09	1.37±0.19	0.002
	17-24	1.30±0.09	1.18±0.18	0.082
	27-32	1.06±0.04	0.94±0.14	0.047
Bilateral Mean resistance index	11-14	0.64±0.213	0.70±0.254	0.214
	17-24	0.58±0.289	0.63±0.184	0.085
	27-32	0.53±0.358	0.58±0.264	0.382

Table 6. Bilateral abdominal mean uterine artery the plausibility index and resistance index in different gestational age according to the presence or absence of PTL

Variables	GA (Weeks)	Abdominal UtA		P-value
		With PTL	Without PTL	
Bilateral Mean plausibility index	11-14	1.48±0.18	1.36±0.20	0.040
	17-24	1.27±0.11	1.17±0.18	0.005
	27-32	1.00±0.13	0.94±0.14	0.058
Bilateral Mean resistance index	11-14	0.69±0.105	0.71±0.800	0.274
	17-24	0.64±0.112	0.64±0.087	0.709
	27-32	0.58±0.119	0.57±0.168	0.542

4. Discussion

Doppler sonography of the uterine artery can predict the maternaloutcome of placental diseases such as preeclampsia and intrauterine growth restriction **(5, 17, 19)**, which are similar to the findings of the present study. Dascau et al **(20)** also reported that with the decrease in UtA-PI, the incidence of premature birth will increase significantly.

The present study showed a significant difference in the mean UtA-PI and the prevalence of bilateral notching between the three time periods measured, so that the prevalence of notching at 11-14 weeks GA was the highest and at 32-27 weeks were the lowest. This finding is in perfect agreement with the results of other studies **(21, 22)**.

The average UtA-PI in the present study showed a progressive decrease in the second and third trimesters. Also, the prevalence of bilateral notching decreased with increasing GA. The most important causes of UtA decrease during pregnancy include the hemodynamic changes in the mother, such as increased cardiac output, decreased blood viscosity and decreased vascular resistance, continued expansion of trophoblasts into the uterus, increased estrogen levels, and increased diameter of uterine arteries **(23, 24)**.

In the present study, the reference intervals for mean uterine artery PI according to gestational ages showed a significant difference between different percentages. This finding is consistent with some studies **(1, 15, 16)** and contradicts other studies **(4, 17, 18)**. The most important reasons for these differences are the time of conducting ultrasound according to the gestational age, the physiological differences between women of different ethnicities, the experience and skill of the perinatologist, and the level of cooperation of the patient **(4, 17, 18)**.

This study had some limitations such as short follow-up time and being a single-center study. It is suggested that another multi-center study with a long follow-up duration be performed, as well as a comparison of the Uterine Artery Doppler Indices between Low-and high-risk pregnant women.

5. Conclusion

The results of this research showed that there is a significant relationship between PI and pregnancy complications, while this was not detected in RI and diastolic notch. These results are relatively consistent with the findings of researchers in other countries.

6. Declarations

Acknowledgments

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Ethical Considerations

All participants signed informed written consent for enrollment in the study. Ethics approval for the study was obtained from the institutional review board of Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1400.1262) according to the Helsinki declaration.

Authors' Contributions

MSH, FR and AJ designed the study and conducted the research. AT, LS, and AV collected and organized data. EF and LA analyzed and interpreted data. FG, BS and FT wrote initial and final draft of the article. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

Conflict of Interest

The authors declare no conflict of interest.

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