Brief communication (Original)

Doppler waveform patterns and reference ranges of fetal renal artery blood flow indices in normal Thai fetuses during the second trimester

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Background: Fetal hemodynamics can be assessed by Doppler ultrasonography, but the normal Doppler waveform pattern and reference range of fetal renal artery blood flow indices in normal Thai fetuses during the second trimester have not been studied.

Objectives: To study the pattern and establish the normal reference range of fetal renal artery blood flow indices in the normal Thai fetus during the second trimester.

Materials and methods: This cross-sectional descriptive study included 512 normal singleton pregnant women, gestational age between $14^{(+0)}$ and $28^{(+6)}$ weeks. Ultrasonography was performed to assess the Doppler waveform pattern and estimate the normal reference range of fetal renal artery blood flow indices. All fetuses were delivered at term with normal outcomes at birth. The mean and 95^{th} and 5^{th} percentiles of the Doppler indices for each gestational week were estimated.

Results: Doppler patterns with absence of diastolic flow in the entire cardiac cycle (type I), and absence of diastolic flow at the end of cardiac cycle (type II) were presented in about 10.4% of normal fetuses during the second trimester of pregnancy. Values for pulsatility index, peak systolic velocity, systolic-to-diastolic ratio, and resistance index (with absent end-diastolic velocity (AEDV) removed) each increased significantly with gestational age. The increase in end-diastolic velocity (with AEDV removed) with gestational age was not significant.

Conclusion: These normative data could serve as a basis for evaluation of the fetal renal artery blood flow, which should be of benefit for pregnancy management, especially in situations that interfere with fetal renal perfusion.

Keywords: Renal artery, second trimester

Doppler ultrasonography is a modality that has been used for assessment of fetal hemodynamics. The ultrasonography is represented as both qualitative findings and quantitative parameters. The qualitative findings describe the pattern of blood flow such as present, absent and reverse flow, whereas the quantitative parameters are considered as Doppler indices such as the systolic-to-diastolic ratio (S/D), pulsatility index (PI), and resistance index (RI). The kidney is an important organ for intrauterine fetal life. Several reports have described the adaptation of vascular anatomy and vasomotor regulation in the renal artery in pathological situations such as hypoxic stress in intrauterine growth restriction and the inflammation process of chorioamnionitis [1, 2]. However, the Doppler waveform pattern and normal reference range of fetal renal artery blood flow indices in normal Thai fetuses during second trimester have not been reported. The aim of this study was to show the normal pattern and establish the normal reference range of fetal renal artery blood flow in the Thai fetus during the second trimester.

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Materials and methods

This was a cross-sectional descriptive study performed at the Maternal-Fetal Medicine Unit, Department of Obstetrics and Gynecology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Thailand, between July 2012 and June 2013. This study was approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University (approval number 55-319-12-3-3). Normal singleton pregnant women with a gestational age between 14⁽⁺⁰⁾ and $28^{(+6)}$ weeks who attended the antenatal care clinic at our hospital were recruited into our study. The gestational age of all participants was documented by the last menstrual period (LMP) and confirmed by ultrasonographic parameters since the first trimester of pregnancy. The exclusion criteria were (1) presentation with fetal malformations or abnormal fetal karyotype, (2) subsequent abnormal fetal growth in the index pregnancy including fetal growth restriction and fetal macrosomia, (3) presentation with an abnormal amount of amniotic fluid, (4) presentation with maternal medical disease such as hypertension, autoimmune disorder, and (5) subsequent obstetric complication in the index pregnancy such as preterm or post-term delivery.

All participants underwent 2-dimensional (2D) real-time ultrasonography conducted by a maternal fetal medicine fellow (PS) who had experience of renal artery Doppler measurement in more than 30 cases before this study using a Voluson E8 (GE Medical Systems, Kretztechnik, Zipf, Austria) with a 2-5 MHz curvilinear probe. First, the number of fetuses, gestational age, amount of amniotic fluid, and standard structural screening were evaluated. Then the fetal kidneys were magnified and displayed in a longitudinal plane. A color Doppler ultrasound with a 60Hz highpass filter was initiated. The fetal renal artery laterally branches from the abdominal aorta and extends directly toward to the kidney hilus. The transducer was adjusted so that the abdominal aorta lay parallel to the ultrasonographic beam. In this position, the insonation angle was as close to 0° as possible. The sample volume was adjusted to 1-3 mm depending on the size of the fetal renal artery and placed approximately 1 cm after it branches off its origin from the abdominal aorta. All examinations were performed during absence of fetal movement or fetal breathing. PI, RI, S/D, peak systolic velocity (PSV) and enddiastolic velocity (EDV) measurements were performed and the presence or absence of end diastolic blood flow assessed. At least three consecutive waveforms from each participant were calculated by an automatic waveform analysis function integrated into the ultrasonographic device.

All participants were followed for maternal and neonatal outcomes until delivery. Only participants free of maternal medical complication, with normal neonatal birthweight and with no fetal anomalies were collected for statistical analysis.

Statistical analysis

The distributions of each Doppler index according to gestational age were examined using scatter plots. Appropriate transformations were then applied to each index to achieve an approximately symmetrical distribution for each gestational age. PI and PSV were log transformed, SD log-log transformed, EDV log transformed after removing fetuses with absent end-diastolic velocity (AEDV), and RI square root transformed after removing fetuses with AEDV. Each of the transformed indices was then regressed against gestational age in days using linear regression models to obtain the estimated mean value for each age, and the residuals of the model checked for near normality and the standard deviation (SD) of the residuals computed. Values of the 95th and 5th percentiles of each index were then estimated using the estimated means \pm 1.64 * SD and the transformed data together with the mean and 95th and 5th percentiles were plotted against gestational age. The regression equations for each Doppler index were then used to tabulate the estimated mean and 95th and 5th percentiles for each day of gestational age. All analyses were conducted using STATA version 10 (StataCorp, College Stations, TX, USA).

Results

All 512 pregnant women were included for final analysis for a Doppler profile of the fetal renal artery. Table 1 shows the basic population characteristic. The mean maternal age was 31.39 (SD 6.11) years (range 15-47 years). About one third (188/512, 36.7%) were nulliparous. Mean gestational age at delivery was 38.22 (SD 1.19) weeks and mean fetal birth weight was 3187.35 (SD 388.94) g. Figure 1 shows the 3 types of normal fetal renal artery Doppler pattern found in normal fetuses during the second trimester of pregnancy, described as absence of diastolic flow in the entire cardiac cycle (type I), absence of diastolic flow at the end of cardiac cycle (type II), presence of diastolic flow in the entire cardiac cycle (type III). Our study found that type I and type II presented in about 10.4% of normal fetuses during second trimester of pregnancy.

Variable	Number	Percentage	
Mother' age (years)			
≤19	25	4.9	
20-34	346	67.6	
≥35	141	27.5	
Gravida			
1	194	37.9	
2	158	30.9	
3	104	20.3	
4	36	7.0	
≥5	20	3.9	
Para			
1	233	45.5	
2	186	36.3	
≥3	65	12.7	

Table 1. The population characteristics



Figure 1. Flow-velocity waveforms in the fetal renal artery. A: Type I (absence of diastolic flow in the entire cardiac cycle) at 15 weeks (systolic waveform is visualized). B: Type II (absence of diastolic flow at the end of cardiac cycle) at 20 weeks (the systolic waveform is present and the diastolic waveform is absent). C: Type III at 24 weeks (systolic waveform is present and the diastolic waveform progresses into the following systolic waveform).

The distributions of Doppler indices according to gestational age from 14⁽⁺⁰⁾ and 28⁽⁺⁶⁾ weeks are shown in **Figure 2**. Transformations achieved a more symmetrical distribution of each index by gestational age (**Figure 3**). The predicted mean and estimated 95th and 5th percentile lines for each index are also shown on **Figure 3**. **Table 2** summarizes the predicted means and estimated 95th and 5th percentiles

of each Doppler index for each week of gestation age between 14 and 28 weeks achieved after backtransformation to the original metric. Values of PI, PSV, S/D and RI (with AEDV removed) each increased significantly with gestational age. The increase in EDV (with AEDV removed) with gestational age was not statistically significant.



Figure 2. Scatter plots Doppler indices of the renal artery according to gestational age



Figure 3. Scatter plots of the transformed Doppler indices of the renal artery according to gestational age, together with predicted mean and estimated 95th and 5th percentiles

GA	No.		PSV			3DV*			S/D			PI		R	*	
(weeks)		Mean	Perce	ntile	Mean	Perc	entile	Mean	Perc	tentile	Mean	Perce	entile	Mean	Percer	ntile
			5th	95th		5th	95th		5th	95th		5th	95th		5th	95th
14	34	17.78	10.36	30.52	2.99	0.89	10.06	5.38	2.54	20.98	1.92	1.20	3.06	0.815	0.622	0.940
15	29	18.85	10.98	32.35	3.04	0.9	10.20	5.59	2.59	22.43	1.95	1.22	3.10	0.823	0.634	0.945
16	31	19.98	11.64	34.29	3.08	0.92	10.34	5.80	2.64	24.02	1.97	1.24	3.15	0.831	0.645	0.949
17	48	21.18	12.34	36.35	3.12	0.93	10.49	6.03	2.7	25.76	2.00	1.26	3.20	0.839	0.657	0.953
18	30	22.45	13.08	38.53	3.17	0.94	10.63	6.27	2.76	27.66	2.03	1.27	3.25	0.847	0.668	0.957
19	32	23.80	13.87	40.84	3.21	0.96	10.78	6.53	2.82	29.76	2.06	1.30	3.29	0.854	0.679	0.961
20	43	25.23	14.70	43.29	3.25	0.97	10.93	6.81	2.89	32.06	2.09	1.31	3.34	0.862	0.690	0.965
21	41	26.74	15.58	45.89	3.30	0.98	11.09	7.10	2.96	34.60	2.13	1.33	3.39	0.869	0.700	0.968
22	37	28.34	16.52	48.64	3.35	1.00	11.24	7.41	3.03	37.40	2.16	1.35	3.44	0.876	0.711	0.971
23	36	30.05	17.51	51.56	3.39	1.01	11.40	7.74	3.10	40.49	2.19	1.37	3.49	0.883	0.722	0.975
24	37	31.85	18.56	54.66	3.44	1.02	11.56	8.10	3.18	43.92	2.22	1.39	3.55	0.889	0.732	0.978
25	26	33.76	19.67	57.94	3.49	1.04	11.72	8.48	3.26	47.73	2.26	1.41	3.60	0.896	0.742	0.981
26	32	35.78	20.85	61.41	3.54	1.05	11.88	8.89	3.35	51.96	2.29	1.44	3.65	0.901	0.752	0.983
27	26	37.93	22.10	65.10	3.59	1.07	12.05	9.33	3.44	56.67	2.32	1.46	3.71	0.908	0.761	0.986
28	30	40.21	23.43	69.00	3.64	1.08	12.22	9.79	3.53	61.92	2.36	1.48	3.76	0.914	0.770	0.988
*after on	vission (of fetuses	with AEL	VC												

Table 2. Doppler indices of the fetal renal artery Doppler indices with 5th and 95th percentiles.

Discussion

To our knowledge, this is the first study to completely demonstrate both qualitative and quantitative fetal renal artery Doppler flow during the second trimester of pregnancy in Thai fetuses. Moreover, the fetal and maternal outcomes were followed until delivery to confirm normal pregnancy outcome. A few previous studies have presented normal values of renal artery Doppler flow [3-9], but the current study is the first to include fetuses in the early second trimester of pregnancy and to have a large sample size. We chose to initiate the fetal renal artery Doppler assessment in the early second trimester because the fetal renal pathologic presentation starts at this time, so reference data on the normal renal artery is required [10]. However, awareness about Doppler assessment in small vessels is important so in our study the sample volume was reduced to be appropriate for the fetal renal artery, which was shown by color Doppler.

Our study found 3 patterns of renal artery Doppler waveform. Most of them were type III. This finding is similar to the previous studies [4, 9], which found that all 3 patterns of renal artery Doppler can be seen among normal fetuses, although the percentages of such patterns differed from those in our study. An explanation may lie in the differences in gestational age in each study and the small sample size in previous studies. Most of cases in previous studies were fetuses in the third trimester of pregnancy [4, 9]. Interestingly, we found that during the second trimester of pregnancy the fetal artery Doppler indices, including of PI, PSV, S/D and RI (with AEDV removed), each increased significantly with gestational age, but the increase in EDV (with AEDV removed) with gestational age was not significant. We postulate that the increase in fetal renal artery PSV was related to the increase in renal blood flow and fetal urine production rate with advancing gestation [11]. Although, the PI, RI, and S/ D increased with advancing gestational age, the values were not high enough to interrupt the renal perfusion. Finally, we constructed best-fitting regression equations and reference ranges for each Doppler index.

The study population included pregnant women between 14 and 28 weeks who mostly resided in urban areas of southern Thai area. Although our participants were mostly Muslim, other basic demographic data including economic status was similar for that of health care in other sites in Thailand. Thus, it should be appropriate to extrapolate the normal reference range for the fetal renal artery to all pregnant Thai women.

In conclusion, these normative data could serve as a basis for evaluation of the fetal renal artery blood flow, which should be of benefit for further pregnancy management, especially in high risk situations that interfere with fetal renal perfusion.

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