Reference Range and Characteristic of Uterine Artery Doppler in Pregnant Thai Women at 11-13^{+6} Gestational Weeks

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Objective: *To determine uterine artery pulsatility index (PI) and to describe the characteristic of uterine artery Doppler velocimetry in pregnant Thai women at 11-13^{+6} gestational weeks.*
Material and Method: *Between July 29, 2010 and September 30, 2010, 150 normal pregnant women at 11-13^{+6} weeks of gestation who were attending at the antenatal care clinic, Department of Obstetrics and Genecology, Faculty of Medicine, Chulalongkorn University were recruited. Pulsatility index (PI) of the uterine artery was measured and mean PI was calculated and plotted against gestational age. Presence or absence of uterine notching in relation to laterality was also noted.*
Results: *The mean $\pm$ SD uterine artery PI was 1.73 $\pm$ 0.42. When segregated for gestation age, uterine artery PI was 1.78 $\pm$ 0.41 at 11 weeks, 1.72 $\pm$ 0.41 at 12 weeks, and 1.66 $\pm$ 0.43 at 13 weeks'gestation. The uterine artery PI was 1.84 $\pm$ 0.37 with presence of notching and was 1.59 $\pm$ 0.43 without notching. The uterine artery notching was presented in 29 (19.3%), 24 (16%), and 27 (18%) of the patients at 11, 12, and 13 weeks respectively. The uterine artery notching was absent in 27 (18%), 23(15.3%), and 20(13.3%) of patients at 11, 12, and 13 weeks respectively. Thirty-nine patients (26%) demonstrated unilateral notch, 12 (8%) of the patients demonstrated ipsilateral notch, 19 patients (12.7%) demonstrated contralateral notch, and eight (5.3%) demonstrated unilateral notch with central placenta.*
Conclusion: *Normal reference range and characteristics of uterine artery Doppler velocimetry in the presented population was established. This may serve as a basis for a future study in patients with abnormal placental function.*

Keywords: *Early diastolic notching, First trimester, Pulsatility index, Uterine artery Doppler*

J Med Assoc Thai 2011; 94 (6): 644-8
Full text. e-Journal: *http://www.mat.or.th/journal*

Pre-eclampsia and intrauterine growth restriction (IUGR) are important obstetric complications leading to an increase in maternal, perinatal morbidity and mortality[1]. Both conditions are caused by a failure in trophoblastic invasion of the spiral arteries and consequently, resulted in an insufficiency in uteroplacental blood flow[2,3]. This rationale has drawn the attention of obstetric community to investigate and employ uterine artery Doppler velocimetry in screening of these abnormal conditions. With an abnormal placentation in pregnancy complicated with uteroplacental insufficiency, the uterine artery blood flow is usually characterized quantitatively by an abnormally high resistive index and qualitatively by presence of a persistent uterine artery diastolic notching. A number of studies have been conducted in using uterine artery Doppler velocimetry in prediction of pre-eclampsia and IUGR with a varying degree of sensitivity and specificity[4-6]. The investigations conventionally complied with the routine structural and chromosomal screening and confined mostly in the second trimester[7,8]. More recently, attention has shifted toward an earlier scanning in the first trimester. Measurement of nuchal translucency in combination with biochemical markers has become a standard measure in screening of chromosomal abnormality in the first trimester[9]. A screening of pre-eclampsia and IUGR has also been studied more extensively between 11 and 14 weeks' gestation. Studies of first trimester uterine artery Doppler have demonstrated a relationship between an increase in the uterine artery resistance and a subsequent development of pre-eclampsia and IUGR[10-12]. There are some western reports of reference range of normal uterine artery Doppler in first trimester

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for a comparison with abnormal pregnancy[13,14], but there is no study on normal reference value of uterine artery Doppler in the authors' population. The objective of the present study is to determine the normal range of the uterine artery Doppler indices and to characterize the uterine artery Doppler waveform in normal pregnant population.

Material and Method

Between July 29, 2010 and September 30, 2010, uterine artery Doppler studies were performed in patients with singleton pregnancies who attended the antenatal clinic at the Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University. Inclusion criteria were singleton pregnancy, gestational age from 11 to 13^{+6} weeks' gestation, and crown-rump length (CRL) between 45 and 84 mm. Exclusion criteria were pregnancy complicated with gestational hypertension, pre-eclampsia, diabetes mellitus, renal disease, and preterm delivery. Fetuses with structural, chromosomal anomalies, IUGR, and intrauterine demise were also excluded. All patients gave informed consent to participate in the study. The present study was approved by the Institutional Ethic Committee. Gestational age was determined by a reliable last menstrual period and confirmed by a crown-rump length (CRL) measurement. All Doppler studies were performed only once in each patient by a single operator (RO) utilizing a Voluson E8, a Voluson 730 Expert, or a Voluson Pro (GE Medical System, USA) with a 5-7 MHz curvilinear transabdominal transducer. Pregnant women were placed in the supine position. The transducer was gently moved laterally from mid sagittal plane of the uterus to determine paracervical plexus. Color Doppler was employed to identify the uterine artery at the level of uterine isthmus as it ascends cephalad to uterine corpus. Pulsed wave Doppler was then activated using a sample gate of 2 mm to cover the whole vessel diameter. The angle of insonation was always kept below 30 degrees. When three similar consecutive waveforms were obtained, the pulsatility index (PI) of both left and right uterine arteries was measured. The mean PI was calculated and recorded. Presence or absence of uterine notching in relation to laterality was also noted. An intraobserver reliability was calculated (by intraclass correlation coefficient statistic) for 10 patients, with each patient examined two times. The mean intraobserver reliability for the PI was 0.8. The data were analyzed with SPSS software package version 17 for Windows. Maternal and neonatal demographic data were obtained from the hospital database. The mean and standard deviation of PI were calculated and plotted against gestational age.

Results

Initially, there were 176 patients enrolled in the present study. The authors excluded 26 patients because 16 had pregnancy complications (5 pre-eclampsia, 1 IUGR, 8 diabetes mellitus, and 2 preterm delivery), two had fetal death in utero, and eight had missing outcome data. This left 150 patients who had a normal pregnancy outcome for further analysis. Maternal and neonatal characteristics are shown in Table 1. Uterine artery PI (mean $\pm$ SD) was 1.73 ± 0.42. The uterine artery PI was 1.84 ± 0.37 with presence of notching and was 1.59 ± 0.43 without notching. When segregated for gestation age, uterine artery PI was 1.78 ± 0.41 at $11\text{-}11^{+6}$ weeks, 1.72 ± 0.41 at $12\text{-}12^{+6}$ weeks and 1.66 ± 0.43 at $13\text{-}13^{+6}$ weeks' gestation (Fig. 1). The uterine artery notching was presented in 29 (19.3%), 24 (16%), and 27 (18%) of the patients at 11, 12, and 13 weeks respectively. The uterine artery notching was absent in 27 (18%), 23 (15.3%), and 20 (13.3%) of

Table 1. Patient characteristics (n = 150)

Characteristics	Mean $\pm$ SD (range)
Maternal age (years)	30.6 ± 5.3 (18-42)
Gravida	1.7 ± 0.9 (1-4)
Gestational age at delivery (weeks)	38.6 ± 1.1 (37-42)
Birth weight (g)	$3{,}142.5 \pm 375.8$ (2290-4000)

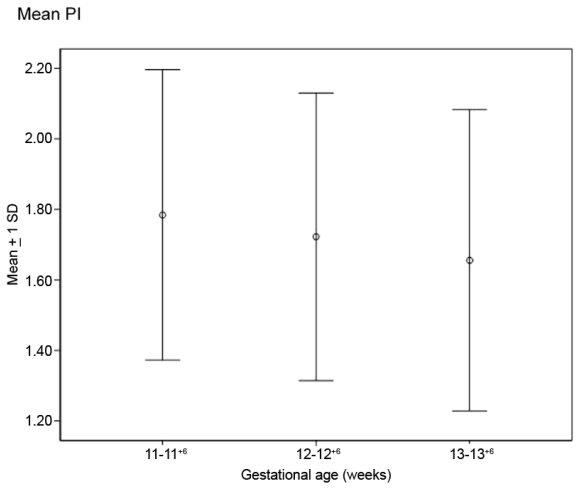

Fig. 1 Uterine artery PI between $11\text{-}13^{+6}$ gestational weeks

Table 2. Notch related to placental location

Placenta	Cases (%)
Ipsilateral notch	12 (8)
Contralateral notch	19 (12.7)

patients at 11, 12, and 13 weeks respectively. Forty-one (27.3%) of the patients demonstrated bilateral notching. Thirty-nine patients (26%) demonstrated unilateral notch (19 on the left side and 20 on the right side), 12 (8%) of the patients demonstrated ipsilateral notch, 19 patients (12.7%) demonstrated contralateral notch and eight (5.3%) demonstrated unilateral notch with central placenta. Seventy patients (46.7%) exhibited no uterine notching. Fifty patients (33.3%) demonstrated right-sided placenta, fifty-eight patients (38.7%) demonstrated left-sided placenta. Forty-two patients (28%) exhibited central placenta. The number of notching related to placental location is shown in Table 2.

Discussion

Pre-eclampsia and IUGR, which are believed to be caused by an abnormal placentation involving an abnormality in trophoblastic invasion of spiral artery[2,3]), are major obstetric complications that posed significant maternal and perinatal morbidity and mortality. In this regard, a prediction of these abnormal conditions with appropriate and timely preventive measures may have a paramount impact in improving maternal and neonatal outcomes. A mid trimester ultrasound has been conventionally employed in screening of both structural and chromosomal abnormalities for decades. Concordantly, uterine artery Doppler velocimetry has also been used to predict a risk for development of pre eclampsia and IUGR at this same period of gestation. A number of studies have revealed an advantage in using mid trimester uterine artery Doppler in prediction of pregnancy complicated with uteroplacental insufficiency[4-6,15]. An increase in uterine artery resistive indices or presence of uterine artery notching has been consistently shown to be associated with an increased risk for pregnancy complicated with pre-eclampsia and IUGR[16]. The shortfall of the uterine artery Doppler screening in mid trimester is that the implementation for minimizing these complications by introducing low dose aspirin is not early enough and is not possible to yield any beneficial effect for the outcomes[6]. More recently, a first trimester ultrasound with a combination of biochemical markers has become a standard test for a screening of fetal aneuploidy[17]. With the same setting, uterine artery velocimetry could also be simultaneously performed for a screening of pre-eclampsia and IUGR. An increase uterine artery PI or presence of an early diastolic notching has been shown in several studies to be associated with maternal and perinatal adverse outcomes with a varying degree of sensitivity and specificity[4-6]. The uterine artery Doppler has also been investigated in combination with several biochemical and clinical markers to increase the predictability of the test[17,18]. Melchiorre et al. demonstrated that an increased uterine artery PI was associated with pre-term pre-eclampsia but not term pre-eclampsia. The sensitivity for detection of preterm pre-eclampsia was 24% at uterine artery PI cut-off of 95 centile with a 5% false positive rate[19]. This is in accordance with the results obtained by Gomez et al who demonstrated the same sensitivity at 95 centile cut-off[20]. In the same study by Melchiorre et al., bilateral uterine notching was not significantly different between normal control and those with pre-eclampsia. They attributed their findings to a high prevalence of bilateral notching in a normal population (45%)[19]. Even though the prevalence of uterine notching was significantly more in preterm pre-eclampsia, the sensitivity was 76% with a poor specificity of 55%. Nevertheless, they still suggested using bilateral uterine notching in combination with other markers for a further pre-eclampsia screening study. In another study, Vainio et al have suggested that presence of bilateral uterine notching in the first trimester could predict one in four pregnancies destined to develop pre-eclampsia. With the absence of bilateral notching, the risk for the same disease would be negligible[16].

Plasencia et al[12] have demonstrated that in the first trimester, the PI of uterine artery decreased from 11 to 13^{+6} weeks of gestation. This is in accordance with the present study, which shows a trend toward a decrease in resistive indices of uterine artery PI from 11 to 13 weeks of gestation. This could result from an increase in trophoblastic invasion of spiral artery at advancing gestation. In contrast with the results of the studies in Western countries, the present study demonstrates a markedly lower prevalence of bilateral uterine notching (27.3%) compared with those described by Melchiorre et al[19] (45%), by Vainio M et al[16] (75%) and by Gadelha Costa et al[14] (84%).

In terms of uterine artery resistive indices, these results demonstrated substantially lower PI of

uterine artery in the presence of diastolic notching compared to the study done by Gadelha Costa et al[14]. The PI of uterine artery with notching in the present study were 1.84 $\pm$ 0.37 compared with 2.32 $\pm$ 0.79 in those of Gadelha Costa et al[14]. The substantial differences in notching prevalence and resistive indices in normal population between the present studies and other Western studies may affect the predictive capability in using uterine artery Doppler velocimetry for detection of pre-eclampsia and IUGR. A further study of uterine artery Doppler in complicated pregnancy in a Thai population is necessary to unveil this question. In terms of uterine artery notching relating to placental laterality, the present study could not demonstrate a statistically significant difference in the prevalence of uterine artery notching between those with ipsilaterally and contralaterally located placenta even though the number of uterine notching is higher in patients with contralaterally located placenta compared with those with ipsilaterally located placenta. It could be that the majority of the presented sample have a centrally located placenta and the number of patients with lateral implantation is rather low. The small sample size could be under power to detect the difference of the prevalence of diastolic notching between those of ipsilaterally and contralaterally located placenta.

In conclusion, the present study has established the reference range and characteristics of uterine artery Doppler velocimetry in a presented normal population. This may serve as a basis for a future study in patients with abnormal placental function.

Acknowledgements

The authors want to thank the staff and nurses, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University for their kind suggestions and assistance.

Potential conflicts of interest

None.

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ค่าอ้างอิงและคุณลักษณะของดอปเปลอร์หลอดเลือดแดงมดลูกในสตรีไทยปกติอายุครรภ์ 11-13^{+6} สัปดาห์

อรพินท์ รัตนพันธมณี, บุญชัย เอื้อไพโรจน์กิจ

วัตถุประสงค์: *เพื่อศึกษาค่าอ้างอิงและคุณลักษณะของดอปเปลอร์หลอดเลือดแดงมดลูกในสตรีไทยปกติ อายุครรภ์ 11-13^{+6} สัปดาห์*

วัสดุและวิธีการ: *เป็นการศึกษาเชิงพรรณนาในหญิงตั้งครรภ์ปกติในช่วงอายุครรภ์ 10-13^{+6} สัปดาห์ จำนวน 150 ราย ที่มาฝากครรภ์ที่โรงพยาบาลจุฬาลงกรณ์ ตั้งแต่เดือน กรกฎาคม พ.ศ. 2553 ถึง กันยายน พ.ศ. 2553 โดยทำการตรวจวัดดัชนีความต้านทานเฉลี่ย และความสัมพันธ์ของตำแหน่งรกกับรอยหยักช่วงหัวใจคลายตัวของหลอดเลือดแดงมดลูก*

ผลการศึกษา: *พบว่าหลอดเลือดแดงมดลูกมีค่าดัชนีความต้านทานเฉลี่ยเท่ากับ 1.73 $\pm$ 0.42 เมื่อแยกรายละเอียดลงไปในแต่ละอายุครรภ์ พบว่าค่าดัชนีความต้านทานเฉลี่ยเท่ากับ 1.78 $\pm$ 0.41, 1.72 $\pm$ 0.41 และ 1.66 $\pm$ 0.43 สำหรับอายุครรภ์ 11, 12 และ 13 สัปดาห์ ตามลำดับ โดยค่าเฉลี่ยดัชนีความต้านทานของหลอดเลือดแดงมดลูกที่มีรอยหยักช่วงหัวใจคลายตัวเท่ากับ 1.84 $\pm$ 0.37 หลอดเลือดแดงมดลูกที่ไม่มีรอยหยักช่วงหัวใจคลายตัวเท่ากับ 1.59 $\pm$ 0.43 ทั้งนี้พบว่าหญิงตั้งครรภ์ที่มารับการตรวจนั้น 41 ราย (27.3%) มีรอยหยักช่วงหัวใจคลายตัวของหลอดเลือดแดงมดลูกทั้งสองข้าง และ 39 ราย (26%) มีรอยหยักช่วงหัวใจคลายตัวของหลอดเลือดแดงมดลูกเพียงข้างเดียว โดยในกลุ่มนี้ 12 ราย (8%) มีรอยหยักช่วงหัวใจคลายตัวอยู่ด้านเดียวกันกับรก และ 19 ราย (12.7%) มีรอยหยักช่วงหัวใจคลายตัวอยู่ด้านตรงข้ามกับรก*

สรุป: *การศึกษานี้ได้ทำการตรวจวัดดัชนีความต้านทานและคุณลักษณะของหลอดเลือดแดงมดลูก เพื่อหาค่าอ้างอิงในกลุ่มหญิงตั้งครรภ์ปกติที่มาฝากครรภ์ โดยทั้งนี้อาจมีประโยชน์ต่อการศึกษาในกลุ่มที่มีการทำงานของรกผิดปกติต่อไป*