Second Trimester Uterine Artery Doppler Screening in Prediction of Adverse Pregnancy Outcome in High Risk Women

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Objective: *To assess the value of uterine artery colour Doppler waveform analysis in the prediction of adverse pregnancy outcome such as preeclampsia, fetal growth restriction in high risk pregnancy women.*
Material and Method: *Uterine artery Doppler screening was performed as part of mid trimester screening between 20 and 24 weeks gestation in high risk pregnancy women at Matermal Fetal Medicine unit, Thammasat University Hospital between June 1, 2008 and May 31, 2009. A pulsatility index (PI) was calculated from each uterine artery and the presence or absence of a notch was determined. A PI of > 1.58 or the presence of any diastolic notch were defined as abnormal. The main outcome measures were pre-eclampsia and small for gestational aged baby (birth weight < 10th centile).*
Results: *Doppler examination of the uterine arteries were performed in 330 singleton pregnancies. Twenty-seven (8.18%) women developed pre-eclampsia, 16 (4.84%) women had SGA babies. The sensitivity of PI > 1.58 and diastolic notch for pre-eclampsia, SGA were 59.25% and 56.25%, respectively.The specificity of PI >1.58 and diastolic notch for these outcomes were 66.67% and 65.60% respectively.*
Conclusion: *In high-risk women, mid trimester uterine artery Doppler waveform analysis can not use as screening method in women at higher risk for the development of severe adverse outcome such as pre-eclampsia and SGA babies. However women with normal uterine artery Doppler results are unlikely to develop pre-eclampsia, fetal growth restriction (FGR) and therefore do not necessarily need repeated Doppler ultrasound follow-up.*

Keywords: *Doppler, Uterine artery, High risk pregnancy*

J Med Assoc Thai 2010; 93 (Suppl. 7) : S127-130
Full text. e-Journal: *http://www.mat.or.th/journal*

Preeclampsia and fetal growth restriction are ones of the most common causes of maternal and fetal morbidity and mortality, however their exact etiology is unknown[1,2]. Although the development of preeclampsia is thought to be a consequence of abnormal trophoblastic invasion of the maternal spiral arteries and their conversion from narrow muscular vessels into wide non-muscular channels but the etiology is still unknown[3,4]. The physiological process of trophoblastic invasion is reflected in the observation from Doppler ultrasound studies that impedance (PI) of flow in the uterine arteries decreases with gestation between 6 and 24 weeks and remains constant thereafter[5,6]. Doppler ultrasound studies of the uterine arteries have demonstrated that the clinical manifestations of preeclampsia are preceded by evidence of impaired placental perfusion[7]. A multicenter screening study using uterine artery Doppler ultrasound imaging at 22-24 weeks of gestation in about 8000 singleton pregnancies showed that the sensitivity for pre-eclampsia with small-for-gestational age (SGA) is substantially higher than that for pre-eclampsia without SGA (69% versus 24%)[8]. Furthermore, a study of more than 30,000 pregnancies showed that the pulsatility index (PI) was above the 95th percentile (> 1.58) in 77% of those that subsequently developed pre-eclampsia requiring delivery before 34 weeks, compared with 36% for late preeclampsia[9]. Doppler studies in high-risk populations for severe pregnancy complications could

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increase the predictive value for adverse pregnancy outcome. Therefore, the aim of this prospective study was to examine the value of uterine artery Doppler in a risk population for the prediction of severe pregnancy complications.

Material and Method

This prospective cohort study was conduct in Maternal Fetal Medicine unit, Thammasat university hospital between June 1,2008 and May 31, 2009. This study was approved by the Ethical Committee of the Faculty of Medicine Thammasat University and received grant support from Thammasat University as well. Singleton pregnant women referring to Maternal Fetal Medicine unit with the follow condition were included: elderly gravidarum, medical disease ex chronic hypertension, renal disease, SLE, previous pre-eclampsia, smoking etc. The pregnant women with fetal anomaly and who did not deliver at Thammasat university hospital were excluded. Genetic sonography was performed as part of routine screening at the Meternal Fetal Medicine unit for pregnant women with high risk of fetal chromosome abnormality, pre-eclampsia, fetal growth restriction. Uterine arteries flow velocity waveforms were obtained using an Aloka alpha-5 (Aloka Co, Tokyo, Japan) ultrasound machine, 3.5 or 5 MHz transducer. The high-pass filter was set at 100 Hz. Flow velocity waveforms were obtained from the uterine artery near to the external iliac artery before division if the uterine artery into branches[10]. Three to five consecutive waveforms from each artery were obtained and the images frozen, the PI was calculated. The presence or absence of an early diastolic notches was also recorded. All ultrasonography and Doppler studies were carried out by subspecialty Maternal Fetal Medicine staffs.

The primary outcome was pre-eclampsia, defined according to American college of Obstetrics and Gynecology (ACOG) as blood pressure of at least 140/90 mmHg measured on two occasions 6 hours apart and proteinuria of 300 mg in 24 hours, or atleast 1+ on dipstick testing[11]. SGA was defined as birth weight less than the 10 percentile for gestational age. Maternal history and Doppler findings were recorded in a computer database at the time of genetic ultrasonography. Data on pregnancy outcomes were obtained from labor ward records. Statistical analysis was performed using SPSS Version 14 for Windows. The sensitivity,specificity, positive predictive value (PPV), negative predictive value (NPV) and relative risk (RR) in the prediction of preeclampsia, FGR were calculated.

Results

A total of 330 pregnancies were recruited into this study. Mean maternal age was 36.8 $\pm$ 2.2 years. One hundred and seventy-nine women were primigravida (Table 1). Twenty seven women (8.18%) developed pre-eclampsia. The babies with birth weight below 10 percentile were sixteen (4.84%). One hundred and seventy seven (53.63%) hand any PI > 1.58. One hundred and twenty two (36.96%) had a notch on any side. One hundred and seventeen (35.45%) had PI > 1.58 and a notch. Sensitivity, specificity, positive and negative predictive values, relative risks and 95% CI of adverse outcomes according to abnormal Doppler results are shown in Table 2 and 3.

Discussion

Impaired uteroplacental blood flow as reflected by abnormal uterine artery Doppler flow velocities remains the important cause for severe pregnancy complications, ex pre-eclampsia and FGR. This has lead to the idea of uterine artery Doppler as a screening test for adverse pregnancy outcome. Variations in Doppler techniques, measurement parameters and study protocols have resulted in disappointing results in the prediction of pre-eclampsia and poor pregnancy outcome in low-risk populations[12]. The clinical value of uterine Doppler as a screening tool in low risk populations is defined by the high negative predictive value of abnormal uterine artery Doppler waveforms. In this study we examined the predictive value for pregnancy complications of second trimester uterine artery Doppler in the high risk population. We used the pulsatility index (PI) above the 95th percentile (> 1.58)

Table 1. Patients' characteristics

Characteristics	Mean $\pm$ SD, n (%)
Age (years)	36.8 $\pm$ 2.2
BMI (kg/m^2)	24.4 $\pm$ 4.2
Time of delivery(weeks)	37.8 $\pm$ 1.7
Cesarean section	254 (76.96%)
Primigravida	179 (54.24%)
Elderly age	317 (96.06%)
Chronic hypertension	7 (2.12%)
Renal disease	3 (0.9%)
Previous pre-eclampsia	3 (0.9%)

Table 2. The prediction of preeclampsia (n = 27) by Doppler parameters

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	RR	95% CI
Any PI > 1.58	81.48	48.84	12.42	96.73	1.59	1.29-1.96
Any notch	62.96	65.34	13.43	95.19	1.81	1.30-2.52
Any PI > 1.58 and notch	59.25	66.67	13.67	94.83	1.77	1.25-2.52

Table 3. The prediction of fetal growth restriction (n = 16) by Doppler parameters

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	RR	95% CI
Any PI > 1.58	81.25	47.77	7.34	98.00	1.55	1.20-2.01
Any notch	56.25	64.0	7.37	96.63	1.56	0.99-2.46
Any PI > 1.58 and notch	56.25	65.60	7.69	96.73	1.63	1.03-2.58

and diastolic notches as screening tool from the study of Onwudiwe N et al, because this study had the largest population in their study. The results of this study show that the use of PI > 1.58 had more sensitivity, but low specificity than the presence of uterine notch in prediction of preeclampsia and FGR. This study also show that uterine Doppler indicies has high negative predictive value as in previous studies[6-9]. Because the result of this study, when using PI > 1.58 and uterine notch, had fair sensitivity and specificity, poor positive predictive value but high negative predictive value in the prediction of preeclampsia and FGR, it cannot used as a good screening test. However, this finding suggests that uterine artery screening might be used to determine the appropriate level of antenatal care in specific women. Women with normal uterine artery Doppler results are unlikely to develop pre-eclampsia, FGR and therefore do not necessarily need repeated Doppler ultrasound follow-up. Future research should focus on further improvement to predict adverse pregnancy outcome, *e.g.*, by a combination of uterine artery Doppler at 20-24 weeks' gestation and biochemical testing (ex, alpha-fetoprotein, beta-human chorionic gonadotropin).

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การตรวจดอพเลอร์หลอดเลือดแดงยูเทอรีนในไตรมาสที่สอง ในการทำนายผล การตั้งครรภ์ที่ไม่ดี ในกลุ่มสตรีตั้งครรภ์ที่มีความเสี่ยงสูง

เด่นศักดิ์ พงศ์โรจน์เผ่า, อธิตา จันทเสนานนท์, ต้องตา นันทโกมล

วัตถุประสงค์*: เพื่อศึกษาประสิทธิภาพของคลื่นเสียงความถี่สูงดอพเลอร์ในการตรวจการไหลเวียนเลือดของหลอดเลือดแดงยูเทอรีนเพื่อช่วยทำนายผลการตั้งครรภ์ที่ไม่ดี เช่น ภาวะครรภ์เป็นพิษและทารกเจริญเติบโตช้าในครรภ์ในสตรีตั้งครรภ์เสี่ยงสูง*

วิธีการ*: สตรีตั้งครรภ์เสี่ยงสูงที่มารับการตรวจด้วยคลื่นเสียงความถี่สูง อายุครรภ์ 20-24 สัปดาห์ระหว่างวันที่ 1 มิถุนายน พ.ศ. 2551 ถึง 31 พฤษภาคม พ.ศ. 2552 ณ หน่วยเวชศาสตร์มารดา และทารกในครรภ์ โรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ ค่า pulsatility index (PI) และ uterine notch จะถูกบันทึกค่า PI > 1.58 หรือการพบ uterine notch ถือว่าผิดปกติ ผลลัพธ์ที่ใช้คือการเกิดภาวะครรภ์เป็นพิษหรือทารกเจริญเติบโตช้าในครรภ์*

ผลการศึกษา*: สตรีตั้งครรภ์กลุ่มเสี่ยงสูงจำนวน 330 ราย ได้รับการตรวจด้วยคลื่นเสียงความถี่สูงดอพเลอร์ พบภาวะครรภ์เป็นพิษ 27 ราย (8.18%) ภาวะทารกเจริญเติบโตช้าในครรภ์ 16 ราย (4.84%) ค่าความไวของการใช้ค่า PI > 1.58 และการพบ uterine notch ในการทำนายภาวะครรภ์เป็นพิษและทารกเจริญเติบโตช้าในครรภ์เท่ากับ 59.25% และ 56.25% ตามลำดับ ค่าความจำเพาะของการใช้ค่า PI > 1.58 และการพบ uterine notch ในการทำนายภาวะครรภ์เป็นพิษและทารกเจริญเติบโตช้าในครรภ์เท่ากับ 66.67% และ 65.60% ตามลำดับ*

สรุป*: การตรวจดอพเลอร์หลอดเลือดแดงยูเทอรีนในไตรมาสที่สองไม่เหมาะสมในการทำนายผลการตั้งครรภ์ที่ไม่ดี เช่น ภาวะครรภ์เป็นพิษและทารกเจริญเติบโตช้าในครรภ์ในกลุ่มสตรีตั้งครรภ์ที่มีความเสี่ยงสูง เนื่องจากมีค่าความไวและความจำเพาะต่ำ แต่สามารถลดการตรวจติดตามในกรณีที่ค่าดอพเลอร์ปกติลงได้เนื่องจากมีโอกาสเกิดภาวะครรภ์เป็นพิษและทารกเจริญเติบโตช้าในครรภ์น้อย*