Prediction of Preeclampsia in a Low-Risk Population Using Diastolic Notch of Uterine Arteries

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Objective : *To assess the performance of diastolic notch of uterine arteries as a predictor for preeclampsia.*
Material and Method : *A prospective study of 378 pregnant women between 18-22 week's gestation who were attending at the Antenatal Care Clinic, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University was conducted. Doppler flow velocity waveform of all subjects was screened for the presence of diastolic notch of uterine artery to be related with the pregnancy outcome.*
Results: *Diastolic notch was found in one or both uterine arteries in 51 subjects, yielding 78.6% sensitivity, 89.0% specificity, 21.6% positive predictive value, 99.1% negative predictive value, 88.6% accuracy, with likelihood ratio of positive and negative test result of 7.2 and 0.2 respectively in the prediction of preeclampsia.*
Conclusion : *Although having high sensitivity and specificity, diastolic notch of uterine artery found in the second trimester provides too low predictive value to be used as a routine screening for preeclampsia.*

Keywords : *Preeclampsia, Diastolic notch, Uterine artery*

J Med Assoc Thai 2004; 87(Suppl 3): S29-33

Preeclampsia is a significant obstetric complication, detrimental not only to the mother but also to the neonate[1,2]. Therefore, prevention and early diagnosis of this condition are crucial. Since there has been no accurate method in predicting preeclampsia [3,4], the intervention to whom potentially to develop this condition cannot be performed. Inability of the uterine artery to increase dilatation with advancing gestational age, like in the normal pregnancy, caused by the pathology of the uterine arterial wall was found in the women with preeclampsia[5].

Doppler ultrasonography is a method that has been used to predict the preeclampsia with various benefits including noninvasiveness, convenience, low cost and no harm to both mother and fetus. High resistance index in the uterine artery demonstrated by the Doppler study was proposed to predict the preeclampsia, however it was found to have a low predictive value with varying cut-off levels reported in the studies[6-12]. Because of this limitation, the association between the diastolic notch of the uterine artery and the development of preeclampsia was explored[13,14] and its accuracy in the prediction of the disease was reported[15-18]. Nonetheless, the results seemed to be discordant and no data was derived from the Thai population, in which the difference in race and ethnicity might give rise to the different results. This study was therefore conducted to evaluate the performance of the presence of the diastolic notch of the uterine artery in predicting the preeclampsia.

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Materials and Method

The study population was the pregnant women between 18-22 week's gestation who were attending at the Antenatal Care Clinic, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University from 1 June 2000 to 31 March 2001. A Doppler ultrasonographic machine used in all subjects was the Aloka, Model SSD 2000 (Japan) with 5 MHz convex probe and pulse wave filtered at 100 MHz. At first, the number of fetus, gestational age, gross anomalies and position of the placenta were evaluated. Then circulation flow of the uterine artery was examined by starting with placing the probe on the 45 degrees to and at the 2 cm above the inguinal ligament in its midline to find the external iliac artery, which was the tubular shape of about 3 mm in diameter and showed

the flow velocity waveform of early reverse type in downward direction. The probe was then moved to the medial, and also slightly to the cephalad, to find the point of intersection between the external iliac artery and the uterine artery. At the distance of 1 cm above this point, the uterine artery was studied and the presence or absence of the notch seen in the artery during diastole was recorded (Fig. 1). Bilateral uterine arteries were studied in each subject.

There were two operators performing the Doppler study of the subjects, in which both were trained to study the uterine artery to get the same standard before commencing this study. The diastolic notch noted by an operator was subsequently confirmed by another. The presence of diastolic notch was recorded only when it was seen by the two operators. The results regarding the diastolic notch were not recorded in the antenatal record book to preclude the bias in the obstetric care. Every subject was advised to be followed-up according to the appointments and to come to the hospital immediately if abnormal symptoms, such as generalized edema, headache, blurred vision or epigastric pain, existed. All subjects were then followed through the whole pregnancy period to see whether preeclampsia developed. Any subject who was found to have hypertension and positive for urine protein would be hospitalized for close observation. The demographic and obstetric data were shown as mean and standard deviation. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, likelihood ratio of positive test result (LR+) and likelihood ratio of negative test result (LR-) of the diastolic notch of the uterine artery in the prediction of preeclampsia were studied. Statistical analyses were performed using the STATA, version 6 statistical software. This study was approved by the Ethics Committee of Khon Kaen University.

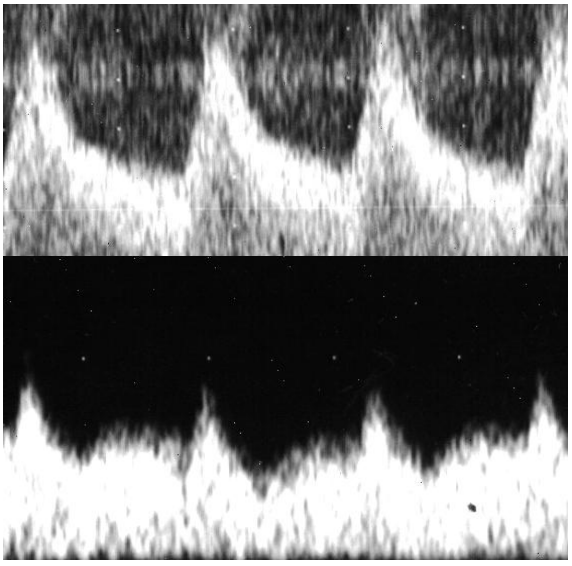

Fig. 1 Demonstration of the normal Doppler flow of the uterine artery (upper row) and the diastolic notch of the uterine artery (lower row)

Results

There were 420 pregnant women included during the study period, in which 32 cases were finally excluded; 10 cases due to lost to perform ultrasonography during the 18-22 week's gestation and 22 cases due to undetermined pregnancy outcome owing to the delivery at other hospitals. The rest 378 cases were enrolled for analysis.

1. Pregnancy-relevant data of the subjects: The study subjects were in the age range of 14-42 years (mean 26.8 + 5.4). Most of them were the second gestation (44.4%) and 19 weeks of gestational age (37.8%). Past medical history was observed in 10 cases including 5 cases (1.3% of all subjects) of thalassemia carrier, 4 cases (1%) of diabetes mellitus; 1 diagnosed before pregnancy and 3 gestational diabetes mellitus, class A1 and a case (0.3%) of thyroid goiter.

2. Data pertinent to Doppler ultrasonoghaphic results and pregnancy outcome Mean duration in performing Doppler ultrasonography was 12.4 + 3.2 minutes. There were 14 subjects (3.7%) found to develop preeclampsia including 9 cases(2.4%) of mild preeclampsia and 5 cases (1.3%) of severe preeclampsia. Distribution of the number of subjects developing preeclampsia according to the age range was shown (Table 1). It was noted that most of the subjects with or without the disease were in the age range of 20-29 years. However, preeclampsia was found in the highest proportion (16.7%) in the subjects of the age range of > 40 years.

The diastolic notch of the uterine artery was found in 51 subjects (13.5%); 48 cases found in unilateral uterine artery and 3 cases found in bilateral uterine arteries. Of these 51 cases, 11 cases developed preeclampsia. There were 3 cases who developed preeclampsia without demonstrated diastolic notch on the Doppler study. (Table 2). Analyses of the diagnostic performance of the diastolic notch of the uterine artery, with the 95% confidence interval (CI) in the parenthesis, in predicting preeclampsia pregnancy outcome were as follows: 78.6% sensitivity (49.2-95.3%), 89.0% specificity (85.3-92.0%), 21.6% PPV

Table 1. Age of the pregnant women who developed and did not develop preeclampsia

Age range (years)	Number of case (% of total subjects)	
	Normal	Preeclampsia
< 19	24 (6.3)	1 (0.3)
20-29	232 (61.4)	7 (1.8)
30-39	103 (27.3)	5 (1.3)
> 40	5 (1.3)	1 (0.3)
Total	364 (96.3)	14 (3.7)

Table 2. Correlation between the presence of diastolic notch of the uterine artery and the development of preeclampsia

Diastolic notch of uterine artery	Preeclampsia		Total
	Present	Absent	
Present	11	40	51
Absent	3	324	327
Total	14	364	378

(11.3-35.3%), 99.1% NPV (97.3-99.8%), 88.6% accuracy (85.0-91.6%), LR+ = 7.2 and LR- = 0.2.

Discussion

The study showed that most of the study subjects were in the age range of 20-29 years and 44.4% of them were the second gestation. Moreover, most of them had no past medical history. This showed that most of our study subjects were in the low risk pregnancy.

The incidence of preeclampsia in our study was 3.7%. Using the diastolic notch of the uterine artery, although having high sensitivity and specificity, 78.6% and 89.0% respectively, were achieved in predicting the disease, this sign provided the wide range of 95% CI of the sensitivity. Additionally, the PPV was found to be low, which could be explained by the low incidence of the disease in the study population.

High sensitivity and specificity but low PPV of the diastolic notch of the uterine artery in predicting the development of preeclampsia found in this study were in accordance with the data found in the previous studies. Bower et al[15] reported that the diastolic notch of the uterine artery yielded 82.0% sensitivity, 86.9% specificity but only 12% PPV in the prediction of preeclampsia. High sensitivity of 77.7% with low PPV of 29.0% were also reported in the study of Harrington et al[18].

However, these data were not agreed with the study of Chan et al[16], which found only 22.0% sensitivity but relatively high specificity and PPV, 97.0% and 35.0% respectively. This low sensitivity but high PPV was probably explained as the criteria used in the prediction of preeclampsia in this study were both the high resistance index of the uterine artery and the presence of the diastolic notch of the uterine artery. Iron et al[19] studied in women with the first gestation at the gestational age of 18 and 26 weeks and found that using the diastolic notch of the uterine artery in the prediction of preeclampsia yielded decreasing sensitivity from 50.0% to 26.0% and increasing specificity from 57.0% to 87.0% with advancing gestational age. The PPV was very low at both gestational ages, 5.0% and 7.0%, whereas the NPV in this study was 99.1%, which was close to those in other studies, indicating that most pregnant women with absent diastolic notch of the uterine artery would not develop preeclampsia. The LR+ of 7.2 in our study was comparable to that of 6.8 reported in the quantitative systematic review of Chien et al[20].

The strength of this study was that only one ultrasound machine used for the whole study, resulting in less variation caused by the machine. The subjects were blinded to the Doppler findings. However, there was a limitation in the study. Although previous training for standardization of the Doppler ultrasonography was done before the study and the positive findings seen by an operator was subsequently confirmed by another, the variability between the two operators probably occurred. Testing for inter-observer variability between the two operators was not performed in this study.

High sensitivity in predicting the development of preeclampsia indicated that this study could highly detect the disease in the women who had high potential in developing preeclampsia. However, low PPV implied that the probability in developing the disease in women with this sign was low. Although showing good performance in predicting the disease as high sensitivity and specificity, this sign, due to having low PPV, should be applied with precaution. It may be used as a surveillance in the development of the disease, in conjunction with a close observation of the symptoms and signs for early detection of the disease and resulting in the preventive measures that do no harm in case of the positive sign but no actual development of the disease in the future. It might not

be appropriate in applying to the preventive measures of high cost or high risk for the pregnant women and fetuses such as the administration of aspirin[21] or other chemical agents to prevent the disease.

Further studies should be conducted in the women with high risk in development of preeclampsia or by using the diastolic notch of the uterine artery in conjunction with other predictive methods in the Thai population to increase the PPV, such as blood pressure in the second trimester, urinary calcium level[3], depth of the diastolic notch of the uterine artery[22] or examining the diastolic notch in the older gestational age such as at the 24 weeks. Since the studies of Bower et al[15] and Antsaklis et al[22] revealed that these predictive methods could increase the PPV.

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การทำนายโรคพิษแห่งครรภ์ระยะก่อนชักในสตรีตั้งครรภ์เสี่ยงต่ำโดยการใช้รอยบุ๋มช่วงหัวใจคลายตัวของหลอดเลือดแดงมดลูก

ถวัลย์วงศ์ รัตนสิริ

วัตถุประสงค์ *: เพื่อประเมินการใช้รอยบุ๋มช่วงหัวใจคลายตัวของหลอดเลือดแดงมดลูกในการทำนายโรคพิษแห่งครรภ์ระยะก่อนชักในสตรีตั้งครรภ์เสี่ยงต่ำ*

วิธีการศึกษา *: เป็นการวิจัยเชิงพรรณนาชนิด diagnostic test study ในสตรีตั้งครรภ์ 378 ราย ที่มาฝากครรภ์ในช่วงอายุครรภ์ 18-22 สัปดาห์ ระหว่างวันที่ 1 มิถุนายน 2543 ถึง วันที่ 31 มีนาคม 2544 ที่โรงพยาบาลศรีนครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่นโดยตรวจหารอยบุ๋มช่วงหัวใจคลายตัวของหลอดเลือดแดงมดลูกโดยคลื่นเสียงความถี่สูงชนิดด็อพเพลอร์*

ผลการศึกษา *: พบสตรีตั้งครรภ์ 51 ราย มีรอยบุ๋มช่วงหัวใจคลายตัวที่หลอดเลือดแดงมดลูกข้างใดข้างหนึ่งหรือทั้งสองข้าง การทำนายโรคพิษแห่งครรภ์ระยะก่อนชักโดยการใช้รอยบุ๋มช่วงหัวใจคลายตัว มีความไวร้อยละ 78.6 ความจำเพาะร้อยละ 89.0 ค่าทำนายผลบวก ร้อยละ 21.6 ค่าทำนายผลลบร้อยละ 99.1 มีความแม่นยำร้อยละ 88.6 LR+เท่ากับ 7.2 และ LR-เท่ากับ 0.2*

สรุป *: การทำนายโรคพิษแห่งครรภ์ระยะก่อนชักโดยตรวจหารอยบุ๋มช่วงหัวใจคลายตัวของหลอดเลือดแดงมดลูกโดยคลื่นเสียงความถี่สูงชนิดด็อพเพลอร์ในไตรมาสที่สอง มีความไวและความจำเพาะสูง แต่มีค่าทำนายผลบวกต่ำจึงไม่เหมาะสมที่จะนำมาใช้เป็นวิธีตรวจคัดกรองโรคในสตรีตั้งครรภ์เสี่ยงต่ำทุกราย*