

Risk Assessment of Preeclampsia in Advanced Maternal Age by Uterine Arteries Doppler at 17-21 Weeks of Gestation

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Objective: To assess the risk of preeclampsia development in elderly gravidarum by uterine arteries Doppler at 17-21 weeks' gestation.

Material and Method: Pulsatility index (PI) of the uterine arteries was measured by color Doppler transabdominal sonography in 298 elderly gravida women at 17 – 21 weeks of gestation. The criterion for abnormal results was PI > 95th percentile of each gestational age and / or the presence of bilateral notches. The major end point was preeclampsia.

Results: Ten woman (3.4%) developed preeclampsia. Two hundred and eighty-four women (95.3%) had a normal Doppler flow of uterine arteries (PI ≤ 95th percentile of each gestational age), and 14 woman (4.7%) had abnormal Doppler flow of uterine arteries. The sensitivity, specificity, and positive and negative predictive values for detecting preeclampsia were 20%, 95.8%, 14.3%, and 97.2%, respectively.

Conclusion: Women with mean PI > 95th of each gestational age have a high risk of developing preeclampsia. With the high negative predictive value, this test may be useful to minimize unnecessary interventions.

Keywords: Uterine artery, Doppler, Preeclampsia, Elderly gravidarum, Pulsatility index

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Preeclampsia affects 5-10% of pregnancies and is a major cause of maternal and fetal morbidity and mortality in developing countries⁽¹⁾. The exact etiology of preeclampsia remains unknown, however, many studies have demonstrated that preeclampsia is associated with failure of trophoblastic invasion of the maternal spiral arteries, leading to increased vascular resistance of the uterine arteries and decreased uteroplacental blood flow⁽²⁾. The ability to predict early, women who have risk of this disease would be of great values. Although there is no proven effective method for the prevention of the preeclampsia, routine antenatal care has the aim to identify women who are at risk for more intensive antenatal care.

Uterine arteries Doppler evaluation is a non-invasive assessment of uteroplacental circulation, and its clinical value in high-risk pregnant women has been encouraging⁽³⁾. Abnormal uterine arteries Doppler waveforms reflect increased impedance in the uterine circulation. Uterine arteries Doppler studies in high-risk groups for severe pregnancy complications could increase predictive values for adverse pregnancy outcomes⁽⁴⁾.

Advanced maternal age is one of the risk factors of preeclampsia^(5,6). Therefore, the aim of the present study was to evaluate the value of uterine arteries Doppler study at 17-21 weeks' gestation as a screening test for preeclampsia in elderly gravidarum.

Material and Method

In this prospective study, uterine arteries Doppler ultrasound was performed on 298 singleton pregnant women of 35 years and older who attended the Antenatal Clinic, Department of Obstetrics and

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Gynecology, Faculty of Medicine, Chulalongkorn University between October 1, 2005 and September 30, 2006. The present study was approved by the Ethics Committee for Human Research of the Faculty of Medicine, Chulalongkorn University. Each subject signed an informed consent before taking the Doppler examination. Exclusion criteria were multiple pregnancies, pregnancy with fetal anomalies, cardiovascular disease, renal disease, diabetes mellitus, smoking, alcohol consumption, or drug addiction. Gestational age was identified by last menstrual period and then confirmed by ultrasonic measurement of the fetal biparietal diameter and femur length at 17-21 gestational weeks. Each subject was offered uterine arteries Doppler studies when they presented for a routine anomaly scan during 17-21 weeks of gestation. Uterine arteries flow velocity waveforms were obtained using an Aloka Prosound 5000 (Aloka Co., Tokyo, Japan) ultrasound machine, 3.5 or 5 MHz. transducer and a 100 Hz. high pass filter. The transducer was placed on the left and right lower quadrant of the maternal abdominal wall to identify the external iliac arteries and the uterine arteries medial to it. Flow velocity waveforms were obtained from each uterine artery near to the external iliac artery, before division if the uterine artery into branches⁽⁷⁾. At least three waveforms from each side were recorded on a strip chart. The pulsatility index (PI) of the left and right of uterine arteries were measured and the mean PI was calculated. The presence or absence of an early diastolic notch was also noted. An abnormal uterine arteries Doppler pattern was defined as a presence of mean PI > 95th of each gestational age and /or a presence of bilateral early diastolic notches.

One operator (SS) performed the measurements. The intra-operator coefficient of variation was calculated in five women with each patient examined three times. The mean intra-observer coefficient of variation for the PI was 6.9%.

Outcome measure was preeclampsia, defined as blood pressure of at least 140/90 mmHg measured on two occasions 6 hours apart, accompanied by proteinuria of at least 300mg per 24 hours, or at least 1+ on dipstick testing⁽⁸⁾. Severe preeclampsia was defined as having one or more of the following criteria: blood pressure of at least 160/110 mmHg measured on two occasions 6 hours apart, proteinuria of at least 5 g per 24 hours, cerebral or visual disturbances, pulmonary edema or cyanosis, epigastric or right upper quadrant pain, impaired liver function, thrombocytopenia, or fetal growth restriction⁽⁸⁾.

The pregnancy outcome and clinical data of all women were collected from hospital records following delivery without knowing the Doppler results.

The data were analyzed with the SPSS software package version 13 for Windows (SPSS Inc, Chicago, III, USA) and expressed in mean \pm standard deviation, range and in 5th, 50th, 95th percentile, term of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and relative risk (RR) with 95% confidence interval. Comparisons of clinical outcome with abnormal and normal uterine arteries were examined by Fishers' Exact test. Linear regression of gestational age and pulsatility index with R² were present. A p-value of less than 0.05 was considered statistically significant.

Results

During the present study period, 298 elderly gravidarum were recruited into the present study. Mean \pm SD maternal age was 36.8 \pm 2.1 years (Table 1). One hundred and thirty six women (45.6%) were nulliparous. Ten woman (3.4%) developed preeclampsia and four delivered newborns (1.3%) whose birth weights were less than 10th percentile.

In the present study, the mean \pm SD scan gestation period was 18.4 \pm 1.0 weeks (ranged 17⁺¹-21⁺⁰ weeks). Two hundred and eighty-eight had normal pregnancy outcome, the distribution of PI of the uterine arteries at 17-21 gestational weeks are shown in Fig. 1. The authors used the 95th percentile PI values of the presented reference interval as the cut-off points in predicting preeclampsia. Two hundred and eighty-four pregnant women (95.3%) had normal Doppler flow of

Table 1. Characteristics of the subjects in this study (n = 298)

Characteristics	Mean \pm SD (range), or n (%)
Mean maternal age (years)	36.8 \pm 2.1 (35-44)
Gravida	2 (1-6)
GA examination (weeks)	18.4 \pm 1.0 (17 ⁺¹ -21 ⁺⁰)
Time of delivery (weeks)	38.4 \pm 1.6 (24 ⁺¹ -42 ⁺⁰)
BMI (kgs/m ²)	22.6 \pm 3.3 (16.0-34.7)
Systolic BP (mmHg)	111 \pm 9 (86-130)
Diastolic BP (mmHg)	69 \pm 8 (50-90)
Route of delivery :	
- Vagina	76 (25.5%)
- Cesarean section	222 (74.5%)
Mean birth weight (g)	3070 \pm 475 (774-4900)

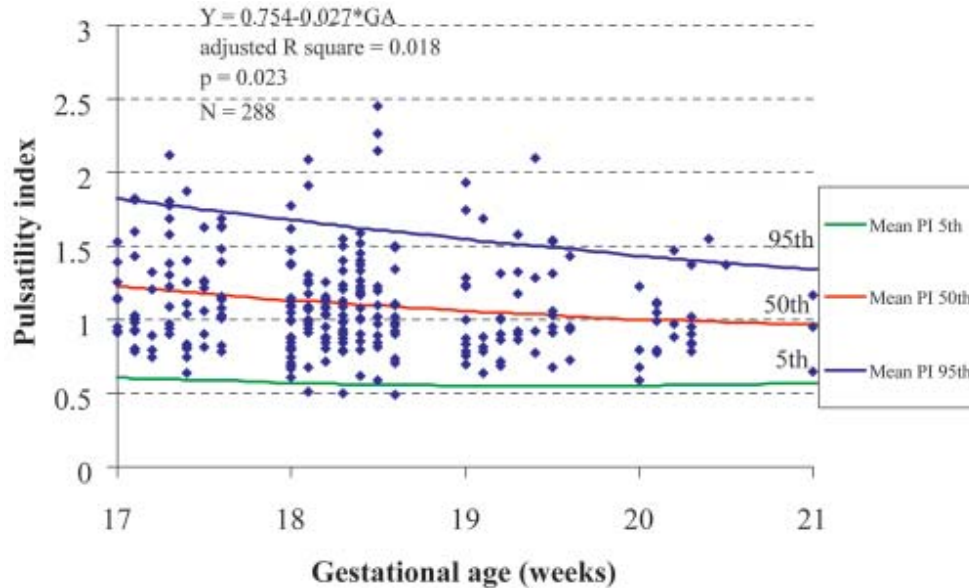


Fig. 1 Pulsatility indices of the uterine arteries in 288 normal pregnancies at 17-21 weeks gestation; the 5th, 50th, 95th percentile of the reference interval

uterine arteries ($PI \leq 95^{\text{th}}$ percentile of gestational age) and 14 cases (4.7%) had abnormal Doppler flow of uterine arteries (Table 2), there were two cases whose $PI > 95^{\text{th}}$ percentile of gestational age developed preeclampsia (Fig. 2). Early diastolic notches were obtained in 37 (12.4%) women. Bilateral early diastolic notches were found in 17 (5.7%) women. So far, no early diastolic notches were found in those who developed preeclampsia.

The screening positive (defined as mean $PI > 95^{\text{th}}$ percentile of each gestational age and/or bilateral notches), sensitivity, specificity, positive and negative predictive values as well as the relative risk of abnormal uterine arteries Doppler waveform (mean $PI > 95^{\text{th}}$ percentile and/or presented bilateral early diastolic notches) was 4.7, 20, 95.8, 14.3, 97.2% and 5.1 (1.2-21.7).

Discussion

Several Doppler studies on the uterine arteries

in the second trimester of pregnancy reported associations between increased mean PI in the uterine arteries at 22-24 weeks and high incidences of preeclampsia and/or fetal growth restriction^(9,10). From the present study, the uterine arteries Doppler study was used to screen a high-risk population at 17-21 weeks' gestation. This was the same period for screening fetal anomalies and performing the genetic amniocentesis. The prevalence of preeclampsia from the present study was similar to those studies on an unselected population⁽¹⁰⁾.

The authors constructed a reference interval of 17-21 weeks of gestation and most of the values lie inside the reference limits (Fig. 1). The definition of abnormal uterine arteries which the authors used in the present study was similar to those of many studies^(9,11-14) and the authors have found that 4.7% of women with mean $PI > 95^{\text{th}}$ percentile, which was similar to Albaiges *et al* and Papageorghiou *et al* studies (5.1%)^(11,12).

Table 2. Comparison of clinical outcomes in women with abnormal versus normal uterine arteries Doppler study

Clinical outcome	Uterine arteries Doppler study		p-value
	Abnormal (n = 14)	Normal (n = 284)	
Preeclampsia	2	8	0.02
- Severe degree	1	3	0.17

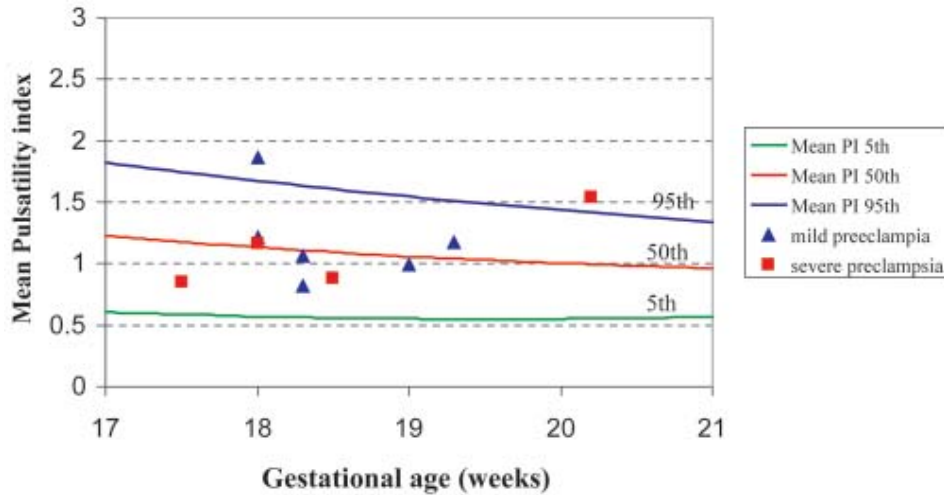


Fig. 2 Pulsatility indices of the uterine arteries in 10 pregnancies who developed preeclampsia related to reference interval

Early diastolic notches can be a physiologic finding till 24-26 weeks' gestation. The prevalence of bilateral diastolic notches at 18-22 weeks is more than 10%⁽¹⁵⁾. In the present study, the bilateral early diastolic notches were found in 5.7% women but no early diastolic notches were presented in any of the preeclampsia cases. Although many studies found that early diastolic notches were presented in preeclampsia cases^(10,16,17), the early diastolic notches in uterine artery analysis were not a better predictive value for preeclampsia^(10,18). Similar to the present study, bilateral notches did not improve screening characteristics for preeclampsia.

The result of prevalence of screening positive for preeclampsia, specificity, and negative predictive value of the present study were similar to Albaiges et al⁽¹¹⁾. It is difficult to make direct comparisons with other studies in high-risk populations because of differences in methodology, time of screening, sites of sampling, and definition of abnormal waveform⁽¹⁹⁾. In the present study, the test results had a low sensitivity and positive predictive value for preeclampsia. It means that this test cannot serve as a good screening test. However, this test had such a high negative predictive value (97.2%) that it implies only 2.8% of women with normal Doppler results developed preeclampsia. In other words, normal Doppler results in the advanced maternal age group appears to confer a low-risk status. The clinical utility of this test depends upon the negative predictive value as a test to avoid unnecessary intensive surveillance. This is the same as in previous study⁽¹⁷⁾.

The authors performed uterine arteries Doppler study at 17-21 weeks' gestation. This test may be added at the time of screening ultrasound or genetic amniocentesis. Many studies that associated the prediction of preeclampsia were performed at 22-24 weeks^(10,17). They may be too late for the benefit of the present study, which was an early screening for those who had risks of preeclampsia.

In conclusion, women who are elderly gravida, with mean PI \leq 95th percentile of each gestational interval age, are unlikely to develop preeclampsia. The test, having high negative predictive values, may be helpful in reducing unnecessary intensive surveillance.

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การประเมินความเสี่ยงต่อการเกิดภาวะครรภ์เป็นพิษในหญิงตั้งครรภ์ที่มีอายุตั้งแต่ 35 ปีขึ้นไป
โดยการตรวจดอปเพลอร์ของหลอดเลือดแดงยูเทอรินขณะอายุครรภ์ 17-21 สัปดาห์

สุชีลา ศรีทิพย์วรรณ, วรพงศ์ ภู่งศ์

วัตถุประสงค์: เพื่อศึกษาความเสี่ยงการเกิดภาวะครรภ์เป็นพิษในหญิงตั้งครรภ์ที่มีอายุตั้งแต่ 35 ปีขึ้นไป โดยการตรวจดอปเพลอร์ของหลอดเลือดแดงยูเทอรินขณะอายุครรภ์ 17-21 สัปดาห์

วัสดุและวิธีการ: การตรวจดอปเพลอร์ของหลอดเลือดแดงยูเทอรินทางหน้าท้องเพื่อวัด pulsatility index ในหญิงตั้งครรภ์ที่มีอายุตั้งแต่ 35 ปีขึ้นไปจำนวน 298 รายที่อายุครรภ์ 17-21 สัปดาห์ เกณฑ์ค่าเฉลี่ย pulsatility index ของหลอดเลือดแดงยูเทอรินที่ผิดปกติ คือ ค่ามากกว่าค่าที่ 95 เปอร์เซนต์ไทล์ของแต่ละอายุครรภ์ และ/หรือ ร่วมกับมี Early diastolic notch ทั้งสองข้างของหลอดเลือดแดงยูเทอริน ผลลัพธ์ที่ต้องการศึกษาคือ การเกิดภาวะครรภ์เป็นพิษ

ผลการศึกษา: ในจำนวนหญิงตั้งครรภ์ที่ศึกษาทั้งหมด 298 ราย มี 10 ราย (3.4%) เกิดภาวะครรภ์เป็นพิษ และพบว่า มี 284 ราย (95.3%) ที่มีค่าเฉลี่ย pulsatility index ของหลอดเลือดแดงยูเทอรินปกติ และมี 14 ราย (4.7%) ที่มีค่าเฉลี่ย pulsatility index ของหลอดเลือดแดงยูเทอรินผิดปกติ ความไว, ความจำเพาะ, positive และ negative predictive value ของการวัด pulsatility index ของหลอดเลือดแดงยูเทอรินในการศึกษานี้ เท่ากับ 20%, 95.8%, 14.3% และ 97.2% ตามลำดับ

สรุป: หญิงตั้งครรภ์ที่มีค่าเฉลี่ย pulsatility index ของหลอดเลือดแดงยูเทอรินมากกว่าที่ 95 เปอร์เซนต์ไทล์ของแต่ละอายุครรภ์จะมีความเสี่ยงต่อการเกิดภาวะครรภ์เป็นพิษ ค่า negative predictive value ที่สูงในการศึกษานี้บ่งว่าการตรวจดังกล่าวจะช่วยลดการเฝ้าระวังที่ไม่จำเป็นในภาวะครรภ์เป็นพิษลงได้
