

The Role of Uterine Artery Doppler Ultrasound in the Second Trimester in Predicting Preeclampsia

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Abstract

Background: Preeclampsia is a specific pregnancy syndrome. Early diagnosis and proper administration of preeclampsia can lead to improved maternal and neonatal outcome. We aimed to investigate the uterine artery Doppler ultrasound in predicting the preeclampsia in women with a high-risk pregnancy.

Materials and Methods: This analytic study was conducted on 160 primigravida women with gestational age of 18 to 26 weeks referring to Ali-Ebne Abi Taleb hospital of Zahedan (Iran). The uterine artery Doppler was considered as abnormal if mean Pulsatility Index (PI) was higher as 95% for gestational age or bilateral notching was observed. All uterine artery sonography was performed by one expert sonographer and with one machine. Then the pregnancy outcomes (such as placenta abruption, postpartum hemorrhage, death, Neonatal Intensive Care Unit admission, low birth weight, preterm labor, etc.) were compared between the two groups.

Results

The mean age of pregnant women was 25.4±5.6 years old. Preeclampsia was seen in 37 (24.7%) of the women and healthy was seen in 113 (75.3%) of the women. A statistically significant difference was seen between the women with normal and abnormal Doppler sonography (P=0.001). The sensitivity of Doppler ultrasonography in predicting early onset, late onset and severe preeclampsia was 73.3 %, 62.5 %, and 100%, respectively. The specificity of Doppler ultrasonography in predicting early onset, late-onset, and severe preeclampsia was 64.4%, 66.1%, and 74.3%, respectively.

Conclusion

The findings of the study showed that uterine artery Doppler (Pulsatility Index) is useful in predicting the occurrence of preeclampsia in second trimester.

Key Words: Preeclampsia, Pregnancy, Uterine artery Doppler.

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1- INTRODUCTION

Preeclampsia is a specific pregnancy syndrome; it is able to affect all organs of the body (1). The condition occurs in 5-8% of pregnancies and leads to 50,000 deaths worldwide annually (2, 3). Preeclampsia is defined as the onset of hypertension $\geq 140/90$ after 20 weeks of pregnancy and proteinuria and characterized by widespread dysfunction of the endothelium of mother (4, 5). Several factors such as nulliparity, molar pregnancy, twin pregnancy, obesity and resistance to insulin, previous history of preeclampsia, antiphospholipid antibody syndrome, familial history of preeclampsia or eclampsia, embryonic aneuploidy, very young and very old mothers have been proposed as risk factors of preeclampsia (6, 7). Etiology and pathogenesis of preeclampsia, despite many studies about the cause of it, is still largely shrouded in mystery and poorly understood (8, 9). The evidence suggests preeclampsia is present in early pregnancy and pathophysiological hidden changes begin from embryonic period, whereas if childbirth does not occur, these changes ultimately lead to multi-organ involvement that might be risky for both mother and fetus (1, 9, 10).

One of the hypotheses discussed in the etiology of preeclampsia is incomplete trophoblast invasion to the uterine artery in normal endovascular implantation process whereby these cells replace the endothelial and muscular lining of blood vessels and cause increase in vascular diameter (1, 9, 10). Thus, by continuing the pregnancy, blood flow impedance of uterine artery is reduced due to change of spiral arteries to vessels with low resistance (11). This situation causes a decrease in placental perfusion and eventually leads to an increase in uterine artery resistance (1). However, early diagnosis and proper administration of preeclampsia can lead to improved maternal and neonatal outcomes. Regarding the prevalence of preeclampsia,

the importance of its proper administration to promote health indicators is clear (12, 13). With the help of Doppler ultrasound, today, uterine arteries can be examined and, by analyzing existing indicators, can largely evaluate the high risk pregnancies (14, 15). In order to estimate the amount of resistance of blood flow in uterus placenta, flow velocity measurement of uterine artery is used (1). Recent studies have shown that increased resistance to uterine vessels will lead to an increased risk of progression towards preeclampsia and intrauterine growth restriction (IUGR) (16). Also, increasing the diastolic velocity of the intercostal cerebrospinal fluid is a sign of brain conservation in chronic fetal hypoxia (17). The study of Roy and Bhosale (2018) indicated that abnormal Doppler velocimetry was associated with poor perinatal outcome (Low Apgar score, low birth weight, Neonatal Intensive Care Unit [NICU] admission) (18). The study of Meler et al. (2010) indicated that neonatal complications and maternal complications were higher in abnormal uterine artery Doppler (3). The study of Ghi et al. (2009) indicated that neonatal complications in the group with abnormal uterine artery Doppler were higher than the group with normal uterine artery but the maternal complications showed no significant difference between two groups (normal vs. abnormal uterine artery Doppler) (19).

According to multiple studies with different results on the role of uterine artery Doppler in predicting preeclampsia and pregnancy outcomes, this study was designed to evaluate the role of uterine artery Doppler ultrasonography in predicting preeclampsia and assessed neonatal and maternal complications in pregnant women with preeclampsia, because in case of early diagnosis of fetal and neonatal complications, preventive measures can be used to improve prenatal prognosis.

2- MATERIALS AND METHODS

2-1. Study design and population

This analytic study was conducted on 160 primiparous women with gestational age of 18-26 weeks referring to Ali-Ebne Abi Taleb hospital of Zahedan (Iran), for prenatal care.

2-2. Method

Patients were advised to follow-up in this center (Ali-Ebne Abi-Taleb) until the end of pregnancy. Patients with a gestational age of 18-26 weeks underwent uterine artery Doppler ultrasound and measurement of blood pressure (at rest). All the data were completed for each patient and recorded in the care card. All uterine artery Doppler ultrasonography was performed by one expert sonographer and with one machine. The uterine artery Doppler was considered as abnormal if mean Pulsatility Index (PI) was higher than 95% for gestational age (mean value of right or left), or bilateral notching was observed (24). Gestational age was calculated according to first-trimester sonography based on Crown-rump length (CRL) at 11 to 13 weeks or Biparietal diameter (BPD) at 19 to 24 weeks.

The PI was compared with blood pressure and urine analysis, and sensitivity and specificity were calculated. The diagnostic criteria of preeclampsia included maternal systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg measured at resting for two times at 4-h intervals, and proteinuria of ≥ 300 mg per 24 h urine collection or at least one positive dipstick after 20 weeks of gestation age in a previously normotensive woman. Severe preeclampsia was defined when maternal blood pressure was $\geq 160/110$ mmHg on two occasions at least 4 h apart and one or more of the following conditions, renal insufficiency, thrombocytopenia, elevated liver transaminases to twice the normal concentrations, cerebral or visual symptoms, pulmonary edema, and severe

right hypochondriac pain (1). To study all patients with late-onset preeclampsia at 34 weeks of pregnancy, they underwent re-measurement of blood pressure and in case of doubt of preeclampsia, urine analysis (Random or 24 h collection) performed respectively. All results at any stage were recorded in primary information form. In the end, pregnancy outcomes in the two groups with normal and abnormal uterine artery Doppler were compared.

2-3. Ethical consideration

Ethical considerations in this study are as following:

- Ethics approval was obtained from the Ethics Committee of the Zahedan University of Medical Sciences (approved by the Ethics Committee: IR.ZAUMS.REC.1392.5884).
- Informed consent was obtained from all pregnant women before participation in the study.
- No charge for any of the participants

2-4. Inclusion and exclusion criteria

Inclusion criteria include consent to participate in the study, history of previous preeclampsia (individual-family), nulliparity, mother's age (less than 35 year-old), or mother's age less than 18 years, abortion history, infertility history. Exclusion criteria were chronic systemic diseases (Endocrinological disorders, cardiovascular, gastrointestinal, immunological, or oncological), Premature rupture of membranes (PROM), pre-term labor, intrauterine fetal death (IUFD), and fetus chromosome abnormalities. In this study 10 patients were excluded as follows: 3 out of 10 with PROM (gestational age of 20, 23 and 25 weeks), 2 patients with IUFD (at 19 and 20 weeks' gestational age), and 5 cases due to lack of constant pursuit. Thus 150 cases were analyzed.

2-5. Data Analysis

The data were analyzed using SPSS version 21.0. Descriptive statistics were used for all variables. Demographic data was compared among groups using t-test. Chi-square test was used for categorical variables. The level of statistical significance was considered as $p < 0.05$.

3- RESULTS

In this study, 150 primigravida women with gestational age between 18 and 26 weeks were enrolled. All women underwent uterine artery Doppler ultrasonography, and 91(60.7%) had normal Doppler sonography, and 59(39.3 %) had abnormal Doppler sonography. The mean age of pregnant women was 25.4 ± 5.6 years old. Mean and standard deviation (SD) age for women with normal and abnormal Doppler was 25.0 ± 5.6 years and 26.1 ± 5.5 years, respectively. There was no statistically significant difference ($P=0.317$). Preeclampsia was seen in 37 (24.7%) of the women and healthy was seen in 113(75.3%) of the women. At the end seven out of 37 women with preeclampsia had normal Doppler (7.7%),

and 30 were those who had abnormal Doppler (50.8%). Statistically significant difference was seen between the women with normal and abnormal Doppler sonography ($P=0.001$). Chi-square test showed no significant difference between severity of preeclampsia in women with normal and abnormal Doppler sonography ($P=0.06$) (**Table.1**). The sensitivity of Doppler ultrasonography in predicting early onset, late onset and severe preeclampsia was 73.3 %, 62.5 %, and 100%, respectively. The specificity of Doppler ultrasonography in predicting early onset, late-onset and severe preeclampsia was 64.4%, 66.1%, and 74.3%, respectively.

Maternal complications included eight patients with placenta abruption and seven patients with postpartum hemorrhage (PPH), and no maternal mortality was observed. Neonatal complications included 17 hospitalizations in the NICU, 18 neonates of Low Birth Weight (LBW), 16 cases of preterm labor and 2 cases with neonate's death (**Table.2**).

Table-1: Compare the severity of preeclampsia by Doppler ultrasound.

Doppler Sonography		Abnormal	Normal	Total	P-value
Preeclampsia	Early-onset	11(36.7%)	4(57.1%)	15(75.3%)	0.06
	Late-onset	5(16.7%)	3(42.9%)	8(24.7%)	
	Severe	14(46.7%)	0(0 %)	14(100%)	
	Total	30(81.8%)	7(18.9%)	37(100%)	

Table-2: Preeclampsia Complications (Maternal and Neonatal).

Preeclampsia Complications		Doppler Sonography		
		Abnormal	Normal	Total
Maternal	Placenta Abruption	5(62.5%)	3(37.5%)	8(100%)
	Postpartum hemorrhage	5(71.4%)	2(28.6%)	7(100%)
	Death	0(0%)	0(0%)	0(0%)
Neonatal	Neonatal Intensive Care Unit admission	11(64.7%)	6(35.3%)	17(100%)
	Low birth weight	14(77.8%)	4(22.2%)	18(100%)
	Preterm labor	11(68.7%)	5(31.3%)	16(100%)
	Death	2(100%)	0(0%)	2(100%)

4- DISCUSSION

The findings indicated that there was a statistically significant difference between the women with normal and abnormal Doppler sonography. In this study, 7.7% of patients with normal Doppler sonography, and 50.8% of patients with abnormal Doppler sonography developed preeclampsia. The sensitivity of Doppler ultrasound in predicting severe preeclampsia in the second trimester of pregnancy was high. Preeclampsia is one of the major causes of maternal and fetal morbidity and mortality worldwide. Different studies have been conducted on this subject, Afrakhteh et al. in 2014 investigated sensitivity and specificity of Doppler ultrasound in the second trimester of pregnancy, and reported acceptable values but it was low in comparison to third trimester (20). Also, Papageorghiou et al. in 2004 showed that abnormal Doppler ultrasound was accompanied with preeclampsia, IUGR, and prenatal death. They mentioned that preeclampsia is predictable with abnormal uterine artery Doppler in the first trimester but its sensitivity is lower than Doppler studies of the second trimester (11).

In a study in 2004, Espinoza et al. also presented abnormal uterine artery Doppler in the second trimester accompanied with an increased risk of preeclampsia and association with early onset or severe preeclampsia (21). Asafi et al. (2011) showed that prevalence of preeclampsia, abortion, and LBW (low birth weight) was higher in the group with abnormal uterine artery Doppler which is consistent with present results but the rate of preterm labor did not differ between the two groups (22). Lijie et al. (2016) conducted a study on 800 patients in the second trimester and investigated the relation of some serum biomarkers and uterine artery Doppler with preeclampsia. They reported that serum inhibin A, activin A, placental growth factor in early second-trimester and

uterine artery Doppler PI in second-trimester may show further information for the prediction of preeclampsia. The combination of the three serum markers and uterine artery Doppler PI has the highest predictive value for preeclampsia (23). Some studies reported that uterine artery Doppler of the second trimester is not a valuable method for predicting preeclampsia (24). In addition, maternal and neonatal morbidity were assessed in the study by Meler et al., in 2008 for 129 patients with early-onset preeclampsia, it showed maternal and neonatal morbidity was higher in the group of abnormal uterine artery Doppler which confirms our results (3). Totally sensitivity of 100% of uterine artery Doppler ultrasonography in predicting severe preeclampsia suggests that uterine artery Doppler ultrasonography, especially in the second trimester of pregnancy can be used as a reliable method for effective prediction of severe preeclampsia. As well as abnormal uterine artery Doppler ultrasonography is helpful in predicting maternal and neonatal morbidity, especially in severe preeclampsia, it seems more studies of this method can be used in predicting preeclampsia and its implications.

4-1. Limitations of the study

The main limitation of this study was that only PI is used. It is recommended that other indexes of the uterine artery Doppler ultrasonography be evaluated.

5- CONCLUSION

The findings of the study showed that the prevalence of preeclampsia in patients with abnormal uterine artery Doppler is higher than in the group with normal Doppler, and the Doppler ultrasound has a powerful diagnostic proper. According to the results of this study, it is suggested that uterine artery Doppler ultrasound can be used in high-risk pregnant women to predict preeclampsia.

6- CONFLICT OF INTEREST: None.

7- ACKNOWLEDGMENTS

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