International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Bommineni BL. Int J Reprod Contracept Obstet Gynecol. 2024 Sep;13(9):2585-2589
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20242527

Review Article

Prediction of preeclampsia and fetal growth restriction by uterine artery Doppler evaluation

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Received: 03 July 2024
Revised: 08 August 2024
Accepted: 09 August 2024

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ABSTRACT

Foetal growth restriction and preeclampsia are important causes of perinatal morbidity and mortality. Studies show a robust correlation between these issues and diffuse endothelial dysfunction. Pregnant women who show significant resistance to uteroplacental blood flow are more likely to develop preeclampsia, according to clinical research. Pregnancies with a higher risk of difficulties due to defective placentation can be predicted by uterine artery Doppler investigations, which can be performed in both the first and second trimesters. These studies had a false positive rate of 5% to 7% and a sensitivity of 80% to 90% in predicting severe preeclampsia. When done between 20 and 24 weeks of gestation, uterine artery Doppler screening is more effective than screening during the first trimester and satisfies all screening test requirements. To find out how well maternal blood indicators and uterine artery Doppler work together to predict unfavorable pregnancy outcomes, more research is required.

Keywords: Preeclampsia, Uterine artery Doppler, Screening, Ultrasound

INTRODUCTION

Preeclampsia is a significant global cause of maternal and neonatal death, particularly in poorer nations.[1,2] It is believed to be caused by compromised placentation, which is influenced by pregnancy-specific modifications and genetically determined maternal variables.[3,4] Preeclampsia patients have insufficient trophoblast invasion of mother spiral arteries, preventing the change of these vessels from high-resistance to low-resistance, high-volume non-responsive vessels.[5]

Preeclampsia has no known cure, so identifying women at risk is crucial for early prenatal surveillance and timely delivery. Early attempts to predict preeclampsia focused on hypertension, proteinuria, edema, excessive weight gain, and increased vascular resistance. However, recent research has shifted focus to biochemical indicators, particularly endothelial dysfunction.[6]

Indirect evidence of aberrant placentation can be seen in preeclamptic women's uterine arteries, where there is persistent high resistance to blood flow.[7] The uterine artery Doppler has been the subject of numerous research as a screening tool for women who may develop preeclampsia.

SECOND TRIMESTER UTERINE ARTERY DOPPLER

Studies have shown increased blood flow impedance in uterine arteries in pregnancies with established preeclampsia or foetal development limitation.[8-10] Doppler ultrasonography has been used to evaluate placental perfusion and vascular resistance problems, both transabdominally at the apparent crossover with the external iliac artery and transvaginally lateral to the uterine cervix at the level of the internal cervical os. In 2004, two systematic reviews were carried out and released, which assessed the clinical utility of various diagnostics in

identifying risk factors for inadequate placental perfusion.[11,12]

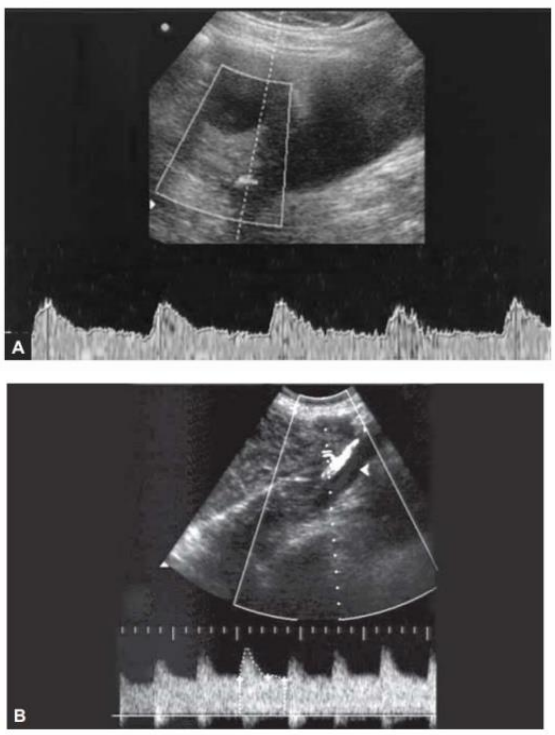

Figure 1: (A) Uterine artery flow measurement (transabdominal approach) at first trimester scan; (B) uterine artery flow measurement (transabdominal approach) at second trimester scan.

The reviewers' criteria were met by 43 studies, including 42,261 cases, that evaluated the accuracy of Doppler ultrasonography. The studies were divided into four categories: individuals utilising flow waveform ratios; individuals utilising the existence or non-existence of any diastolic notch; individuals utilising the existence or non-existence of bilateral diastolic notches; and individuals utilising both flow waveform ratios and diastolic notches.

Severe preeclampsia can be predicted more accurately than moderate illness. Steel et al found that gestational hypertension and preeclampsia were associated with sensitivity levels of increased impedance in the uterine arteries of 39% and 63%, respectively.[13] Papageorgiou et al found that the sensitivity was 24% for preeclampsia without foetal growth restriction (FGR) and 69% for preeclampsia with FGR.[14]

The gestational age at which delivery is attempted is an additional indicator of the disease's severity that has been documented in certain studies. Harrington et al found that bilateral notching at 24 weeks detected 55% of women who went on to develop preeclampsia, increasing to 81% in cases of preeclampsia that required delivery before 34 weeks.[15] Albaiges et al demonstrated that for preeclampsia necessitating delivery before 34 weeks, the sensitivity was 90%, but for elevated PI or bilateral notches in the second trimester, the sensitivity was 45%.[16]

The value of the uterine artery Doppler in the second trimester and the 3D placental volume in the first trimester were compared by Hafner et al and discovered that their sensitivity to the prediction was comparable of foetal development limitation and preeclampsia.[17]

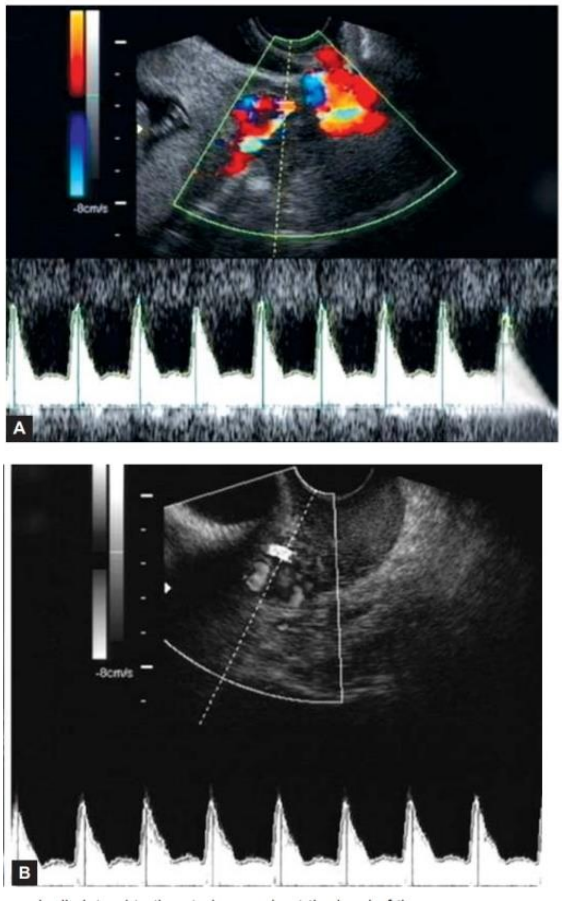

Figure 2: (A) Uterine artery flow measurement transvaginally lateral to the uterine cervix at the level of the internal cervical os (first trimester) on right side; (B) uterine artery flow measurement transvaginally lateral to the uterine cervix at the level of the internal cervical os (first trimester) on left side.

Toal et al investigated the value of a placental profile in high-risk pregnancies during the second trimester, which included maternal serum screening, uterine artery Doppler, and placental morphology.[18] They discovered that the odds ratio for unfavourable perinatal outcomes was considerably lowered by a normal profile.

Certain risk factors related to maternal history may improve the uterine artery Doppler's sensitivity. Papageorgiou et al concluded that uterine artery Doppler could be used to estimate a patient's specific risk of developing preeclampsia by combining risk factors from the mother's past, including race, smoking habit, essential

hypertension, previous preeclampsia, family history, body mass index, and parity.[19]

According to Yu et al study of 32,157 pregnant women who were not chosen for screening, Doppler ultrasound of the uterine arteries in the second trimester combined with risk factors like ethnicity, history of preeclampsia, previous term birth, and smoking habit yielded a more accurate estimate of preeclampsia risk than ultrasound alone.[20]

FIRST TRIMESTER UTERINE ARTERY DOPPLER

Uterine artery Doppler is a useful tool in early pregnancy screening for trophoblast invasion. Studies have shown a link between hypertension diseases and foetal growth restriction (FGR) and the pulsatility index, with women with higher pulsatility indexes having a higher risk of FGR and preeclampsia. Recent research has shown that Doppler ultrasonography can identify women at risk of developing intrauterine growth restriction and preeclampsia.

Martin et al conducted the largest screening multicenter study at 11 to 14 weeks, showing a sensitivity of 27.0% for the mean uterine artery pulsatility index above the 95th percentile in identifying preeclampsia.[22] However, 55% of instances had early diastolic notches, which reduced their usefulness for screening at this gestational age. Gomez et al observed a significant shift in the mean uterine artery pulsatility index's 95th percentile as gestation progressed, resulting in a sensitivity of 24% for predicting preeclampsia among 22 instances of preeclampsia.[23]

Pilalis et al found that the mean uterine artery pulsatility index (PI) >95th percentile had a sensitivity of 23% and a positive predictive value of 6.7% at 11 to 14 weeks.[24] Plasencia et al concluded that combining maternal history with aberrant uterine artery Doppler at 11 to 14 weeks produces better results than either test alone.[25]

Detti et al concluded that complications during a second or third trimester cannot be predicted by a first trimester Doppler examination of the uterine circulation.[26] Khaw et al found changes in uterine artery Doppler and maternal cardiac function in nulliparous women who later experienced preeclampsia and/or foetal growth restriction.[27] Rizzo et al found that the combined test performed better in predicting preeclampsia than either test performed alone.[28]

COMBINATION OF UTERINE ARTERY DOPPLER AND MATERNAL SERUM MARKERS

Research has shown that combining multiple markers of oxidative stress and placental malfunction with combined uterine Doppler examinations can effectively predict preeclampsia. Aquilina et al study found that three types of markers were highly predictive of developing preeclampsia in women at high risk for the illness, including placental growth factor, leptin, and plasminogen activator inhibitor (PAI-1/PAI-2 ratio).[29] Two recent nested case-control studies revealed important findings in preeclampsia prediction: sFlt-1 and the placental growth factor (PlGF), which were predicted by lower first-trimester serum levels of PlGF and higher levels of fms-like tyrosine kinase 1 (sFlt-1), its soluble inhibitor.

Indicators of poor placentation and oxidative stress could be found prior to the clinical manifestation of preeclampsia, such as an abnormal PAI-1/PAI-2 ratio, an increase in the plasma concentration of 8-epi-prostaglandin F2α, a marker of oxidative stress, a decrease in PlGF, and an increase in circulating sFlt-1. The results suggest that early alterations in these biomarkers may function as predictive markers for the onset of preeclampsia, providing chances for early intervention and management techniques in pregnancies at risk.

Finding the mean uterine artery resistance index and maternal plasma factor II (FII) at mid-trimester may help predict preeclampsia in women with early-onset gestational hypertension. Ay et al found that uterine artery Doppler and maternal serum inhibin A and activin A levels seem to be helpful screening tools for preeclampsia in the second trimester. However, the therapeutic value of these hormone indicators is limited because their addition to Doppler velocimetry only marginally increases prediction effectiveness.

Two more variables have been assessed as preeclampsia predictors in the first trimester: oxidative stress and placental dysfunction indicators. These variables play a critical role in early detection of pregnancies at risk for preeclampsia, enabling prompt interventions and better outcomes for both the mother and the foetus.

Yaron et al investigated the possibility that low levels of maternal pregnancy-associated plasma protein-A (PAPP-A) could be used as a predictor of unfavourable pregnancy outcomes. Spencer et al found that the detection rates for preeclampsia were 14.1% for maternal PAPP-A, 54.7% for Doppler, and 62.1% for the combination. Anastasakis et al. discovered that preeclampsia was more likely to occur in women with elevated malondialdehyde levels and aberrant uterine artery Doppler imaging. To determine the true prognostic significance of each of these indicators, prospective, long-term studies are required.

CONCLUSION

The uterine artery Doppler screening is a promising method for predicting preeclampsia, with a low false positive rate and high sensitivity. Second trimester screening, between 20 and 24 weeks of gestation, performs better and is more reliable than first trimester screening. However, uterine artery screening programs are not widely implemented in hospitals due to the lack of effective preventative medicines. To improve predictive accuracy, efforts should be made to support the broader use of

screening programs, possibly combining them with other indicators of oxidative stress and placental dysfunction.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Bommineni BL. Prediction of preeclampsia and fetal growth restriction by uterine artery Doppler evaluation. Int J Reprod Contracept Obstet Gynecol 2024;13:2585-9.