

Mid-trimester uterine artery doppler in high risk pregnancies as a predictor of adverse pregnancy outcomes

Authors

- 1) Sravani Mukka, Assistant Professor, Department of Obstetrics & Gynecology, ESIC Medical College, Hyderabad, Telangana, India.
- 2) Swathi Emmadisetty, Assistant Professor, Department of Obstetrics & Gynecology, ESIC Medical College, Hyderabad, Telangana, India.

Corresponding Author : Dr. Sravani Mukka, Assistant Professor, Department of Obstetrics & Gynecology, ESIC Medical College, Hyderabad, Telangana, India; Email: mukka.sravani@yahoo.com

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Abstract:

Objectives: The present study aims at demonstrating an association between abnormal uterine artery doppler waveform in high risk pregnancies at 18-24 weeks of gestation and subsequent development of adverse pregnancy outcomes. **Methods:** Uterine artery doppler was performed in high risk pregnant women between 18-24 weeks of gestation attending antenatal OPD at ESIC Medical College, Sanathnagar, during the period between March 2018 to February 2019. Presence of pulsatility index (PI) >1.45 or presence of bilateral uterine artery notching was considered as abnormal doppler waveforms. Outcomes measured were preeclampsia, small for gestation (<10th centile), abruption and intrauterine fetal death. **Results:** Doppler examination was performed in 115 high risk pregnant women. 34.78% had abnormal doppler waveforms. Overall 42 (36.52%) women had Small for gestational age (SGA) babies and 31(26.95%) developed preeclampsia, of which 76% and 70% had abnormal doppler respectively. The sensitivity, specificity, PPV and NPV of PI > 1.45 and bilateral uterine artery notching for predicting preeclampsia were 70%,78.57%,55% and 88% respectively (95% CI 2.3361-8.9923;P value < 0.0001) and that for SGA being 76.19%,89.04%,80% and 86.67% respectively (95% CI 3.3013-10.904; P value <0.0001). **Conclusion:** Mid-trimester uterine artery doppler waveform analysis performed in high risk women have a high negative predictive value. Hence, women with normal doppler waveforms are unlikely to develop adverse pregnancy outcomes.

Keywords: Abnormal doppler, preeclampsia, pulsatility index, mid-trimester, small for gestational age, uterine artery doppler, uterine artery notching.

Impaired placentation is considered as one of the major risk factor for adverse pregnancy outcomes¹. This is due to failure of trophoblastic invasion of muscular spiral arteries and their conversion from narrow muscular to wide non muscular low resistance vessels.^{2,3}

Direct assessment of trophoblastic invasion is not possible in human pregnancy. Doppler imaging permits a non invasive evaluation of uteroplacental circulation by comparing systolic and diastolic waveforms^{4,5}. The physiological process of trophoblastic invasion is reflected in the observation from doppler ultrasound studies that impedance (PI) of flow in uterine arteries decreases with gestation between 6 weeks and 24 weeks and remains constant thereafter^{6,7}. Impedance to flow is reflected by either persistence of the uterine artery diastolic notch or abnormal doppler waveforms. This led to the idea of uterine artery doppler as screening test for adverse pregnancy outcomes.

Variation in doppler techniques, measurement parameters and study protocols have resulted in disappointing results in the prediction of poor pregnancy outcomes in low risk population with positive predictive values between 4 and 20⁸⁻¹⁰. In high risk women doppler screening of uterine circulation would double the PPV for estimating either preeclampsia or small for gestation baby compared to the clinical risk assessment or prevalence¹¹. Hence, predicting the risk of these complications may improve the outcome by providing appropriate antenatal surveillance and therapeutic intervention.

The present study aims at demonstrating an association between abnormal uterine artery doppler waveform in high risk pregnancies at 18-24 weeks of gestation and subsequent development of adverse pregnancy outcomes.

Materials and methods

This was a prospective study conducted at ESIC Medical College, Sanathnagar during the period between March 2018 to February 2019 after obtaining ethical clearance. Uterine artery doppler was performed as a part of routine clinical care in high risk pregnancies between 18-24 weeks of gestation. 115 High risk pregnant women attending antenatal OPD were enrolled based on their previous pregnancy history and willingness to participate in the study. A written informed consent was taken from the participants after explaining the objectives of the study.

Inclusion criteria (Previous pregnancies) -

- H/o preeclampsia or eclampsia
- H/o abruption
- H/o recurrent abortions (>3)
- H/o intrauterine fetal demise
- H/o oligohydramnios

Exclusion criteria -

- Chronic hypertension
- Multiple pregnancy
- Renal disease
- Fetal anomalies
- Diabetes mellitus

Procedure: With the transducer in the longitudinal plane, external iliac artery is visualised at the pelvic sidewalls. The transducer is turned medially towards the uterine arteries where they cross the external iliac arteries. 4 different waveforms are obtained from each uterine artery and average was taken each side. Parameters of mean PI and presence or absence of notch in bilateral uterine arteries were analysed.

Presence of PI >1.45 or presence of bilateral notching was considered as abnormal doppler forms. A prescribed proforma was filled up and record was maintained. Follow up was done till the end of pregnancy. No intervention was done based on the doppler results. The main outcomes measured were preeclampsia, small for gestation (<10th centile), abruption and intra uterine fetal death.

Preeclampsia: Blood pressure of $\geq 140/90$ mm of Hg on two occasions 6 hrs apart in a previously normotensive women after 20 weeks of gestation with proteinuria (excretion of more than 300mg in 24hrs urine sample or single void urine protein/creatinine ratio ≥ 0.3 or dipstick 1+ persistent) or signs of end organ damage with or without proteinuria (platelet count < 1 lakh/mm³; raised serum creatinine >1.1 mg/dl; elevated liver enzymes 2 times their normal values; evidence of pulmonary edema; new onset of visual/cerebral symptoms)^{12,13}.

Small for gestational age: Birth weight less than 10th percentile for the gestational age¹⁴.

Abruption: Premature separation of a normally situated placenta from the lining of the uterus before the completion of second stage labour¹⁵.

Intrauterine fetal death: Delivery of a fetus showing no signs of life at 20 weeks or greater of gestation or a weight equal to or greater than 350gms (50th percentile for weight) if the gestational age is not known^{16,17}.

The validity of doppler as a predictor of preeclampsia and small for gestational age babies was tested based on sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratios and negative likelihood ratios. The statistical analysis was done by chi square test and 2×2 contingency table using MedCalc statistical software, version 19.6.

Results

A total of 115 pregnant women were selected based on the risk factors in their previous pregnancy and the doppler study was performed in them. Majority of the women had hypertensive disorders (43.47%) during their previous pregnancy, followed by oligohydramnios (22.60%) (table 1).

Table 1: High risk categorisation		
Risk factors	Total (n = 115)	%
Preeclampsia	46	40%
Eclampsia	04	3.47%
Oligohydramnios	26	22.60%
Recurrent abortions	19	16.52%
Intra uterine fetal death	14	12.17%
Abruption	04	5.21%

Table 2 : Uterine artery doppler results in the present pregnancy		
Doppler results	Total (n=115)	%
Normal Doppler	75	65.20%
Abnormal Doppler	40	34.78%

Table 3: Adverse pregnancy outcomes observed				
Pregnancy Outcomes	Normal doppler(n)	Abnormal doppler (n)	Total (n=115) N	%
Preeclampsia	9	22	31	26.95
Small for gestation age	10	32	42	36.52
Abruption	0	05	05	4.34
Intrauterine fetal death	0	03	03	2.60

Out of the total 115 high risk pregnancies studied 34.78% had abnormal doppler based on the doppler indices of PI >1.45 and bilateral uterine notching (table 2). On follow up of all the cases 42 (36.52%) had small for gestational age babies and 31(26.95%) developed preeclampsia of which 76% and 70% respectively had abnormal doppler (table 3). Of the three cases of intrauterine fetal death two cases were due to abruption and one case eclampsia.

Table 4 : Diagnostic validity and accuracy								
Pregnancy outcome	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Relative risk	Chi square test	95% CI	P value
Hypertensive disorders	70	78.57	55	88	4.58	24.284	2.3361-8.9923	0.00*
Small for gestational age	76.19	89.04	80	86.67	6.00	49.576	3.3013-10.9049	0.00*

The relative risk of having preeclampsia and SGA with abnormal doppler was 4.58 and 6.00 respectively. The negative predictive value for both the conditions is high (88% and 86.67% respectively) and significant (table 4).

Discussion

The validity of uterine artery doppler as a predictor of adverse pregnancy outcomes has been explored by several investigators. Trophoblastic invasion is maximum in the first trimester and that preeclampsia deriving from a

relative failure of this event, validates doppler evaluation of uterine artery from first trimester¹⁸. In our institute majority of the women have their first antenatal check up from second trimester. Hence the study was conducted between 18-24 weeks.

In the present study out of the 115 high risk pregnant women 40 (34.78%) had either PI>1.45 or bilateral uterine artery notching. This is similar to a study by Coleman et al¹¹ in New Zealand in which 40% of high risk patients at 22-24 weeks had atleast one uterine artery notching, this rate was 38% in a study by El Hamedi⁴.

70.9% and 76% of the pregnant women who developed preeclampsia and small for gestational age in the present study had abnormal doppler waveforms during their midtrimester with the sensitivity, specificity, positive predictive value and negative predictive values for preeclampsia and small for gestational age being 70, 78.57, 55.88 (95 % CI 2.3361 - 8.992; P value <0.0001) and 76.19, 89.04, 80, 86.67 (95% CI 3.3013-10.9049 ; P value <0.0001) respectively. Of the 5 cases of abruption two cases presented with intra uterine fetal death and it was a retrospective finding during caesarean section in one case.

Densak in his study used PI and doppler notching in high risk women has shown sensitivity of preeclampsia and small for gestation as 59.25% and 56.25 % respectively and the specificity for these outcomes as 66.67% & 65.70% respectively¹.

A study by Pranita et al in 140 women has shown RI as a predictor of preeclampsia with sensitivity of 50%, specificity of 93.9%, positive predictive value 33.3% and negative predictive value 96.9% and notching had a sensitivity of 62.5%, specificity 94.7%, positive predictive value 41.7% and negative predictive value 97.7%¹⁹.

Padmalatha in her study with 217 random singleton pregnancies and doppler studies included PI, RI and notching. The sensitivity, specificity, PPV and NPV of PI and notching in the prediction of preeclampsia were 60, 92, 16, 99 and 80, 94, 25, 100 respectively. Further the validation of PI and notching in the prediction of FGR being 21, 92, 21, 92 and 26, 94, 31, 93 respectively. The study also concluded doppler as a better tool for high risk women than low risk²⁰.

A multicentric study using uterine artery doppler ultrasound imaging at 22-24 weeks of gestation in about 8000 singleton showed that the sensitivity for preeclampsia with small for gestational age is substantially higher than that for preeclampsia without small for gestational age (69% vs 24%)²¹. Furthermore, a study of more than 30,000 pregnancies showed that the PI > 1.58 in 77% of those that substantially developed pre-eclampsia requires delivery before 34weeks compared with 36% of late preeclampsia²².

Conclusion

Mid trimester uterine artery doppler waveform analysis performed in high risk women have a high negative predictive value. Hence, women with normal doppler waveforms are unlikely to develop adverse pregnancy outcomes.

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