



FIRST AND SECOND TRIMESTER UTERINE ARTERY DOPPLER IN PREDICTING HYPERTENSIVE DISORDERS IN PREGNANCY LOW-RISK MOTHERS

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ABSTRACT

Background: This study was conducted to investigate whether uterine artery spectral Doppler screening is able to identify patients who will develop hypertensive disorders in pregnancy (HDP). Besides HDP, delivery of SGA babies, their APGAR scores and whether admitted in NICU is also studied.

Methods: In this single-centre prospective cohort study, 200 low-risk antenatal women attending a tertiary care teaching hospital in eastern India between July 2020 and August 2023 underwent transabdominal uterine artery Doppler assessment at 11–13⁺6 weeks. Mean pulsatility index (PI), resistance index (RI), and systolic/diastolic ratio were recorded; the 95th percentile was used to classify women as Doppler-normal or Doppler-abnormal. Participants were followed prospectively for development of HDP, delivery of a small-for-gestational-age (SGA) neonate, neonatal intensive care unit (NICU) admission, and APGAR scores. Groups were compared using the independent-samples t-test for continuous variables and the chi-square or Fisher exact test for categorical variables; $P < 0.05$ was considered significant.

Results: Twenty-four women (12.0%) had abnormal first-trimester Doppler indices. HDP developed in 18 women overall and 16 of these had abnormal Doppler findings. HDP occurred in 66.7% of the Doppler-abnormal group versus 1.1% of the Doppler-normal group ($P < 0.001$). Abnormal Doppler was also associated with a higher rate of SGA neonates (25.0% vs 5.1%, $P = 0.001$) and NICU admission (50.0% vs 23.9%, $P = 0.007$).

Conclusion: Abnormal first-trimester uterine artery Doppler velocimetry was strongly associated with subsequent development of HDP and with SGA and NICU admission in this low-risk cohort. These findings support incorporation of first-trimester uterine artery Doppler into routine antenatal screening to identify women who may benefit from closer surveillance and prophylactic low-dose aspirin, although confirmation in larger, multicentric cohorts with a priori sample size calculation is required.

KEYWORDS: Pregnancy-induced Hypertension, Pre-eclampsia, Uterine Artery Doppler, Pulsatility Index, First-trimester Screening, Small for Gestational Age.

Introduction

Hypertensive disorders of pregnancy remain among the leading causes of maternal and perinatal morbidity and mortality worldwide, accounting for approximately 14% of maternal deaths globally[1]. In India, the incidence of preeclampsia was found to be 10.3 % (NER) National Eclampsia Registry and incidence of eclampsia is 1.9% of all pregnancies[2], translating into a substantial national burden given the country's annual delivery volume.

Normal placentation depends on trophoblastic invasion of the maternal spiral arteries, which converts these vessels from a high-resistance to a low-resistance, high-capacitance system capable of supporting the markedly increased uteroplacental blood flow of pregnancy. In preeclampsia, this remodelling is incomplete, leaving the spiral arteries partially muscularised and unable to dilate appropriately; the resulting uteroplacental ischaemia and oxidative stress are considered central to the disease's pathogenesis[3,4]. Because this defect originates early in pregnancy and precedes clinical manifestations by many weeks, it is, in principle, detectable non-invasively by Doppler ultrasound of the uterine arteries before the onset of overt disease[3].

Several large cohorts and meta-analyses have examined the performance of uterine artery Doppler indices — pulsatility index (PI), resistance index (RI), and the presence of diastolic notching — as first-trimester predictors of preeclampsia and fetal growth restriction. A meta-analysis of 55,974 women found that an abnormal first-trimester uterine artery PI predicted preeclampsia with a sensitivity of 26.4%, rising to 47.8% for early-onset disease[5], while combined screening models incorporating maternal characteristics, biochemical markers, and Doppler indices have achieved detection rates exceeding 90% for early-onset preeclampsia at a 10% false-positive rate[6]. Serial assessment across the first and second trimesters, as proposed by Plasencia et al.[7] and Gomez et al.[8], suggests that a persistently elevated Doppler index carries an even greater risk of adverse outcome, and that a normalising Doppler index between trimesters does not fully reassure against later complications.

Reference ranges for uterine artery PI across gestation, validated in large prospective cohorts, are now well established[9], and international guidance recommends standardised transabdominal technique for reproducible measurement[10]. Contingent, staged screening — reserving detailed second-trimester surveillance for women identified as high-risk on first-trimester assessment — has been proposed as an efficient model of antenatal care[11], particularly as low-dose aspirin initiated before 16 weeks in women with abnormal first-trimester Doppler has been shown in meta-analyses to reduce the risk of preeclampsia and its complications[12,13,14].

Despite this body of evidence, most published data originate from high-income settings, and locally generated evidence

on the predictive performance of first-trimester uterine artery Doppler in low-risk Indian women remains limited. We conducted a prospective cohort study to evaluate whether first-trimester uterine artery Doppler velocimetry predicts the subsequent development of HDP, and to characterise its association with SGA, NICU admission, mode of delivery, gestational age at delivery, and APGAR scores, in a low-risk antenatal population attending a tertiary care hospital in eastern India.

Methods

Study Design and Setting

This was an institution-based prospective cohort study conducted in the Department of Obstetrics & Gynaecology and the Department of Radiodiagnosis, Institute of Postgraduate Medical Education and Research (IPGMER) & SSKM Hospital, Kolkata, India, a tertiary care teaching hospital. Recruitment and follow-up were conducted between July 2020 and August 2023. This study was approved by the Institutional Ethics Committee, IPGMER & SSKM Hospital, Kolkata. Written informed consent was obtained from all participants prior to enrolment.

Participants

Antenatal women attending the outpatient department before 11 weeks of gestation were eligible. Women were excluded if they were aged 40 years or older, had a body mass index (BMI) ≥ 35 kg/m², had a multiple pregnancy, had an inter-pregnancy interval exceeding 10 years, or had a history of hypertensive disease in a previous pregnancy, chronic hypertension, a family history of HDP, chronic kidney disease, type 1 or type 2 diabetes mellitus, or autoimmune disease such as systemic lupus erythematosus or antiphospholipid syndrome. Two hundred women meeting these criteria were enrolled by convenience sampling; a formal a priori sample size calculation was not performed, and this is addressed as a limitation below.

Uterine Artery Doppler Protocol

Doppler assessment was performed transabdominally at 11–13⁺₆ weeks' gestation, coinciding with the routine nuchal translucency scan. A sagittal section of the uterus was obtained and the cervical canal and internal cervical os identified; colour flow mapping was used to locate each uterine artery at the level of the internal os. Pulsed-wave Doppler was applied with the sampling gate set at 2 mm, an angle of insonation $< 30^\circ$, and a peak systolic velocity > 60 cm/s to ensure sampling of the main uterine artery rather than the arcuate branches, following standard technique[10]. Once three consecutive similar waveforms were obtained, PI was recorded and the mean of the left and right uterine artery PI, RI, and systolic/diastolic ratio was calculated. The 95th percentile for each index — PI 2.48, RI 0.85, and S/D ratio 3.30 — was used as the cut-off for classifying Doppler findings as normal or abnormal, consistent with published reference ranges for this gestational window[9].

Women also underwent a second Doppler assessment at the time of the routine anomaly scan (18–21⁺⁶ weeks) as part of departmental protocol; for reasons detailed in the Limitations, the second-trimester dataset could not be verified as independent of the first-trimester classification during manuscript preparation and second-trimester Doppler findings are therefore not reported as a separate analysis in this manuscript.

Outcome Definitions

HDP was assessed according to National Institute for Health and Care Excellence (NICE) criteria[15], encompassing gestational hypertension (blood pressure ≥ 140/90 mmHg arising after 20 weeks without proteinuria) and preeclampsia (new hypertension after 20 weeks accompanied by proteinuria and/or evidence of maternal acute kidney injury, liver dysfunction, neurological features, haemolysis, thrombocytopenia, or fetal growth restriction). Chronic hypertension and superimposed preeclampsia were exclusion criteria and are not represented in this cohort. SGA was defined as birthweight below the 10th percentile for gestational age[16]. APGAR scores were recorded at 1 and 5 minutes for all neonates as per standard practice, with a score > 7 considered reassuring[17].

Statistical Analysis

Data were tabulated in Microsoft Excel and analysed using SPSS version 24 (IBM Corp., Armonk, NY). Normally

distributed continuous variables are presented as mean ± standard deviation and compared using the independent-samples t-test. Categorical variables are presented as counts and percentages and compared using the chi-square test or Fisher exact test as appropriate. A P value ≤ 0.05 was considered statistically significant.

Results

Two hundred women met the inclusion criteria and completed follow-up to delivery. Twenty-four (12.0%) had abnormal first-trimester uterine artery Doppler indices and 176 (88.0%) had normal indices.

Baseline maternal age (24.19 ± 3.47 vs 24.25 ± 5.33 years, P = 0.944) and gravidity (P = 0.446) did not differ significantly between the Doppler-normal and Doppler-abnormal groups. BMI, however, differed markedly: 54.2% of the Doppler-abnormal group were obese compared with none of the Doppler-normal group (P < 0.001) (Table 1).

Overall, 18 of 200 women (9.0%) developed HDP during the study period. HDP developed in 66.7% (16/24) of the Doppler-abnormal group compared with 1.1% (2/176) of the Doppler-normal group (P < 0.001). SGA neonates were delivered by 25.0% of the Doppler-abnormal group versus 5.1% of the Doppler-normal group (P = 0.001), and NICU admission occurred in 50.0% versus 23.9%, respectively (P = 0.007) (Figure 1).

Table 1: Baseline maternal characteristics by first-trimester Doppler status

Characteristics	Doppler normal (n = 176)	Doppler abnormal (n = 24)	P value
Maternal age, years (mean ± SD)	24.19 ± 3.47	24.25 ± 5.33	0.944
Gravidity, n (%)			
Primigravida	73 (41.5)	8 (33.3)	0.446
Multigravida	103 (58.5)	16 (66.7)	
Body mass index, n (%)			
Normal	103 (58.5)	2 (8.3)	<0.001*
Overweight	73 (41.5)	9 (37.5)	
Obese	0 (0.0)	13 (54.2)	

*Statistically significant (P < 0.05).

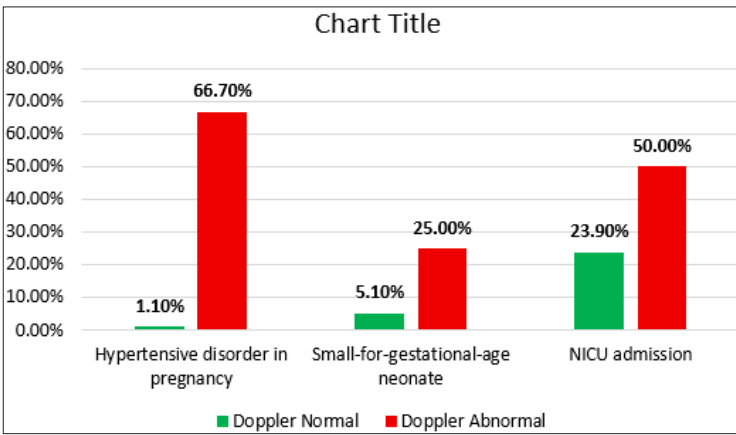


Figure 1. Pregnancy and neonatal outcomes which are significantly higher in Doppler-abnormal group

Table 2: Pregnancy and neonatal outcomes by first-trimester Doppler status

Outcome	Doppler normal (n = 176)	Doppler abnormal (n = 24)	P value
Caesarean section, n (%)	116 (65.9)	18 (75.0)	0.374
Gestational age at delivery, weeks (mean $\pm$ SD)	39.09 $\pm$ 1.34	37.83 $\pm$ 1.31	<0.001*
APGAR score at 1 minute (mean $\pm$ SD)	6.34 $\pm$ 1.00	6.00 $\pm$ 1.14	0.124
APGAR score at 5 minutes (mean $\pm$ SD)	7.70 $\pm$ 0.74	7.42 $\pm$ 0.78	0.085

*Statistically significant ($P < 0.05$).

Gestational age at delivery was significantly earlier in the Doppler-abnormal group (37.83 ± 1.31 vs 39.09 ± 1.34 weeks, $P < 0.001$). Caesarean section rate was numerically higher in the Doppler-abnormal group (75.0% vs 65.9%) but the difference was not statistically significant ($P = 0.374$), and APGAR scores at 1 and 5 minutes did not differ significantly between groups ($P = 0.124$ and $P = 0.085$, respectively) (Table 2). The diagnostic performance of an abnormal first-trimester uterine artery Doppler for predicting subsequent HDP shows that the sensitivity was 88.9%, specificity 95.6%, positive predictive value 66.7%, and negative predictive value 98.9%.

Discussion

In this prospective cohort of 200 low-risk women, an abnormal first-trimester uterine artery Doppler was strongly associated with the subsequent development of HDP, with a sensitivity of 88.9% and a negative predictive value of 98.9% — figures at the favourable end of those reported in the literature. The Velauthar meta-analysis of 55,974 women reported a pooled sensitivity of only 26.4% (47.8% for early-onset disease) for an abnormal PI[5], considerably lower than observed here. This discrepancy most likely reflects differences in population risk profile, disease definition, and the pragmatic, single-centre design of our study relative to large multicentre meta-analyses, and should be interpreted with appropriate caution given our modest sample size and the wide confidence intervals implied by only 24 Doppler-abnormal and 18 HDP cases.

Our finding that abnormal Doppler was also associated with SGA delivery and NICU admission, but not with APGAR score, mirrors the pattern reported by van den Elzen et al.[18], who found a four-fold increase in hypertensive disorders and a two-fold increase in fetal growth restriction among women in the highest quartile of first-trimester uterine artery PI, and by Harrington et al.[19], who reported a seven-parameter first-trimester Doppler-based model with 93% sensitivity and 85% specificity for preeclampsia. Combined screening algorithms incorporating maternal factors, biochemical markers, and Doppler indices have achieved even higher detection rates for both early-onset preeclampsia and SGA[6,20,21,22], suggesting that Doppler velocimetry alone — as used in the present study — captures only part of the overall predictive information available in the first trimester.

The marked association between obesity and abnormal Doppler findings observed in our cohort (54.2% obese in the Doppler-abnormal group versus none in the Doppler-normal group) is consistent with the broader literature linking maternal adiposity to impaired trophoblastic invasion and uteroplacental dysfunction, and reinforces obesity as an important, modifiable risk factor to incorporate alongside Doppler findings when counselling and risk-stratifying women in early pregnancy.

Because uterine artery Doppler assessment identifies at-risk women well before clinical disease manifests, it lends itself to a staged model of antenatal care in which first-trimester screening determines the intensity of subsequent surveillance, as proposed by Nicolaidis[11]. Meta-analyses of antiplatelet therapy indicate that low-dose aspirin commenced before 16 weeks in women identified as high-risk reduces the incidence of preeclampsia and adverse perinatal outcome[12,13,14]. Our data — in particular the high negative predictive value of a normal first-trimester Doppler — support the use of this scan to reassure the majority of low-risk women while directing the minority with abnormal findings toward closer surveillance and consideration of prophylactic aspirin, consistent with the sequential screening strategy described by Plasencia et al.[7], in which second-trimester testing is reserved for the subset of women flagged as high-risk in the first trimester.

Conclusion

In this low-risk cohort, abnormal first-trimester uterine artery Doppler velocimetry was strongly associated with subsequent development of HDP, delivery of an SGA neonate, and NICU admission, with a negative predictive value of 98.9% for HDP. These findings support the potential value of incorporating first-trimester uterine artery Doppler into routine antenatal screening as a means of identifying women who may benefit from closer surveillance and prophylactic low-dose aspirin. Given the pragmatic sample size and single-centre design, confirmation in larger, adequately powered, multicentric prospective cohorts — with a priori sample size calculation and independently verified second-trimester follow-up data — is warranted before these findings can inform routine clinical policy.

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None

Conflict of Interests

None

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