Uterine artery Doppler velocimetry in hypertensive disorder of pregnancy in Nigeria

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Abstract

Aim of the study: To evaluate the value of uterine artery Doppler indices and waveform pattern in predicting fetuses at risk for intrauterine growth restriction in hypertensive disorders of pregnancy. Materials and methods: This was a prospective cross-sectional study including 80 pregnant subjects with hypertensive disorders of pregnancy and two control groups. Uterine artery Doppler sonography was performed in all study participants. Uterine artery Doppler indices across the groups were compared using the analysis of variance (ANOVA) while the presence of prediastolic notch was analyzed with the Chi Square test. Results: For the hypertensive disorders of pregnancy group, resistivity index > 0.66 had a sensitivity of 50.0%, specificity of 69.1% and a positive predictive value of 22.2% for predicting intrauterine growth restriction. The odds ratio was 2.2 with a 95% confidence interval of 0.6–7.8. The presence of prediastolic notching had a sensitivity of 100.0%, specificity of 96.0% and a positive predictive value of 80.0% for predicting intrauterine growth restriction. The odds ratio was 22.7 with a 95% confidence interval of 7.5–68.5. Conclusion: Uterine artery Doppler sonography is useful for predicting fetuses at risk for intrauterine growth restriction in hypertensive disorder of pregnancy. Prediastolic notching is more sensitive and more specific than uterine artery resistivity index in predicting fetuses at risk of intrauterine growth restriction in established hypertensive disorder of pregnancy.

Keywords
hypertensive disorder of pregnancy, uterine artery, Doppler sonography, intrauterine growth restriction

Introduction

Hypertensive disorder of pregnancy (HDP) is a major cause of maternal and perinatal morbidity and mortality in developing countries, including Nigeria(1). HDP is considered to be the result of abnormal placenta formation, involving abnormal trophoblast invasion of spiral arteries leading to an increase in vascular resistance in the uteroplacental circulation(2). Subsequently, intrauterine growth restriction (IUGR) occurs if there is no intervention.

Hypertension in pregnancy is said to occur when the systolic blood pressure is greater than 140 mmHg and diastolic blood pressure is greater than 90 mmHg on at least two occasions, six hours apart. Hypertensive disorder of pregnancy encompasses gestational hypertension in pregnancy (hypertension without proteinuria), pre-eclampsia (hypertension with proteinuria) and eclampsia (pre-eclampsia with convulsions)(3). In our environment, it is estimated that 5–10% of pregnancies are complicated by hypertensive disorders(4).

With the already established role of Doppler sonography in evaluating human vascular hemodynamics, it is rea-
Doppler ultrasound assessments were performed at 20–24 weeks gestational age at the commencement of medication in the HDP group. Each subject was placed in supine position on an examination couch. After appropriate exposure, coupling gel was applied on the abdomen and a routine obstetric scan was performed to establish the estimated fetal weight (EFW) using the Hadlock formula on Mindray® DC-7 (Shenzhen Mindray Bio-Medical Electronics Co., LTD. Shenzhen, China) as well as to rule out any fetal congenital anomalies. The fetuses were classified as small-for-gestational-age (SGA) or IUGR based on their EFW from ultrasound scanning. The American College of Obstetrician and Gynecologists defines IUGR as EFW below the 10th percentile for gestational age\(^{(6)}\).

The transducer was then placed on the lower quadrant of the abdomen, angled medially, and then color Doppler imaging was used to identify both uterine arteries at their apparent crossover with the external iliac artery. Measurements were taken approximately 1 cm distal to the crossover point\(^{(8)}\). This point was chosen after a pilot study showed that it is more easily reproducible.

The side at which the placenta is located reportedly has an influence on uterine artery Doppler indices in pregnant women; however, we examined both uterine arteries in all pregnant subjects in this study and found no statistically significant difference in the uterine artery Doppler indices between the two sides. Subsequently, for convenience, the right side was used for further analysis.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) for Windows (SPSS Inc, USA) version 20. One-way analysis of variance (ANOVA) was used to compare the means of variables across the three groups while the presence of prediastolic notch was analyzed with the Chi Square test, and a \(p\)-value \(\leq 0.05\) was considered statistically significant.

### Results

There was no statistically significant difference \((p = 0.99)\) in the mean age across the three study groups (Tab. 1).

The highest blood pressure was recorded in the HDP group, with a mean systolic blood pressure (SBP) of 149.8 ± 11.5 mmHg while the lowest blood pressure with a mean SBP of 117.6 ± 8.8 mmHg was found in the PC group (Tab. 2). The differences in the mean SBP, diastolic blood pressure (DBP) and mean arterial pressure (MAP) across the

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**Fig. 1.** Triplex ultrasound image showing the uterine artery Doppler waveform in normal pregnancy.

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**Materials and methods**

This was a prospective cross-sectional study including 3 groups of 80 age-matched subjects. The groups included pregnant subjects with HDP, apparently healthy pregnant controls (PC) with normal blood pressure, and apparently healthy non-pregnant controls (NPC) with normal blood pressure. All pregnant subjects were recruited from the antenatal unit. Written informed consent was obtained from all study participants. Approval for the study was obtained from the institution’s ethics committee. The study was conducted at the Department of Radiology of our institution from February 2014 to January 2015.

Patients with diabetes mellitus, chronic hypertension, cardiovascular disorders, chronic renal disease, fetal congenital anomalies and smokers were excluded from the HDP and PC groups while patients with uterine pathologies and post-menopausal women were excluded from the NPC group.

The operative definition of HDP used in this study was pregnancy at ≥ 20 weeks gestational age (GA) with hypertension, proteinuria and/or convulsions induced by pregnancy. Medical histories of the subjects were reviewed and their blood pressures were taken with a mercury sphygmomanometer. Early morning urine samples were collected from the HDP group and screened for proteinuria using urinalysis test strips/dipsticks. Patients were defined as being proteinuric in the presence of protein of ≥ 0.3 g/L of urine (≥ 1 + reading on dipstick).

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groups were all statistically significant \( (p < 0.001; \text{Tab. 2}) \). Similarly, the observed difference in the mean weight of the PC and HDP groups was statistically significant \( (p < 0.001) \). However, no statistically significant \( (p = 0.057) \) difference was detected in the mean SBP between NPC and PC groups.

Urinalysis in HDP subjects revealed no proteinuria in 56 (70.0%) patients, while 24 (30%) patients were proteinuric. Statistical comparison between the mean RI of the right and the left uterine artery in all study groups showed no statistically significant differences. Therefore, for convenience, the right uterine artery RI was chosen for further analysis of RI.

The mean RI of the right uterine artery was the highest in the NPC group followed by the HDP group and was lowest in the PC group \( (p < 0.001, \text{Tab. 3}) \). A similar tendency was observed for PI and S/D ratio (Tab. 3). Scheffe post-hoc analyses for inter-group differences in the mean values of the Doppler parameters showed a significant statistical difference (Tab. 4).

Prediastolic notching (Fig. 2) was present in HDP and NPC groups only. There was no prediastolic notching recorded in the PC group. In the HDP group, 15 (18.8%) out of 80 subjects had prediastolic notch as opposed to the other 65 (81.2%). Similarly, prediastolic notch was present in 14 (17.5%) and absent in 66 (82.5%) patients in the NPC group, as shown in Tab. 5.

Out of the 80 HDP subjects investigated, 12 had their EFW below the 10\(^{th}\) percentile and thus were at high risk for IUGR; the remaining 68 had their EFW above the 10\(^{th}\) percentile. The uterine artery mean RI was significantly

| Variables | NPC | PC | HDP | \( \chi^2 \) | df | \( p \) value |
|-----------|-----|----|-----|-------------|----|-------------|
| Age in years | | | | | | |
| Mean ± SD* | 31.7 ± 5.5 | 31.8 ± 5.6 | 31.8 ± 4.7 | 0.009 | 2.237 | 0.991 |
| (Range) | 20–42 | 20–42 | 20–40 | 8.818 | 8 | 0.358 |
| \( n \) (%) | | | | | | |
| <25 | 9 (11.2) | 8 (10.0) | 6 (7.5) | | | |
| 25–29 | 15 (18.8) | 19 (23.8) | 14 (17.5) | | | |
| 30–34 | 34 (42.5) | 24 (30.0) | 35 (43.8) | | | |
| 35–39 | 13 (16.2) | 24 (30.0) | 20 (25.0) | | | |
| ≥40 | 9 (11.2) | 5 (6.2) | 5 (6.2) | | | |

\* One way ANOVA used to compare means

\( \chi^2 \) – chi square test statistic; NPC – non-pregnant controls; PC – pregnant controls; HDP – hypertensive disorder of pregnancy

| Variables | NPC | PC | HDP | \( F \) | df | \( p \) value |
|-----------|-----|----|-----|-------|----|-------------|
| Height (m) | 1.61 ± 0.09 | 1.60 ± 0.11 | 1.63 ± 0.06 | 2.684 | 2.237 | 0.070 |
| Weight (kg) | – | 72.8 ± 12.7 | 86.0 ± 18.1 | 4.4631 | 158 | <0.001 |
| Blood pressure | | | | | | |
| SBP (mmHg) | 121.4 ± 9.1 | 117.6 ± 8.8 | 149.8 ± 11.5 | 254.42 | 2.237 | <0.001 |
| DBP (mmHg) | 79.8 ± 5.7 | 68.5 ± 8.3 | 95.8 ± 8.8 | 251.18 | 2.237 | <0.001 |
| MAP (mmHg) | 93.67 ± 5.8 | 84.9 ± 6.9 | 113.8 ± 7.8 | 371.65 | 2.237 | <0.001 |

\( F \) – means One way ANOVA; NPC – non-pregnant controls; PC – pregnant controls; HDP – hypertensive disorder of pregnancy; SBP – systolic blood pressure; DBP – diastolic blood pressure; MAP – mean arterial pressure

| Variables | NPC | PC | HDP | \( F \) | df | \( p \) value |
|-----------|-----|----|-----|-------|----|-------------|
| Right uterine artery RI | 0.76±0.09 | 0.50±0.08 | 0.61±0.14 | 109.51 | 2.237 | <0.001 |
| Right uterine artery PI | 1.74±0.40 | 0.87±0.22 | 1.39±0.86 | 47.71 | 2.237 | <0.001 |
| Right uterine artery S/D | 5.18±1.62 | 2.07±0.33 | 2.98±1.53 | 3.06 | 2.237 | <0.001 |

\* One way ANOVA applied

NPC – non-pregnant controls; PC – pregnant controls; HDP – hypertensive disorder of pregnancy; RI – resistive index; PI – pulsatility index; S/D – systolic/diastolic ratio

Tab. 1. Demographic characteristics of subjects

Tab. 2. Clinical parameters of the subjects across the 3 groups

Tab. 3. Comparison of uterine artery Doppler parameters across the 3 groups*
higher in the at-risk-for IUGR subjects (0.69 ± 0.07) compared to those with EFW above the 10th percentile (0.59 ± 0.15); \( p = 0.025 \).

Further analysis of the HDP group was performed using the RI of 0.66 as normal upper limit/cut-off value. This cut-off value was obtained in this study from the mean RI of the normal pregnant control group, which was 0.50 ± 0.08, with a 95th percentile RI of 0.66 (i.e., 95th percentile = mean RI + 2 standard deviations).

Out of 12 patients with IUGR (EFW < 10th percentile), six (50%) had the RI above 0.66, while the remaining 6 (50%) had their RI below 0.66. In contrast, in the group of 68 patients with EFW above the 10th percentile, a greater proportion (69.1%, \( n = 47 \)) had the RI below 0.66 (\( p = 0.20 \)).

In the PC group, of 8 subjects with EFW below the 10th percentile, none had RI above 0.66. However, 3 out of 72 patients with EFW above the 10th percentile had RI above 0.66 (\( p = 0.726 \)). More subjects in the HDP group [27 (33.8%) out of 80] had RI greater than 0.66 compared to the PC group with only 3 (3.8%) patients with RI > 0.66 out of 80 subjects in the group (\( p < 0.001 \)).

All 12 (100.0%) subjects in the HDP group with EFW < 10th percentile had prediastolic notching of their right uterine artery waveform. Of the remaining 68 subjects with EFW > 10th percentile, only 3 (4.4%) had prediastolic notching of their right uterine artery waveform. The presence of prediastolic notching in those at-risk-for IUGR (i.e. EFW < 10th percentile) was statistically significant (\( p < 0.001 \)).

Out of 80 right uterine arteries investigated in the HDP subjects, 15 (18.8%) had prediastolic notching in their waveform. These also had higher mean RI of 0.73 ± 0.10 compared to the remaining 65 without prediastolic notch with a mean RI of 0.58 ± 0.12 (\( p < 0.001 \)). Furthermore, all these 15 HDP subjects with prediastolic notching on their uterine artery waveform had proteinuria.

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of RI > 0.66 and prediastolic notching for predicting IUGR are shown in Tab. 6.

### Discussion

Pre-eclampsia and IUGR are postulated to be the result of abnormal placenta formation involving abnormal trophoblast invasion of spiral arteries subsequently leading to an increase in vascular resistance in the uteroplacental circulation\(^9\). This eventually leads to a decrease in blood flow to the uterus and the fetus. Thus, early diagnosis of IUGR, as evidenced by detailed Doppler velocimetry, is needed for timely intervention.

Audibert et al.\(^{10}\) reported that the presence of a uterine artery notch was associated with a significantly higher risk of both preeclampsia and IUGR in the general pregnant population. In another study\(^{11}\), the sensitivity of detecting a uterine artery notch at 20–24 weeks gestational age for predicting future development of HDP and/or IUGR in the

### Table 4

| Variables                  | NPC vs PC | NPC vs HDP | HDP vs PC |
|----------------------------|-----------|------------|-----------|
| Right uterine artery RI    | <0.001    | <0.001     | <0.001    |
| Right uterine artery PI    | <0.001    | <0.001     | <0.001    |
| Right uterine artery S/D   | <0.001    | <0.001     | <0.001    |

NPC – non-pregnant controls; PC – pregnant controls; HDP – hypertensive disorder of pregnancy; RI – resistive index; PI – pulsatility index; S/D – systolic/diastolic ratio

### Table 5

| Study group | \( N \) | Uterine artery side | Prediastolic notching | \( \chi^2 \) | \( df \) | \( p \) value |
|-------------|--------|---------------------|-----------------------|-----------|--------|-------------|
| NPC group   | 80     | Right uterine artery| Present: 14 (17.5%) Absent: 66 (82.5%) | 73.117    | 1      | <0.001      |
| PC group    | 80     | Right uterine artery| Present: 0 (0.0%) Absent: 0 (0.0%) | –         | –      | –           |
| HDP group   | 80     | Right uterine artery| Present: 15 (18.8%) Absent: 65 (81.2%) | 29.32     | 1      | <0.001      |

NPC – non-pregnant controls; PC – pregnant controls; HDP – hypertensive disorder of pregnancy; \( \chi^2 \) – chi square test statistic

### Table 6

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of RI > 0.66 and prediastolic notching for predicting IUGR are shown in Tab. 6.

## Fig. 2

Triplex ultrasound of the uterine artery in one of the HDP group showing the presence of prediastolic notch (red arrows).
third trimester was 73.68% and the specificity was 97.15%. These findings correspond to our study.

Among the various uterine waveform parameters, prediastolic notch was found to have the highest sensitivity and specificity (50%). Its presence in late pregnancy is an indicator of increased uterine vascular resistance and impaired uterine circulation (12). However, the presence of prediastolic notch could be a normal finding in a non-pregnant uterus and even in a gravid uterus up to 16 weeks gestational age (13). According to some researchers (14,15), the use of prediastolic notch as the definition of abnormality has improved the reliability and predictive value of uterine Doppler studies in pregnancy as per pre-eclampsia and IUGR. The presence of prediastolic notch signals that the uteroplacental circulation is greatly impaired, and indicates the worst prognosis for the fetus (16).

The mean RI in the HDP group was higher than that in the PC group but lower compared to the NPC group (p < 0.001). This is in line with what various researchers documented previously (2,14). The placenta, through implantation and development, modifies the uterine circulation from one characterized by low flow and high resistance to the one showing high flow and low resistance in normal pregnancy (14). The primary defect that predisposes pregnancies to uteroplacental complications appears to be partial or complete failure of trophoblastic invasion (2) in HDP subjects (17), although the reason for this failure is still unclear (14).

The uterine artery waveform in a non-pregnant uterus demonstrates notchig at the beginning of diastole with low flow at the end of diastole because of high resistance to blood flow (thus usually have a high RI). Our findings correspond to this observation, with the NPC group showing the highest mean RI compared to the other groups. Once pregnancy occurs, placental vessels develop, resulting in a low resistance to blood flow with a concomitant increase in the height of the diastolic waveform and increased blood flow to the gravid uterus (14). This is confirmed by the lowest mean RI recorded in normal pregnant subjects (PC group). The 95th percentile of uterine artery RI in the PC group was 0.66, which is the basis of using 0.66 as a cut-off RI value in this study.

Persistent diastolic notch (beyond 24 weeks’ gestation) or abnormal flow velocity ratios have been associated with inadequate trophoblastic invasion in HDP subjects (18). This is reflected in the high RI values in HDP subjects compared to normal pregnant subjects (PC group) in this study and previous studies (2,14).

We found that RI > 0.66 had a sensitivity of 50.0%, specificity of 69.1% and positive predictive value of 22.2% in predicting fetuses at-risk-for IUGR. This corresponds to the findings of Zimmermann et al. (19). During a 20-month period, they (19) studied 175 pregnant women at high risk for hypertensive disorders of pregnancy, and 172 low-risk patients in a prospective cross-sectional trial. They found that persistent notches in the main stem uterine arteries and elevated resistance indices of > 0.68 in the uterine arteries and > 0.38 in the uteroplacental arteries defined abnormal waveforms.

The PI in the HDP group in this study was notably higher compared to the PC group (Tab. 2). This is similar to some researchers’ findings that an increase in flow resistance as measured by PI or RI greater than a chosen value (1.45 or 0.58, respectively) or the presence of unilateral or bilateral diastolic notches have been considered abnormal for pregnant uterus (20,21). The primary importance of prediastolic notchig was further emphasized by a longitudinal study (22) which evaluated Doppler indices in the first trimester (at 11–13 weeks gestational age) and followed up the subjects clinically until a week after delivery. Aworinde et al. (22) found that the positive predictive value (PPV) of PI for the development of hypertension in pregnancy was 12%; the PPV of RI for development of hypertension in pregnancy was 11% while the PPV of early diastolic notchig for the development of hypertension in pregnancy was 35%.

In conclusion, uterine artery Doppler ultrasound is invaluable in predicting fetuses at risk for IUGR in the clinical setting of established HDP. The presence of prediastolic notchig is significantly more sensitive and specific than uterine artery resistance index for this purpose.

**Conflict of interest**

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

| RI > 0.66 | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Odd ratio | 95% CI |
|-----------|----------------|----------------|---------|---------|-----------|-------|
| Prediastolic notch | 50.0 | 69.1 | 22.2 | 88.7 | 2.2 | 0.6–7.8 |

Tab. 6. Predictability of intrauterine growth restriction in the hypertensive disease of pregnancy group using RI and prediastolic notchig
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