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Uterine artery Doppler velocimetry in hypertensive disorder of pregnancy in Nigeria

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

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.

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-

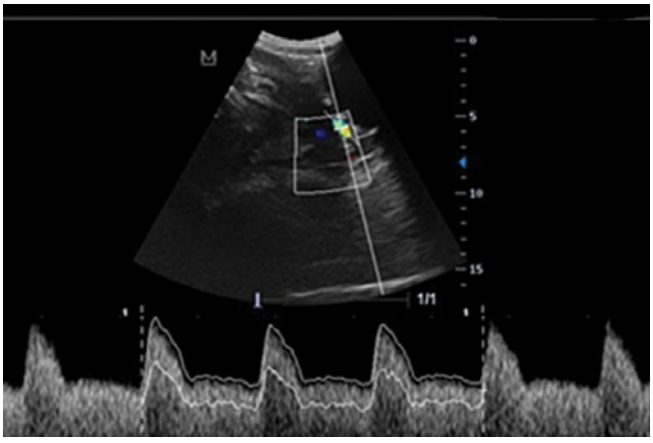

Fig. 1. *Triplex ultrasound image showing the uterine artery Doppler waveform in normal pregnancy.*

sonable to surmise that the effect(s) of HDP on the fetus could be predicted and/or monitored using this technique. Uterine artery Doppler parameters, namely the resistivity index (RI), pulsatility index (PI) and systolic/diastolic (S/D) ratio are reportedly more sensitive and specific than umbilical artery Doppler parameters in fetal monitoring[5–7]. The aim of this study is to evaluate the usefulness of maternal uterine artery Doppler parameters in HDP subjects for predicting those fetuses that are likely to develop IUGR in our environment.

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 postmenopausal 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).

Doppler ultrasound assessments were performed at 20–24 weeks gestational age before 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 1cm distal to the crossover point[8]. This point was chosen after a pilot study showed that it is more easily reproducible.

The pulsed Doppler gate was placed in the middle of the vessel and the signal was updated until three similar consecutive waveforms were obtained. It was ensured in all cases that the angle of insonation was less than 60^0. The RI, PI and S/D ratio of the uterine arteries were measured using autotrace (Fig. 1). These measurements were taken 3 times by the first author and then averaged. The presence or absence of prediastolic notching was noted.

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 ≤ 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

Variables	NPC	PC	HDP	χ2	*df*	*p* value
	n = 80	*n* = 80	*n* = 80			
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			
***n* (%)**						
<25	9 (11.2)	8 (10.0)	6 (7.5)	8.818	8	0.358
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

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

Tab. 1. *Demographic characteristics of subjects*

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

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

groups were all statistically significant ($p < 0.001$; 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 ($p < 0.001$, 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 10th percentile and thus were at high risk for IUGR; the remaining 68 had their EFW above the 10th percentile. The uterine artery mean RI was significantly

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	119.05	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. 3. *Comparison of uterine artery Doppler parameters across the 3 groups**

Variables	*p* value		
	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

Tab. 4. *Scheffe post-hoc analyses for the differences in Doppler parameters between 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 ($p < 0.001$).

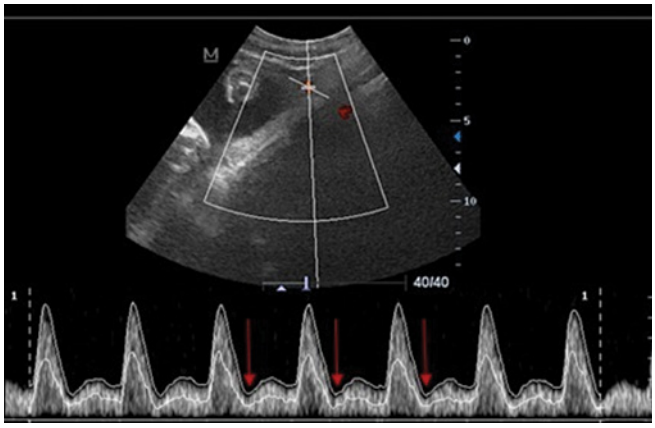

Fig. 2. *Triplex ultrasound of the uterine artery in one of the HDP group showing the presence of prediastolic notch (red arrows).*

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 (PPV) 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

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

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

Tab. 5. *Comparison of uterine artery prediastolic notching among the three study groups*

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Odd ratio	95% CI
RI >0,66	50.0	69.1	22.2	88.7	2.2	0.6–7.8
Prediastolic notching	100.0	96.0	80.0	100.0	22.7	7.5–68.5
RI – resistive index; PPV – positive predictive value; NPV – negative predictive value; CI – confidence interval						

Tab. 6. *Predictability of intrauterine growth restriction in the hypertenive disease of pregnancy group using RI and prediastolic notching*

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[5]. 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 notching 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 notching 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 the 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 notching 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 notching 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 notching 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 notching 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.

References

1. Ebeigbe P, Aziken M: Early onset pregnancy-induced hypertension/eclampsia in Benin City, Nigeria. Niger J Clin Pract 2010; 13: 388–393.
2. Khong TY, De Wolf F, Robertson WB, Brosens I: Inadequate maternal vascular response to placentation in pregnancies complicated by pre-eclampsia and by small-for-gestational age infants. Br J Obstet Gynaecol 1986; 93: 1049–1059.
3. Program NHBPE: Report of the national high blood pressure education program working group on high blood pressure in pregnancy. Am J Obstet Gynecol 2000; 183(1): S1–S22.
4. Singh S, Ahmed EB, Egondu SC, Ikechukwu NE: Hypertensive disorders in pregnancy among pregnant women in a Nigerian Teaching Hospital. Niger Med J 2014; 55: 384–388.
5. Lakhkar BN, Ahamed SA: Doppler velocimetry of uterine and umbilical arteries during pregnancy. Indian J Radiol Imaging 1999; 9: 119–125.
6. Law TL, Korte JE, Katikaneni LD, Wagner CL, Ebeling MD, Newman RB: Ultrasound assessment of intrauterine growth restriction: relationship to neonatal body composition. Am J Obstet Gynecol 2011; 205: 255.e1–255.e6.
7. Platz E, Newman R: Diagnosis of IUGR: Traditional Biometry. Seminars in Perinatology 2008; 32:140–147.
8. Gómez O, Figueras F, Fernández S, Bennasar M, Martínez JM, Puerto B *et al.*: Reference ranges for uterine artery mean pulsatility index at 11–41 weeks of gestation. Ultrasound Obstet Gynecol 2008; 32: 128–132.
9. Steel SA, Pearce JM, Chamberlain G: Doppler ultrasound of the uteroplacental circulation as a screening test for severe pre-eclampsia with intra-uterine growth retardation. Eur J Obstet Gynecol Reprod Biol 1988; 28: 279–287.
10. Audibert F, Benchimol Y, Benattar C, Champagne C, Frydman R: Prediction of preeclampsia or intrauterine growth restriction by second trimester serum screening and uterine Doppler velocimetry. Fetal Diagn Ther 2005; 20: 48–53.
11. Sieroszewski P, Guzowski G: [Prognostic value of the uterine doppler velocimetry at 20–24 gestation weeks for PIH and IUGR development in pregnancy]. Ginekol Pol 2005; 76: 348–357.
12. Ochi H, Matsubara K, Kusanagi Y, Taniguchi H, Ito M: Significance of a diastolic notch in the uterine artery flow velocity waveform induced by uterine embolisation in the pregnant ewe. Int J Obstet Gynaecol 1998; 105: 1118–1121.
13. Bashir O, Weerakkody Y: Uterine artery flow notching. Available from: http://radiopaedia.org/articles/uterine-artery-flow-notching.
14. Harrington K, Cooper D, Lees C, Hecher K, Campbell S: Doppler ultrasound of the uterine arteries: the importance of bilateral notching in the prediction of pre-eclampsia, placental abruption or delivery of a small-for-gestational-age baby. Ultrasound Obstet Gynecol 1996; 7: 182–188.
15. Fleischer A, Schulman H, Farmakides G, Bracelo M, Grunfeld L,Rolchelson B *et al.*: Uterine artery Doppler velocimetry in pregnant women with hypertension. Am J Obstet Gynecol 1986; 154: 806–813.
16. Thaler I, Weiner Z, Itskovitz J: Systolic or diastolic notch in uterine artery blood flow velocity waveforms in hypertensive pregnant patients: relationship to outcome. Obstet Gynecol 1992; 80: 277–282.
17. Shanklin DR, Sibai BM: Ultrastructural aspects of preeclampsia. I. Placental bed and uterine boundary vessels. Am J Obstet Gynecol 1989; 161: 735–741.
18. Cnossen JS, Morris RK, ter Riet G, Mol BW, van der Post JA, Coomarasamy A *et al.*: Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis. CMAJ 2008; 178: 701–711.
19. Zimmermann P, Eiriö V, Koskinen J, Kujansuu E, Ranta T: Doppler assessment of the uterine and uteroplacental circulation in the second trimester in pregnancies at high risk for pre-eclampsia and/or intrauterine growth retardation: comparison and correlation between different Doppler parameters. Ultrasound Obstet Gynecol 1997; 9: 330–338.
20. Zhong Y, Tuuli M, Odibo AO: First-trimester assessment of placenta function and the prediction of preeclampsia and intrauterine growth restriction. Prenat Diagn 2010; 30: 293–308.
21. Chappell L, Bewley S: Pre-eclamptic toxaemia: the role of uterine artery Doppler. Br J Obstet Gynecol 1998; 105: 379–382.
22. Aworinde O, Ayoola O, Loto O, Olufemi-Aworinde K, Idowu M, Adeniji AO *et al.*: First trimester prediction of hypertensive disorders in pregnancy using Doppler ultrasonography in an African population. Int J Pharm Res Health Sci 2015; 3: 886–890.