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Original Article

Comparative study of uterine and umbilical artery Doppler and pregnancy risk status in predicting adverse pregnancy outcome

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ABSTRACT

Background: The rising rate of adverse pregnancy outcomes, particularly in low-and middle-income countries, calls for simple, accurate diagnostic tools to avert the associated high morbidity and mortality. **Objective**: To determine the relationship of uterine/umbilicalDoppler ultrasound with adverse pregnancy outcomes and high-risk pregnancies(HRP). To compare the predictive efficacy of uteroplacental versus pregnancy risk status in predicting adverse pregnancy outcomes. **Materials and Methods**: This was a comparative longitudinal study of the uterine and umbilical Doppler and pregnancy outcomes among cohorts of HRP and normal pregnancies (NPs). The data was analyzed by IBM SPSS version 23.0. The student t-test and Chi-square tested association Doppler parameters and; adverse pregnancy outcomes and pregnancy outcomes. Multiple regression analysis assessed the best predictor of adverse pregnancy outcomes. Pvalues <0.05 were statistically significant. **Results**: Uterine end-diastolic volume (EDV) was 15.9±8.59cm/s and 29.8± 15.9cm/s (p=0.014), whilst umbilical EDV=19.1± 8.59cm/s and 35.2±13.6cm/s (p=0.016) in adverse pregnancy outcome and normal outcome cases respectively. Uterine artery resistance index(RI=0.57 ± 0.14), pulsatility index (PI=1.23 ± 0.68) and S/D ratio (S/D=2.56 ± 0.97). Similar Doppler parameters of low EDV and high RI, PI, and S/D were recorded in women with adverse pregnancy outcomes in the umbilical arteries. In HRP, the uterine and umbilical artery PI, RI, and S/D were higher than in NPs (P-value<0.05). The uterine PI independently predicted adverse pregnancy outcome in 76.5 % (AUC 95% CI: 0.693; 0.837, p<0.001). While the combination of uterine PI and HRP status predicted adverse pregnancy outcomes in 80.1% (AUC 95% CI: 0.735; 0.867, p<0.001). **Conclusion**: High Doppler impedance to blood flow and low diastolic flow occur in both uterine

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and umbilical arteries, in pregnancies with adverse outcomes and high-risk pregnancies. Uterine PI independently predicts adverse outcomes in pregnancy. **Keywords**: Uterine, Umbilical, Doppler Ultrasound, High-risk pregnancy, Pregnancy outcome.

Introduction

Adverse pregnancy outcome has become a serious public health issue globally, especially in low- and middle-income countries. More than eight hundred women die each day from pregnancy and childbirth complications, with an additional twenty suffering serious injuries, infections, or disabilities.[1] Worldwide, 15 million premature babies are born each year, of which more than a million die immediately after birth, while many others suffer from lifelong disabilities.[2] Pregnancies with maternal or fetal complications or any other complications peculiar to pregnancy are at "high risk" of having adverse pregnancy outcomes with associated perinatal mortality and morbidity of about 75%.[3]

Efforts in recent times have been geared towards specialized obstetric care to ensure the best outcome for mother and child through early detection and prompt treatment of high-risk pregnancy, thereby preventing maternal and fetal morbidity and mortality.[4,5]

Despite recent advances in antenatal care, maternal and fetal complications like pre-eclampsia, eclampsia, fetal growth restriction, and other placenta abnormalities remain part of the major causes of adverse pregnancy outcomes.[6,7] Therefore, there is a need for a more robust strategy for early screening of high-risk pregnancies to avert adverse pregnancy outcomes. In a developing country like Nigeria, the commonly used categorization of pregnancy into low or high risk is based on maternal factors. These factors such as body mass index, mean arterial pressure, and previous medical history do not sufficiently reflect the variety of risk that exists for all pregnant women or consider the limited clinical value of current strategies for the prediction of obstetric risk in some subgroups of pregnant women.[8]

In the last four decades, Doppler techniques have been the focus of interest and research in obstetrics. From current literature, obstetric Doppler evaluation reflects signs of fetal compromise and adverse fetal outcomes earlier than clinical evaluation.[9] Obstetric Doppler can identify adverse pregnancy outcomes from an array of clinical complications attributable to chronic placental disease.[10] However, there is an inconsistent report on the Doppler parameters to be measured and the general role of Doppler ultrasound in predicting pregnancy outcome.[11-14] Recent studies have reported that a multi-parametric test combining multiple biomarkers may be more suitable than any single test for identifying high-risk pregnancy.[13,15-17]

The commonly used Doppler parameters in obstetric include the Uterine and Umbilical artery blood flow; the End diastolic volume (EDV) and Peak systolic volume (PSV), as well as the impedance parameters; resistivity index (RI), Pulsatility index (PI), and Systolic to Diastolic ratio (S/D).[18]

In addition to evaluating the role of the doppler parameter in predicting pregnancy outcome, this study aims to examine the value of combining obstetrics Doppler velocimetry and maternal characteristics in the prediction of pregnancy outcome.

Materials and Methods

This was a hospital-based comparative longitudinal clinical study involving singleton gestation pregnancies recruited at the antenatal clinic and the booking clinic of the Obstetrics and Gynecology department of our institution. The participants were subdivided into High-Risk Pregnancy (HRP) patients and Normal Pregnancy (NP) patients. We evaluated the uterine and umbilical arteries and

pregnancy outcomes in all participants.

The Oyo State Research Ethical Review Committee, Department of Planning, Research and Statistics, Ministry of Health Oyo State, approved the study (Approval number AD 13/479/701).

Recruitment of subjects who fulfilled the inclusion criteria was done by an experienced obstetrician and gynecologist and trained nursing staff from the antenatal clinic of our institution, from April 2015 to October 2015, and participants followed up till April 2016, when all recruited subjects had delivered. This study was a continuation of a previously published study that evaluated preeclampsia cases.[19]

Participation in this study was completely voluntary after a written informed consent following a detailed explanation of the intents and purpose of the study and interpretation in local dialects in appropriate cases. Participants were free to discontinue the study at any time, which did not affect the participants' care, as every pregnant woman had the standard care according to the hospital management protocol.

A previous pilot study showed that four to five HRP cases were seen per week, giving a total of eighty-four to one hundred and thirty patients. Using the sample size calculation; $n = N^* X/(X+N - 1)$ where $X = Z_{\alpha/2}^{2} * p*(1-p)/e^2$ and $Z_{\alpha/2}$ is 1.96 at confidence level of 95%, α is 0.05, e = significance level (0.05), *P* is sample proportion and N, the population size.[20] The minimum sample size was, therefore, 82-98 cases. However, because of possible non-responders, a non-probability sampling method was adopted for the study to include all consecutive consenting participants with high-risk pregnancies and normal pregnancies recruited during the study period. All subjects were followed up till delivery/ termination of pregnancy.

Inclusion criteria

a) **High-Risk Pregnancy**: Singleton pregnant women with pre-existing hypertension, diabetes mellitus, kidney disease, heart disease, previous intra-uterine growth restriction, elderly primigravidas, previous PE, hemoglobinopathies, and human immune deficiency syndrome.

ii) **Normal Pregnancies**: Singleton pregnancies without any of the conditions mentioned above

Exclusion criteria

All cases of multiple pregnancies, fetal malformations, and unknown last menstrual period without early dating scans.

a) **Clinical Evaluation**: All consenting pregnant women that fit into the inclusion criteria had their socio-demographics, obstetric parameters, and history of high-risk factors documented for each patient. Adverse pregnancy outcomes evaluated in this study were: Abortion (Expulsion of a product of conception before 28 completed weeks), stillbirth, preterm birth(before 37 completed weeks of gestation), and Low birth weight (<2.5kg).

b) **Ultrasonography evaluation:** The sonographic evaluation was done with a GENERAL ELECTRIC LOGIQ P5 ultrasound scanner machine with a curved array 3.5 -5.0 MHz trans-abdominal transducer. All subjects had an initial obstetric ultrasound scan to confirm pregnancy date with the last menstrual period date, document obstetric biometry, number of fetuses to exclude multiple gestations, and any fetal anomaly. All recruited participants had uterine and fetal umbilical arteries Doppler interrogation at the second trimester (2224 weeks) and third trimester (3234 weeks) periods. Some HRP had more frequent Obstetric Doppler to monitor fetal wellbeing.

c) **Uterine artery Doppler**: All participants were scanned in a semi-recumbent position with a slight lateral tilt, and the abdomen exposed from the xiphisternum to the pelvic hairline. Ultrasound gel was applied to the abdomen to exclude air from the transducer and abdominal wall interface. An obstetric Ultrasound was

first performed and followed by a Doppler study. The transducer was placed longitudinally in the lower lateral quadrant of the abdomen with slight medial angulation and using the color Doppler. The uterine artery was identified as it crosses the external iliac artery.[21] The Pulsed wave Doppler was applied with the wall filter set at 5060 Hz, angle of insonation was below 20°, and a gate size of 2 mm was placed over the uterine artery at about 1 cm below the crossover point[21] of the uterine artery and the external iliac artery to generate the spectral wave pattern.

d) **Umbilical artery Doppler**: after locating a free loop of the cord at a time when there is no fetal movement or uterine contraction. The color and pulsed wave Doppler interrogation of the umbilical artery generated the spectral waveform following the technique of Bramham et al.,[21] and the International Society of Ultrasound in Obstetrics and Gynaecology.[22]

For both the uterine and umbilical arteries spectral waveform analysis, we employed automatic tracing. At the same time, manual tracing of the waveforms was also done in appropriate cases to generate the Doppler parameters. The mean values of three consecutive waveforms were recorded for each Doppler parameter measured.

The Doppler parameters recorded for each participant includes peak systolic velocity (PSV), end-diastolic velocity (EDV), RI, PI, and the systolic-diastolic ratio (S/D).

All subjects were monitored until delivery or termination of pregnancy to assess the pregnancy outcome.

Data analysis

Demographic variables were summarized and tabulated. All data were analyzed using the IBM SPSS Statistical Package for the social sciences) statistics for windows, version 23.0 (IBM Corp., Armonk, NY: USA), and frequency distributions generated with appropriate graphs and tables. Chi-square was used to test the association between pregnancy risk status and pregnancy outcomes. We employed the student t-test to test the association between Doppler parameters and adverse pregnancy outcomes. The Doppler parameter that best predicts pregnancy outcomes was assessed using multiple regression analysis. Pregnancy type, the uterine and umbilical artery Doppler, and the combination of pregnancy type and uterine/ umbilical Doppler were evaluated by receiver operator curve to determine their predictability of adverse pregnancy outcomes. P values <0.05 were statistically significant in this study.

Result

A total of one hundred and ninety pregnant women were recruited in this study and followed till delivery. The mean age of the pregnant women was 31.5 ± 4.38 years. Most of the women (40.0%) were within the age group 30 to 34 years. Seventy-three (38.4%) of the pregnant women were nulliparous. More than half (58.4%) of the pregnant women were in the third trimester of pregnancy. Eighty-seven (45.8%) of the pregnant women were classified as a high-risk pregnancies. Table 1

Among all study participants, there were adverse pregnancy outcomes in 75 (39.5%) cases, while 115(60.5%) had normal pregnancy outcomes. Among women with adverse pregnancy outcomes, 61 (81.3%) had low birth weight, 48 (64.0%) had a preterm delivery, and 5 (6.7%) had a stillbirth (Figure 1).

Relationship Between Uterine and Umbilical Artery Doppler Parameters and Pregnancy Outcome

Table 2 shows the Relationship between Uterine and Umbilical Doppler velocimetry parameters and pregnancy outcomes. The women with adverse pregnancy outcomes had significant lower Uterine and Umbilical artery EDV (29.8± 15.9 cm/s), (15.9 ± 8.59 cm/s) respectively compared to women with normal pregnancy outcome with EDV of (35.2 ± 13.6 cm/s) ($p = 0.014$)., (19.1 ± 8.59 cm/s) $p=0.016$ respectively. Higher significant mean Uterine artery RI(0.57 ± 0.14) PI(1.23

± 0.68) and S/D(2.56 ± 0.97) and mean Umbilical artery RI(0.61 ± 0.16)., PI(1.16 ± 0.64), and S/D(3.00 ± 1.49) were observed in women with adverse pregnancy outcome than in women with normal pregnancy outcome that recorded lower mean Uterine artery RI(0.49 ± 0.15) (p =0.001), PI(0.74 ± 0.25) (p<0.001), and S/D(1.90 ± 0.44) (p<0.001) and Umbilical artery RI(0.58 ± 0.11) p = 0.016. PI (0.96 ± 0.38) p = 0.025 and S/D (2.39 ± 0.59) p=0.002

Uterine and Umbilical Artery Doppler in the high risk and normal pregnancy groups

Table 3 showed the Uterine and Umbilical artery Doppler Velocimetry parameters in the Study Population. The mean uterine EDV of women with High-risk pregnancies (29.4 ± 14.4) cm/s (p = 0.001) was significantly lower than the mean EDV of the women with normal pregnancies (36.2 ± 14.4) cm/s. However, there was significantly higher S/D ratio in the HRP (2.47 ± 0.97) compared with normal pregnancy (1.91 ± 0.40) (p < 0.001) The mean uterine RI(0.56 ± 0.14) and PI(1.17 ± 0.66) of women with HRP are significantly higher than the RI (0.49 ± 0.16) (p=0.003). and PI (0.73 ± 0.24) (p <0.001) of women with normal pregnancy. although the uterine PSV was lower in the HRP group compared to the NP, this was not statistically significantly.

Furthermore, there was a statistically significantly higher S/D ratio in the umbilical artery in women with high-risk pregnancies (2.97 ± 1.43) than in the normal pregnancy group (2.36 ± 0.59) (p = 0.001). furthermore, there was a significant higher RI(0.62 ± 0.14) and PI(1.13 ± 0.60) in HRP than in women with NP with RI(0.57 ± 0.12) (p=0.004), and PI(0.96 ± 0.40) (p = 0.035) respectively. The umbilical artery PSV and EDV, however, did not show significant differences in the two groups.

Figure 2 showed that normal spontaneous vaginal delivery was achieved largely in women with normal pregnancies (58.3%) compared to the fewer proportion recorded in High-Risk pregnancy (24.1%), p was <0.001. The high-risk pregnancy (46.4%) cohort also had higher preterm deliveries compared to women with normal pregnancy (8.7%) (p <0.001). Low birth weight was statistically associated with pregnancy status (p <0.001).

Multivariate analysis of Doppler velocimetry, as predictors of pregnancy outcome, among the population studied, show that the mean uterine PI independently predict pregnancy outcome (AOR= 21.2, 95% CI: 7.04; 63.5) p<0.001

The AUC of the mean uterine PI in predicting pregnancy outcome was 0.765 (AUC 95% CI: 0.693; 0.837, p<0.001). When HRP status alone was also used to predict adverse pregnancy outcomes, the AUC rated HRP status high 0.728 (AUC 95% CI: 0.653; 0.802, p<0.001) in predicting pregnancy outcomes. In addition, the combination of the mean uterine PI and HRP pregnancy status was used in predicting pregnancy outcome; the AUC was 0.801 (AUC 95% CI: 0.735; 0.867, p<0.001), as shown in figure 3.

Table 1: Clinico Demographic Characteristics Of The Study Population

CLINICO-DEMOGRAPHIC PARAMETERS	Frequency	Percentage
Age Group (Years)		
Below 25	7	3.7
25 - 29	58	30.5
30 - 34	76	40.0
35 and above	49	25.8
PARITY		
Nulliparous	73	38.4
Primiparous	65	34.2
Multiparous	52	27.4
GRAVIDA		
1	40	21.1
2	82	43.2
>2	68	35.8
GESTATIONAL AGE (WEEKS)		
Second trimester	79	41.6
Third trimester	111	58.4
Pregnancy status		
Normal pregnancy	103	54.2
High Risk	87	45.8

Table 2: Relationship Between Doppler Velocimetry Parameters and Pregnancy Outcome

	Pregnancy outcome		
Variables	**Adverse (Mean ± SD)**	**Normal (Mean ± SD)**	**P-value**
Uterine Artery			
Peak Systolic velocity	64.2 ± 23.0	63.8 ± 22.2	0.897
End Diastolic velocity	29.8± 15.9	35.2 ± 13.6	0.014
Systolic to Diastolic Ratio	2.56 ± 0.97	1.90 ± 0.44	<0.001
Resistive Index	0.57 ± 0.14	0.49 ± 0.15	0.001
Pulsatility Index	1.23 ± 0.68	0.74 ± 0.25	<0.001
Umbilical Artery			
Peak Systolic Volume	39.6 ± 13.2	42.8 ± 11.3	0.086
End Diastolic Volume	15.9 ± 8.59	19.1 ± 8.59	0.016
Systolic to Diastolic Ratio	3.00 ± 1.49	2.39 ± 0.59	0.002
Resistive Index	0.61 ± 0.16	0.58 ± 0.11	0.017
Pulsatility Index	1.16 ± 0.64	0.96 ± 0.38	0.025

SD = Standard deviation.

Table 3: Doppler Velocimetry Parameters in Normal and High-Risk Pregnancy

	Pregnancy outcome		
Variables	**HRP (Mean ± SD)**	**Normal (Mean ± SD)**	**P-value**
Uterine Artery			
Peak Systolic Volume	61.9 ± 20.6	65.6 ± 23.9	0.251
End Diastolic Volume	29.4 ± 14.4	36.2 ± 14.4	0.001
Systolic/Diastolic Ratio	2.47 ± 0.97	1.91 ± 0.40	<0.001
Resistivity Index	0.56 ± 0.14	0.49 ± 0.16	0.003
Pulsatility Index	1.17 ± 0.66	0.73 ± 0.24	<0.001
Umbilical Artery			
Peak Systolic Volume	41.3 ± 13.9	41.8 ± 10.5	0.795
End Diastolic Volume	16.7 ± 9.07	18.9 ± 8.33	0.094
Systolic/ Diastolic Ratio	2.97 ± 1.43	2.36 ± 0.59	0.001
Resistivity Index	0.62 ± 0.14	0.57 ± 0.12	0.004
Pulsatility Index	1.13 ± 0.60	0.96 ± 0.40	0.035

SD = Standard deviation, HRP = High risk pregnancies

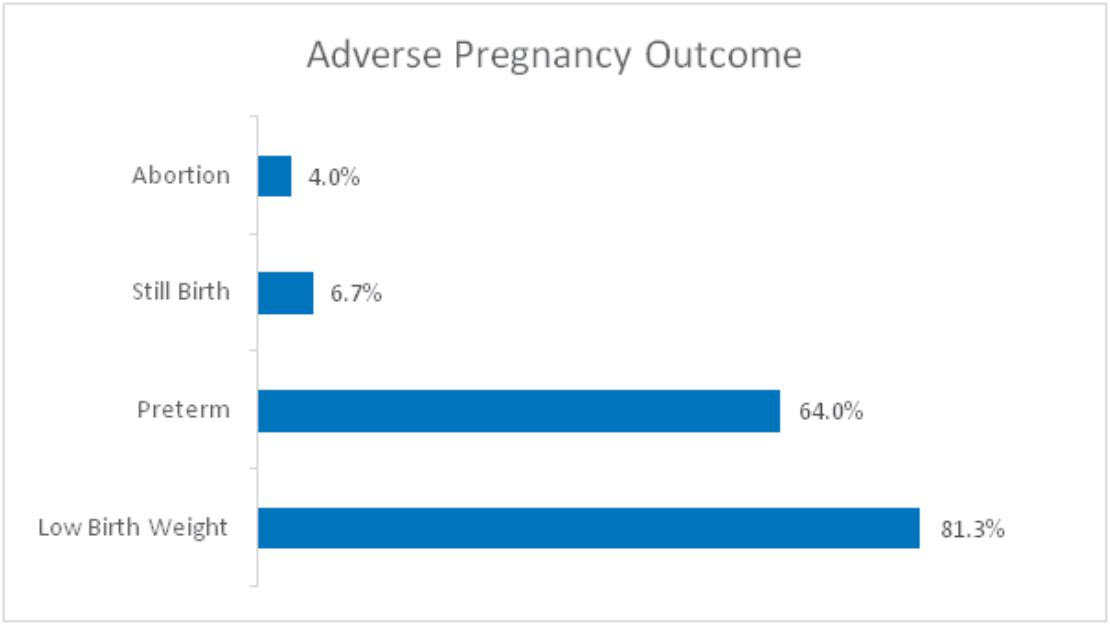

Figure 1: Major adverse pregnancy outcome in the study population

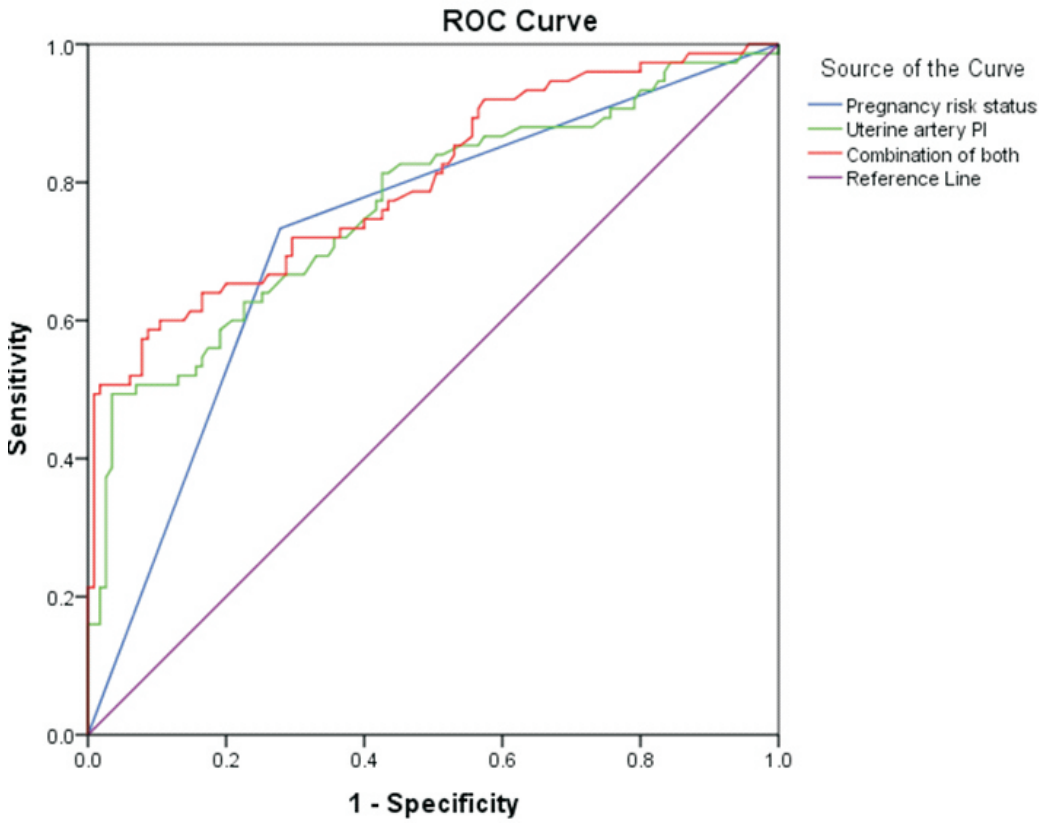

Figure 2: ROC curve showing uterine PI, pregnancy risk status and combination of both in predicting adverse pregnancy outcome.

Discussion

The uterine and umbilical artery flow resistance decreases with advancing gestational age in normal pregnancy, and the presence of a high resistant circulation is associated with an increased risk of adverse pregnancy outcome.[3] Doppler Ultrasound of the Uterine and Umbilical arteries have been used to detect obstetrics complications resulting from uteroplacental insufficiency and situations that may increase the risk of adverse effect on both the mother and the fetus during pregnancy, labour and delivery.[24-27]

Consistent with previous findings,[15,27,28] our study showed that the uterine and umbilical artery SD ratio, PI, RI and EDV values were significantly associated with adverse pregnancy outcomes. Our study's low diastolic flow and high resistance indices are due to the high resistant circulation that might have resulted from defective placenta development.[15,28]

While Jamal et al.[23] and Barati et al.[29] studied the uterine PI and documented its association with adverse pregnancy outcomes. Rabiu and Abubakar[30] and Hazra et al.[31] confirmed that in addition to the uterine artery Doppler parameters, abnormal Umbilical artery Doppler parameters also predict adverse pregnancy outcomes, particularly in the fetus. This suggests that the abnormal hemodynamic changes resulting from maldevelopment at the placental also affect umbilical artery circulation.

Impaired placentation resulting from defective

trophoblastic invasion of the uterine spiral arteries has been said to be responsible for the reduced blood flow and high vascular resistance in HRP such as hypertension in pregnancy, preeclampsia, and intrauterine growth restriction,[18,25] with scientific evidencethat Doppler studies are morebeneficial in high-risk pregnancies in the management of perinatal and neonataloutcomes. Our findings of low EDV but high PI, RI, and S/D among the high-risk pregnancy group compared to the control group agrees with the reports ofHazra et al.[28] This may suggest the same pathophysiologic basis of defective trophoblastic spiral artery invasion in other cases of high-risk pregnancy.

Sieroszewski et al.[31] had a similar result in a study to analyze the use of uterine artery Doppler velocimetry in high-risk pregnancy diagnosis among 530 single normal pregnancies and 80 high-risk pregnancies between 19 and 39 gestation weeks in which the mean uterine PI, RI, and S/D ratio were significantly higher in high-risk pregnancy than in normal pregnancy. Likewise, Arathi et al.[27] in a study to determine the role of color Doppler sonography in evaluating fetal outcome in high-risk pregnancies and normal patients, reported a significantly higher obstetric Doppler value for umbilical S/D ratio and resistivity index (RI) among the high-risk group compared to the control. However, Urmila and Beena[32] showed that there was a significant difference in the uterine artery in the uterine artery only in the mean S/D ratio between the two groups, while in the umbilical artery, there was a significant difference in the mean PI, RI, and S/D ratio between the two groups. This difference may be due to differences in study design and population characteristics.[33,34] However, the association between Doppler parameters and high-risk pregnancies in this study agrees with other studies by Gupta et al. and Farooq et al., that obstetric doppler velocimetry may be useful in detecting pathology in pregnancy.[35,36]

A previous study done by Rabiu and abubakar[30] showed that Women with high-risk pregnancies had higher preterm delivery and abortions than women with normal pregnancies, which agrees with the findings in this current study.

Further analysis in this study showed that the uterine artery PI alone independently predicted pregnancy outcome among all uterine and umbilical artery parameters studied. This implies that an increased uterine artery PI is associated with an increased risk of adverse pregnancy outcomes[31,37] and may be useful in predicting both adverse maternal/and perinatal outcomes in high-risk pregnancy.[38,39] Test of predictor that correlates adverse pregnancy outcomes with the uterine PI and pregnancy risk status showed slightly higher accuracy with uterine PI in predicting adverse pregnancy outcomes than pregnancy status.

In line with previous studies,[13,15,16,40] report that a combination of doppler parameters and maternal clinical characteristics or any other biomarker to predict pregnancy outcomes yields better results than either parameter, findings from our study showed that a combination of pregnancy status and the mean uterine PI for predicting pregnancy outcome had higher accuracy than using either pregnancy status or the mean uterine PI alone as predictors of pregnancy outcomes.

Conclusion

This study showed an inverse relationship between the uterine and umbilical artery diastolic flow but directly links impedance parameters (S/D, RI and PI) and adverse pregnancy outcomes and high-risk pregnancies.

Uterine PI independently predicts adverse pregnancy outcomes. A combination of uterine PI and pregnancy status better predicts adverse pregnancy outcomes.

Conflict of Interest

The authors declare that no conflict of interest exists in this work.

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