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ORIGINAL ARTICLE

Role of venous Doppler evaluation of intrauterine growth retardation

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KEYWORDS

Intrauterine growth restriction;
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Abstract *Aim of the work:* The aim of this work is to determine the role of venous Doppler Ultrasonography for the prediction of adverse perinatal outcome in "intrauterine growth restricted fetus", providing the obstetrician with additional information about the time frame and significance of the IUGR to help determine the optimal time of delivery.
Patients and methods: Sixty pregnant females with their age ranging between 28 and 35 years, gestational age between 27 and 37 weeks of gestation were enrolled in the study. All patients in the study were subjected to Doppler examination of the umbilical vein (UV), Ductus venosus (DV), right hepatic vein (HV) and umbilical artery (UA).
Results: Abnormal UA Doppler was found in 40 patients. Abnormal DV Doppler was found in 40 patients. Abnormal UV Doppler was found in 10 patients. Abnormal Rt. HV Doppler was found in 20 patients. All parameters studied were strongly related to perinatal mortality, however, none had 100% sensitivity, the pulsatility index in the Rt. HV and DV were the best single indices to use in the prediction of perinatal mortality.
Conclusion: We observed that venous Doppler is superior to arterial Doppler in predicting poor perinatal outcome and that the abnormal equivocal BPP scoring significantly correlated with adverse outcome. We also, concluded that multi-vessel Doppler Ultrasonography and BPP can

Abbreviations: UV, umbilical vein; DV, Ductus venosus; HV, hepatic vein; UA, umbilical artery; PI, pulsatility index; IUGR, intrauterine growth retardation; EDV, end diastolic velocity; RF, reversed flow; AEDF, absent end diastolic flow; REDF, reversed end diastolic flow; FGR, fetal growth restriction; A/R, absent or reversed flow; pH, power of hydrogen; BPP, biophysical profile

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effectively stratify IUGR fetuses with placental vascular insufficiency into risk categories. Fetal deterioration appears to be independently reflected in these two testing modalities; their combined use is likely to be complementary.

1. Introduction

Intrauterine growth retardation is a common condition affecting about 10–15% of the general maternity population (1). It is associated with increased risk of intrauterine fetal death, intracranial hemorrhage, respiratory distress syndrome, neonatal lung diseases, necrotizing enterocolitis, chronic cardiovascular disorders, and renal diseases (2). IUGR fetus have a low growth potential as a result of genetic disease or environmental damage, or due to reduced placental perfusion and 'utero-placental insufficiency'; and they are at increased risk of perinatal morbidity and mortality (3). Fetal venous Doppler studies represent valuable diagnostic techniques that can influence the management of intrauterine growth retardation fetus as it helps in identification of the fetus at risk for perinatal complications and help in prediction of neonatal complications (4). Alterations of venous flow volume forms precede fetal heart rate deceleration offering a warning sign to act before a fetal life-threatening situation occurs (5). Doppler assessment of the venous system is important in the surveillance of compromised intrauterine growth restricted fetus (6), as it can improve perinatal mortality and morbidity by optimizing timing of delivery (7).

2. Patients and methods

2.1. Patients

This prospective study was conducted according to the guidelines of the ethics committee of our university and was approved by our institutional review board, all females gave us written informed consent.

This prospective study was done between December 2013 and August 2014 including 60 pregnant females with their age ranging between 28 and 35 years, gestational age between 27 and 37 weeks of gestation (mean 33.02 Weeks), with high risk features, single viable fetus and growth retardation determined by fetal weight less than 10% for gestational age and abdominal circumference less than 5% (2).

2.2. Methods

All patients in the study were subjected to Doppler examination—using 3.5 MHz transducer in a PHILIPS HD11 instrument—of the umbilical vein (UV), Ductus venosus (DV), right hepatic vein (HV) and umbilical artery (UA).

2.3. Umbilical vein examination

The sampling site of the UV is in the intra-abdominal part of the UV. The physiologic UV Doppler pattern shows linear forward flow. Pulsatile flow in the UV including monophasic, biphasic or triphasic pulsations was considered abnormal.

2.4. Ductus venosus examination

The Ductus venosus (DV) could be visualized either in the midsagittal longitudinal plane of the fetal trunk or in an oblique transverse plane through the upper abdomen, Doppler flow spectra were obtained from the DV at its origin from the UV. The flow velocity waveform displays continuous forward flow throughout the cardiac cycle, consisting of 2 surges of velocity peaks, the first corresponding to ventricular systole (S wave) and the second to ventricular diastole (D wave). These are followed by reduction in velocity during atrial systole (a wave). The DV waveforms were considered normal when the pulsatility index (PI) of DV is less than 1 between the 2nd trimester and term, PI more than 1 is an indication of DV dilatation and indicating poor outcome in severe fetal growth retardation. Absence or reversal of flow during atrial contraction (a wave) (deep a wave in the DV) indicates failure of fetal circulatory compensation to supply well oxygenated blood to vital organ.

2.5. Right hepatic vein

HVs were located in a transverse view between DV and right atrium by color Doppler. The right HV waveforms were considered abnormal when PI was elevated above 95% or reverse flow which is considered as an earlier predictor of impending mortality.

2.6. Umbilical artery examination

The Umbilical artery (UA) could be visualized at the midsection of the free loop of the umbilical cord. The UA waveforms were considered abnormal when PI was elevated above the upper limit of gestational age (at 33 weeks, 0.93–1.03) or in the absence or reversal of end-diastolic velocities.

2.7. Statistical analysis

All radiographic findings were compared with operative and pathological data. Statistical analysis was performed using SPSS software package version 16.0 (statistical package for social science TM) and $P < 0.05$ was considered to be statistical significant.

3. Results

This study included sixty patients with clinical high risk features. The median age was 28 years (range 28–35 years), the majority of cases were primigravidae, the mean gestational age was 33.02 (range 27–37 weeks) (Table 1).

Maternal pathology in the study group is presented in Table 2. Idiopathic, pregnancy induced hypertension and preeclampsia were the most common medical disorders.

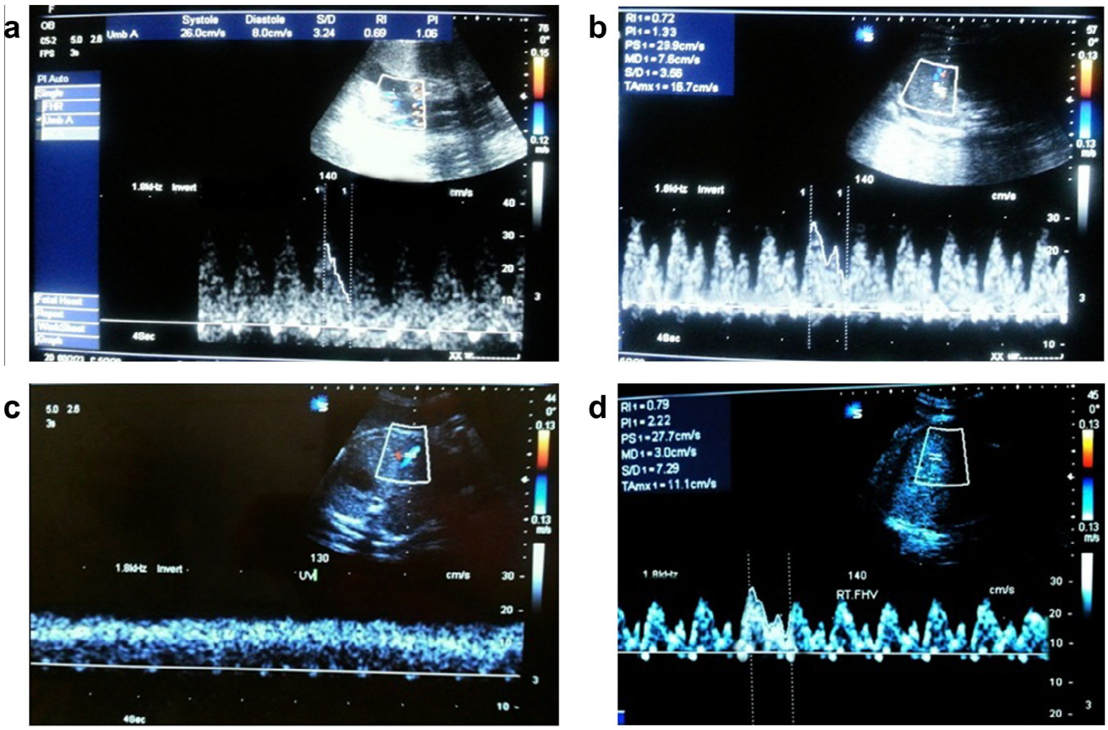

Fig. 1 (a) UA RI: 0.69 (Upper limit = 0.72), UA PI: 1.06 (Upper limit = 1.07), Qualitative evaluation: Normal wave. (b) DV PI: 1.33 (mean 0.45 + 0.19). Qualitative evaluation: abnormal DV wave with decreased flow velocity during atrial contraction (decreased a wave) and increased pulsatility. (c) Qualitative evaluation: normal wave. (d) RT.FHV PI: 2.22, Qualitative evaluation: normal wave. The perinatal outcome: the patient was 25 weeks of gestation, delivery on the next day of examination, the fetus was admitted to the ICU and developed septicemia and was released 3 weeks later.

Table 1 Dermographic data.

	Min	Max	Mean	SD
Age	28	35	28.6	3.62
Parity	0	4	2.65	0.58
GA	27	37	33.02	2.464

Maternal pathology in the study group is presented in Table 2.

Table 2 Maternal pathology in the study group.

	Frequency	%
Pregnancy induced hypertension	16	26.6
Preeclampsia	14	23.3
Idiopathic	18	30
Chronic hypertension	6	10
Diabetes mellitus	4	6.66
Mitral stenosis	2	3.33

Table 3 Doppler study of the umbilical artery.

	Number	%
Normal	20	33.33
High PI	22	36.66
Absence EDF	10	16.66
Reversal EDF	8	13.33
Total	60	100

Table 4 Doppler study of the umbilical vein.

	Number	%
Normal	50	83.33
Monophasic	8	13.33
Triphasic	2	3.33
Total	60	100

The UA-EDF was preserved in 20 patients with normal PI (1.33–1.35), in patients with gestational age 27–28 weeks of gestation (2nd trimester) and 1.16–1.18 in more than 28 weeks of gestation (3rd trimester). It was increased to 3.4–3.6 in intact survivors (7/22 patient), 5.07–5.09 in major morbidity (13/22 patient) and 7.7–7.9 in stillbirth (2/22 patient). UA-AEDF was present in 10 patients and UA-REDF was present in 8 patients (Table 3, Fig. 4).

UV continuous pulsation (normal) was preserved in 50 patients, monophasic pulsation in 8 patients and triphasic in 2 patients. These changes could be in both 2nd and 3rd trimester. Table 4 shows the Doppler characteristics of the umbilical vein.

The Rt. Hepatic vein was normal in 40 patients, high PIV in 14 patients and high PIV with RF in 6 patients. Table 5 shows the Doppler characteristics of the Rt. Hepatic vein.

Table 5 Doppler study of the Rt. Hepatic vein.

	Number	%
Normal	40	66.66
High PIV	14	23.33
High PIV with RF	6	10
Total	60	100

Table 6 Doppler study of the Ductus venosus.

	Number	%
Normal PIV with +ve a-wave (intact survivors)	20	3.33
High PIV with low a-wave		
Major morbidity	10	16.6
Still birth	4	6.6
Absent a-wave	14	23.33
Reversed a-wave	12	20
Total	60	100

The DV-PI was normal (less than 1) with positive a-wave in 20 patients (intact survivors), high PIV (2.44–2.48) with +ve a-wave, in 10 patients (major morbidity), 2.8–3 in 4 patients, absent a-wave was present in 14 patients, reversed a-wave was present in 12 patients. Table 6 shows the Doppler characteristics of the Ductus venosus (see Figs. 1, 2 and 3).

Sensitivity, specificity, PPV and NPV of Doppler in relation to perinatal mortality in fetus with growth restriction are shown in Table 7.

A/R EDV of UA had 27% sensitivity and 86% specificity for perinatal death, 14% sensitivity and 86.4% specificity for neonatal death, 10.8% sensitivity and 92.1% specificity for NICU admission and 17.6% sensitivity and 86.2% specificity for acidosis of cord blood while A/R DV a-wave had 63.3% sensitivity and 98.7% specificity for perinatal death, 27% sensitivity and 92% specificity for neonatal death, 18.4% sensitivity and 97% specificity for NICU admission and 37.1% sensitivity and 95.3% specificity for acidosis of cord blood. A/R DV a-wave showed more sensitivity and specificity for prediction of poor perinatal outcome when compared with A/R EDV of UA (see Table 8).

In cases with BPP 4, the mean UA-PI was 3.34, the mean DV-PI was 1.402, the mean Rt. HV-PI was 3.91 and UV showed 6 patients with monophasic pulsation and two patients with triphasic pulsation. In cases with BPP 6, the mean UA-PI was 2.816, the mean DV-PI was 1.01, the mean Rt. HV-PI was 3.49 and UV showed two patients with monophasic pulsation. While in cases with BPP 8, the mean UA-PI was 1.774, the mean DV-PI was 0.814, the mean Rt. HV-PI was 2.33 and UV Doppler showed normal continuous pulsation. The mean UA-PI, Rt HV-PI and UV pulsation were significantly different between cases of normal and abnormal BPP ($P < 0.05$), while the mean DV-PI showed a high significant difference ($P < 0.01$) (Table 9).

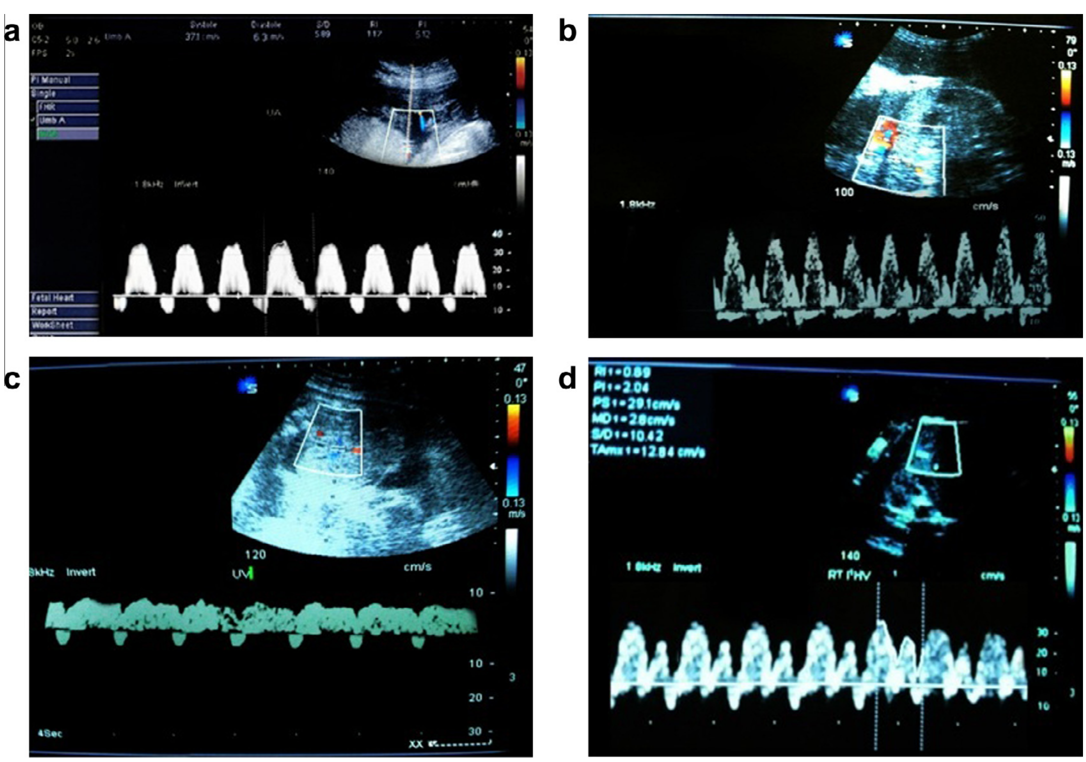

Fig. 2 (a) UA RI: 1.17 (Upper limit = 0.7), UA PI: 5.12 (Upper limit = 1.06), Qualitative evaluation: REDV. (b) Qualitative evaluation: abnormal DV wave with absent flow velocity during atrial contraction (absent a wave). (c) Qualitative evaluation: abnormal umbilical venous flow, triphasic pulsation. (d) Rt. HV PI: 2.04, Qualitative evaluation: normal wave. The perinatal outcome: delivery on the 30 weeks of gestation, stillbirth.

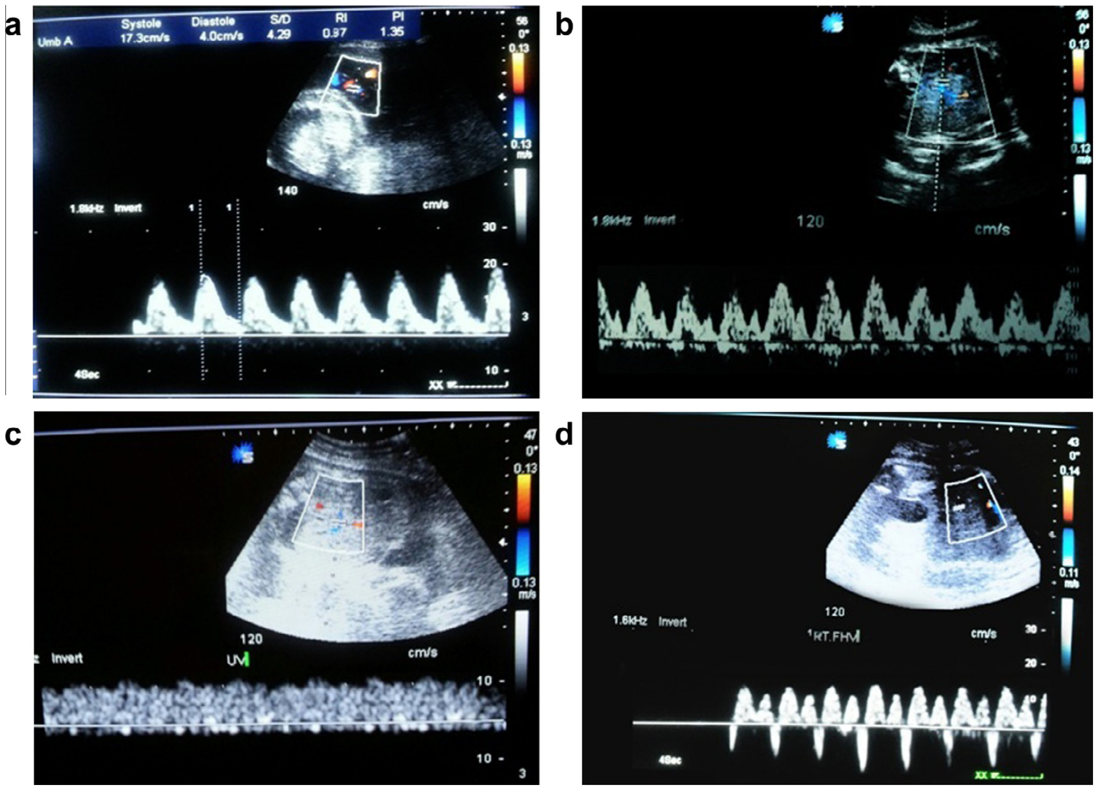

Fig. 3 (a) UA RI: 0.97 (Mean = 0.6, Upper limit = 0.7), UA PI: 1.35 (Mean = 0.98, Upper limit = 1.06). Qualitative evaluation: increased umbilical pulsatility and resistivity but forward velocity. (b) Qualitative evaluation: abnormal DV wave with absent flow velocity during atrial contraction (absent a wave). (c) Qualitative evaluation: normal wave. (d) Qualitative evaluation: there is a considerable increase in reverse velocities during atrial contraction which exceeds forward velocities during early diastole. The perinatal outcome: delivery on the 35 weeks of gestation, neonatal death after admission to ICU.

Table 7 Sensitivity, specificity, PPV and NPV of Doppler in relation to perinatal mortality in fetus with growth restriction.

	Sensitivity	Specificity	PPV	NPV
UA-PI	58.6	65.3	33.5	89.6
HV-PI	79.6	88.6	63	76
DV-PI	85.1	82	57	70
UV pulsation	76.3	97.2	70	78
HV-RF	79.3	91.8	74	80
A/R DV a-wave	63.3	98.7	81	83

4. Discussion

Fetal venous Doppler studies represent valuable diagnostic techniques that can influence the management on intrauterine growth restricted fetuses as it helps in identification of the fetuses at risk for perinatal complications and helps in prediction of neonatal complications (4). Abnormalities in venous system Doppler waveforms are sensitive tools for the assessment of fetal well-being especially before 32 weeks' gestation, and may help to fine-tune our decision-making concerning time of delivery in affected fetuses. It is a more instantaneous indicator for hemodynamic performance than is the umbilical artery velocity pattern (8). The present study included 30 patients diagnosed with IUGR. All patients in the study underwent uniform antenatal assessment protocol that includes Doppler examination of the UA, UV, DV and Rt. HV. These were conducted either twice weekly or daily according to the severity of the condition and results of the last examination before delivery were analyzed. The main concern in the study was the prediction of perinatal outcome with an objective to identify the sequence of progression of venous Doppler abnormalities from the onset of placental insufficiency in IUGR till the time of delivery. In this study, there was no significant difference in GA at the time of termination in cases of IUGR. Gestational age of the fetus is a critical component of the delivery decision-making process. Baschat et al. (9) reported that gestational age was the most significant determinant of total survival of growth restricted fetuses until 26 weeks, and intact survival until 29 weeks. A single case in the present study was terminated before 28 weeks owing to its non-reassuring Doppler parameters with an unfavorable perinatal outcome and early neonatal death.

The UA-EDF was preserved in 20 patients with normal PI (1.33–1.35), in patients with gestational age 27–28 weeks of gestation (2nd trimester) and 1.16–1.18 in more than 28 weeks of gestation (3rd trimester). It was increased to 3.4–3.6 in intact survivors (7/22 patient), 5.07–5.09 in major morbidity (13/22 patient) and 7.7–7.9 in stillbirth (2/22 patient). UA-AEDF was present in 10 patients and UA-REDF was present in 8 patients.

The DV-PI was normal (less than 1) with positive a-wave in 20 patients (intact survivors), high PIV (2.44–2.48) with +ve

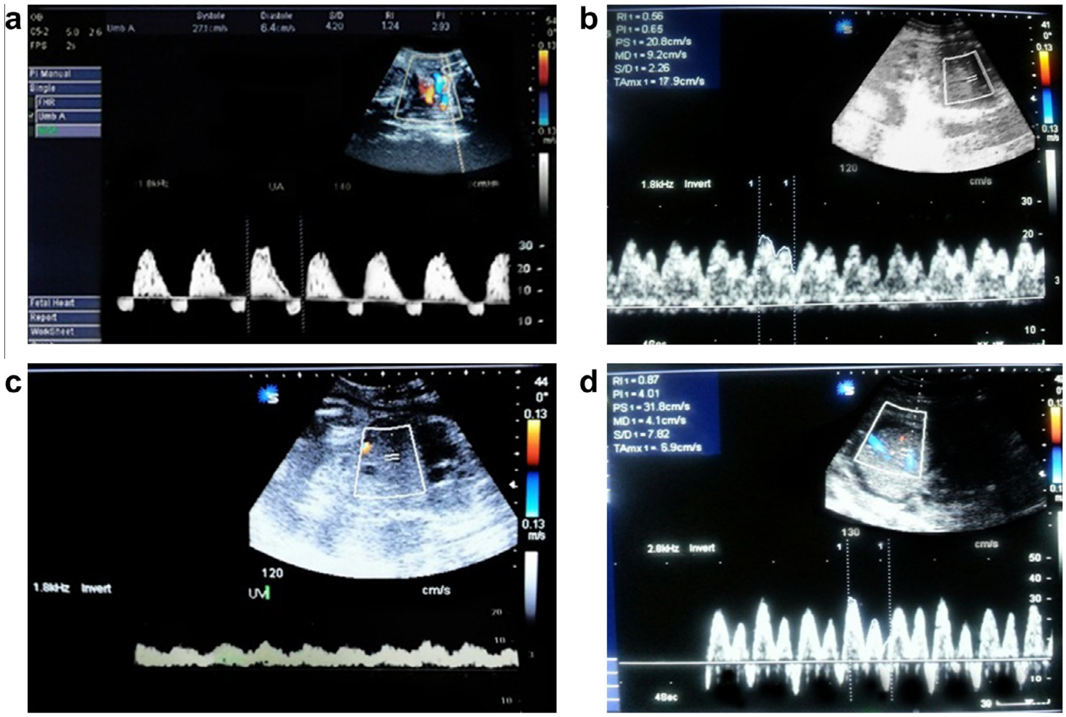

Fig. 4 (a) UA RI: 1.24 (Upper limit = 0.7), UA PI: 2.93 (Upper limit = 1.06), Qualitative evaluation: REDV. (b) DV PI: 0.65 (mean 0.47 + 0.22), Qualitative evaluation: normal wave. (c) Qualitative evaluation: abnormal umbilical venous flow, monophasic pulsation. (d) Rt. HV PI: 4.01, Qualitative evaluation: there is an increase in reverse velocities during atrial contraction with increased pulsatility. The perinatal outcome: delivery on the 27 weeks of gestation, neonatal death during the first week in the ICU.

Table 8 Sensitivity, specificity, PPV and NPV of absent or reverse flow in UA and absent or reverse a-wave in DV for perinatal outcome.

	Sensitivity		Specificity		PPV		NPV	
	A/R DV a-wave	UA-A/R EDV	A/R DV a-wave	UA-A/R EDV	A/R DV a-wave	UA-A/R EDV	A/R DV a-wave	UA-A/R EDV
Perinatal death	63.3	27	98.7	86	81	20	83	95
Neonatal death	27	14	92	86.4	17	5	97	98
NICU admission	18.4	10.8	97	92.1	92	72	96	76
pH <7.2	37.1	17.6	95.3	86.2	34	12	95	78

Table 9 BPP in relation to Doppler.

		UA-PI	DV-PI	Rt-HVPI	UV pulsation
4	Mean	3.344	1.402	3.91	3 monophasic
	SD	0.458	0.605	0.34	1 triphasic
	Min	2.7	0.70	3.24	
	Max	5.1	1.92	4.36	
6	Mean	2.816	1.01	3.49	1 monophasic
	SD	0.84	0.54	0.33	
	Min	1	0.68	3.17	
	Max	3.9	2.09	3.89	
8	Mean	1.774	0.81	2.33	All normal
	SD	0.93	0.30	0.33	
	Min	1	0.66	1.9	
	Max	3.8	2.1	2.92	
t test		3.956	4.526	3.669	2.663
p value		0.024	0.009	0.049	0.017

a-wave in 10 patients (major morbidity), PIV was 2.8–3 in 4 patients, absent a-wave was present in 14 patients, reversed a-wave was present in 12 patients.

Abnormal UV Doppler was found in 10 patients (16.6%); 8 of them showed monophasic pulsation (13.33%) and 2 showed triphasic pulsation (3.33%).

Abnormal Rt. HV Doppler was found in 20 patients (33.3%); 14 of them showed high PI (23.3%) and 6 showed reversal of flow (10%). All parameters studied were strongly related to perinatal mortality, however, none had 100% sensitivity, the PIV in the Rt. HV and DV were the best single indices to use in the prediction of perinatal mortality because they are easy to calculate, DV-PI had 85% sensitivity than HV-PI which had 79% but it had more specificity for detecting perinatal mortality than DV-PI with 88.6% for HV-PI and 82% for DV-PI. The blood velocity waveforms in the HV were slightly better than those in the DV at predicting outcome, a great difference was noted in HV-PI between survivors and non survivors with better significance than DV-PI. By qualitative evaluation, HV-RF followed by pulsations in the UV and a-wave abnormalities in the DV were most sensitive parameters for detection of perinatal mortality with higher PPV value than UA-PI. In the present study, the DV, UV and HV Doppler abnormalities were significantly related to poor outcome parameter and perinatal mortality when compared with abnormal UA Doppler ($p < 0.05$).

Hofstaetter et al. (10) used the same multi-vessel Doppler US in the surveillance of 154 growth restricted fetuses and among the vessels tested HV and DV-PIV were the most useful indices as well as UV pulsations in prediction of perinatal outcome, DV-PI had 82% sensitivity than HV-PI which had 76% sensitivity for detection of perinatal mortality. The blood velocity waveforms in the HV were slightly better than those in DV at predicting outcome and the venous parameters studied were highly related to perinatal outcome which were similar to the results in the present study.

Morris et al. (11) investigated the accuracy of fetal UA Doppler to predict the risk of compromise of fetal/neonatal wellbeing in a high-risk population by a systematic review, concluding that in a high risk population, fetal UA Doppler is a moderately useful test with which to predict mortality and risk of compromise. In the present study, raised UA-PI constituted 55% of the UA abnormality while the extreme end of the spectrum represented by AEDF and REDF constituted 45%, this stratification of abnormalities leads to the UA being reported as insignificantly related to poor perinatal outcome.

The umbilical vein was investigated by Hofstaetter et al. (10), they stated that pulsation in the umbilical venous flow is known to be a characteristic sign of fetal heart failure and imminent asphyxia, double pulsation is known to be a more severe sign of fetal compromise and associated with stillbirth, perinatal and neonatal mortality. In the present study, UV pulsations had a high sensitivity to perinatal mortality with 76.3% sensitivity, the case of stillbirth reported in the study had a triphasic umbilical venous pulsation, results were similar to previous studies.

The Rt. HV was studied by Hecher et al. (12) in which the Rt. HV showed significant differences between the compromised and non-compromised fetuses before 32 weeks and may be due to the fact that the earlier that growth retardation occurs, the more severe is the disease, and, therefore, the more severe are the alterations in the venous circulation. Hofstaetter et al. (10) stated that a compromised fetal state was expressed better in the HV than in the DV as the fetal left ventricle in severely compromised fetuses usually has to work against a lower after load than the right ventricle due to brain sparing in chronic hypoxia. According to the author of that study, the HV was an earlier predictor of impending mortality than the DV. In our study, a high significant difference was noted in the HV-PI ($p + 0.048$) with better specificity of the Rt. HV-PI than DV-PI in predicting perinatal mortality and HV-RF had a higher sensitivity (79%) than A/R DV a-wave (63%) in predicting perinatal mortality which was in accordance with Hofstaetter et al. (10).

Hung et al. (13) study concluded that compared with single vessel assessment, combining the PI of the UA and DV provides greatest accuracy in predicting growth restricted neonates with acidemia.

Baschat et al. (9) stated that abnormal DV-PI proved to be the best predictor of poor neonatal outcome in severe FGR which was in accordance with the present study. Baschat et al. (6) and Schwarze et al. (14) stated that pulsation in the UV followed by waveform abnormalities in the DV was the most sensitive Doppler parameter for identifying fetuses at risk for stillbirth, perinatal or neonatal death and that the most specific parameters with higher positive predictive values regarding adverse perinatal outcomes were abnormal venous Doppler values, which supports the results in the present study. According to the relation between BPP and Doppler study, we found that, the mean UA-PI, Rt. HV-PI, and UV pulsation were significantly different between cases of normal and abnormal BPP (*P* less than 0.05), while the mean DV-PI showed a high significant difference (*P* less than 0.01). Baschat et al. (15), stated that Doppler and biophysical variables are endpoints reflecting different mechanisms of fetal compromise in IUGR, and as such they have the potential for truly complementing each other. Application of biophysical profile scoring to a population of IUGR fetuses that has been preselected by Doppler examination yields good results. One important factor that explains these results is that Doppler and biophysical deterioration can occur independently of each other. This has been previously suggested by Pillai and James (16) based on the concurrent analysis of the umbilical circulation and fetal behavior. Baschat et al. (15), results suggest that even when DV Doppler Ultrasonography is taken into account, Doppler and BPP results appear to be independent. This provides strong evidence that Doppler examination and BPP are complementary antenatal modalities.

5. Conclusion

We observed that venous Doppler is superior to arterial Doppler in predicting poor perinatal outcome and that the abnormal equivocal BPP scoring significantly correlated with adverse outcome. We also, concluded that multi-vessel Doppler Ultrasonography and BPP can effectively stratify IUGR fetuses with placental vascular insufficiency into risk categories. Fetal deterioration appears to be independently reflected in these two testing modalities; their combined use is likely to be complementary.

Conflict of interest

There is no conflict of interest.

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