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FETAL VENOUS DOPPLER VELOCIMETRY: ROLE IN PREDICTION OF PERINATAL OUTCOME IN INTRAUTERINE GROWTH RESTRICTION

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ABSTRACT

Background: Uteroplacental insufficiency is a major cause of perinatal mortality and morbidity in growth-restricted fetuses. Doppler ultrasound effectively measures the changes that sequentially appear in fetal arterial and venous systems and can predict adverse perinatal outcome. Venous changes in Doppler, when monitored, are preterminal events that can help frame delivery decisions in preterm infants. **Objective:** To determine Venous Doppler parameters in Intra uterine growth restricted fetuses (IUGR) and correlate with adverse perinatal outcome. **Methods:** 77 singleton pregnancies beyond 28 weeks of gestation, without fetal anomalies, that had estimated fetal weight below the 10th percentile for gestational age, were examined by Doppler ultrasound to record fetal cerebro-umbilical, Ductus venosus (DV) and umbilical vein (UV) indices. Fetal perinatal outcomes were noted. **Results:** The sensitivity, specificity, positive & negative predictive value of DV PI to predict IUGR in the present study was 58.3%, 100%, 100% & 40.5%. The sensitivity, specificity, positive & negative predictive value of DV PI to predict adverse perinatal outcome was 59.5%, 71.4%, 71.4% & 59.52% respectively. The incidence of IUD & neonatal mortality was higher in cases with abnormal DV PI (26%, 20%) than in cases with normal DV PI (4%, 4%) (p 0.026, 0.016), increasing with appearance of absence or reversal of a-wave in DV. 100% cases with pulsations in UV had intrauterine or perinatal demise. **Conclusion:** Abnormal DV PI and decreased UV velocity is a predictor of adverse perinatal outcome in the setting of abnormal fetal arterial Doppler. These parameters can be monitored in preterm infants to help frame delivery decisions.

KEYWORDS: Ductus venosus, Umbilical vein, Doppler, Intrauterine growth restriction, perinatal mortality, adverse perinatal outcome.

INTRODUCTION

Infants with birth weight below the 10th percentile for gestational age with a pathological restriction of fetal growth are considered as intrauterine growth restricted fetuses (IUGR).[1] The incidence of IUGR is estimated to be between 3 to 7 percent.[2] "Pathologically" small fetuses have a recognizable maternal pathology such as chronic hypertension or advanced-stage diabetes mellitus causing placental insufficiency and abnormal fetal Doppler.[3]

Uteroplacental insufficiency is a major cause of perinatal mortality and morbidity in growth-restricted fetuses. Doppler provides for repetitive non-invasive hemodynamic monitoring of fetal circulation and can reliably predict adverse perinatal outcome in IUGR pregnancy by providing both qualitative waveform analyses and quantitative blood flow measurements.

The Doppler patterns follow a longitudinal trend with early changes in the feto-placental arterial blood vessels. If timely adequate measures are not taken, venous changes appear in the severely compromised fetus. These are strong predictors of poor perinatal outcome and indicate impending irreversible damage.[4]

Absent end-diastolic or reversed flow in the ductus venosus and pulsation in the umbilical vein are less frequent findings in IUGR fetuses than abnormal arterial Doppler waveforms that are associated with a high risk of perinatal death. It seems that the presence of alterations of the venous system could constitute a sufficient and adequate reason to optimize the timing of delivery.[5]

The present study is an attempt to detect and monitor venous Doppler parameters in Intra uterine growth restricted fetuses and predict fetal complications so that they can be prevented by timely intervention.

AIMS AND OBJECTIVES

1) To determine the Doppler indices in fetal arterial and venous circulation in Intrauterine Growth Restricted fetuses.

2) To correlate the Doppler findings with perinatal outcome in Intrauterine Growth Restricted fetuses.
3) To determine the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of Ductus venosus PI for predicting IUGR and adverse perinatal outcome.

MATERIALS AND METHODS

Study Design - Hospital based, Prospective, Observational study

Study population- All pregnant women admitted with singleton pregnancy complicated by intrauterine growth restriction diagnosed clinically and/or on ultrasound, which require further Doppler sonographic evaluation.

Study Period - 18 Months

Sample Size – 77

Inclusion Criteria

1. Singleton pregnancy.
2. Pregnancies with known LMP (Last Menstrual Period).
3. Clinical suspicion of IUGR and/or ultrasonographic estimated fetal weight below the 10th percentile for gestational age.
4. Fetal gestational age beyond 28 weeks.

Exclusion Criteria

1. Multiple pregnancies.
2. Fetal anomalies.

METHODOLOGY

All pregnant female patients fitting the inclusion criteria were selected for the study. After obtaining an informed consent, they were subjected to a detailed history and examination. Routine laboratory investigations like CBC, RBS and urine albumin and sugar were done in all cases to look for maternal anemia and diabetic status. Fetal morphometric parameters, placental status, AFI (Amniotic Fluid Index) were recorded in each case. During examination, patient was in semirecumbent position and fetus was in quiet, resting state. A preliminary Doppler velocimetry evaluation was done in all cases on Phillips iu22 machine using 3.5 MHz curvilinear probe and low pass filter, keeping the power output at the minimum level. Subsequent Doppler evaluations were individualised. USG and Doppler findings last done were considered for evaluation of pregnancy outcome. Follow up was done to see perinatal outcome (till 7 days of life).

Statistical Analysis: Analysis was done using SPSS software (version 20). Descriptive data was presented as Mean ± Standard Deviation and percentages. Data was tabulated and Chi square test was done to asses association among categorical parameters. Sensitivity and specificity were calculated to see the accuracy of predicting variables like perinatal outcome. For all statistical analysis, $p<0.05$ was considered statistically significant.

RESULTS

The age of patients observed in the study ranged from 18 to 40 years. Maximum number of patients belonged to 21- 25 years age group. Mean age of the patients was 24.76 ± 3.73years. 37% of patients were primigravida and 63% of the patients were multigravida. Most patients (52%) delivered between 34 to 36 weeks. Mean gestational age at the time of delivery was 35.04 ± 2.26weeks. Birth weight of <1kg was present in 9 cases (12%), 19 cases (25%) had B. wt ≥ 1 kg but <1.5 kg, 32 cases (41%) had B.wt ≥1.5 but <2 kg & rest of the 17 cases (22%) had B.wt ≥2kg but <2.5 kg. Mean birth weight was found to be 1564.5 ± 459.88g. Of the 77 cases, 60 were proven to be IUGR as they had abnormal Doppler velocimetry in one or more feto-placental vessels, while 17 were seen to be SGA (small for gestational age) as they had normal Doppler values on USG.

Table 1: Sensitivity, specificity, PPV and NPV of Ductus Venosus (DV) PI to predict IUGR.

Fetus	IUGR (n=60)	SGA (n=17)
DV PI AbN (n=35)	35	0
DV PI N (n=42)	25	17
Sensitivity= [25/(25+35)] x 100 = 58.3%		
Specificity= [17/(0+17)] x 100 =100%		
Positive predictive value (PPV)= [25/(25+0)] x 100 =100%		
Negative predictive value (NPV)= [17/(35+17)] x 100 =40.5%		

Table 2: Sensitivity, specificity, PPV and NPV of Ductus Venosus (DV) PI to predict adverse perinatal outcome

IUGR	Adverse perinatal outcome present (n=42)	Adverse perinatal outcome absent (n=35)
DV PI AbN (n=35)	25	10
DV PI N (n=42)	17	25
Sensitivity= [25/(25+17)] x 100 = 59.5%		
Specificity= [25/(10+25)] x 100 = 71.4%		
Positive predictive value (PPV)= [25/(25+10)] x 100 = 71.4%		
Negative predictive value (NPV)= [25/(17+25)] x 100 = 59.5%		

Table 3: Perinatal outcome in IUGR(n=60) in relation to Ductus Venosus (DV) PI

Perinatal outcome	DV Pulsatility index (PI)		*P* value (Chi Square test)
Parameters	**1 DV PI N* (n=25, 42%)**	**2 DV PI Abn* (n=35, 58%)**	
a) Fetal distress (n=13)	4	9	0.314
b) IUD (n=10)	1	9	0.026
c) AS <7 at 5 min (n=7)	3	4	0.112
d) Resuscitation (n=7)	2	5	0.045
e)Respiratory distress at birth (n=28)	14	14	0.020
f) Acidemia(Cord ph<7.2) (n=25) [Of this Cord ph<7 (n=7)]	10 [2]	15 [5]	0.004
g) Increased duration(>7d) of hospital stay (n=12)	5	7	0.012
h) Early neonatal Mortality (<7d) (n=8)	1	7	0.016
i) Adverse outcome† (n=42)	17	25	0.006

** DV PI of > 2 S.D. was taken as abnormal [6]*

†Usually a case had more than one adverse outcome. Postnatal outcomes after exclusion of IUD.

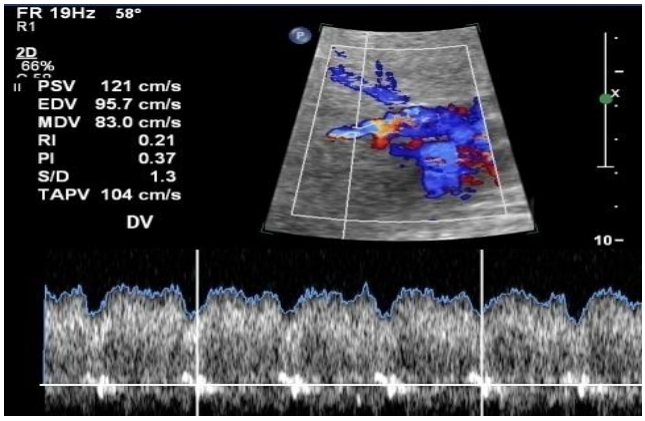

Fig 1. Normal Ductus venosus showing aliasing effect with forward antegrade flow through cardiac cycle seen in waveform. Three antegrade waves are seen – 'S' wave caused by ventricular contraction, 'D' wave due to passive ventricular filling in early diastole and 'a' wave caused by atrial contraction.

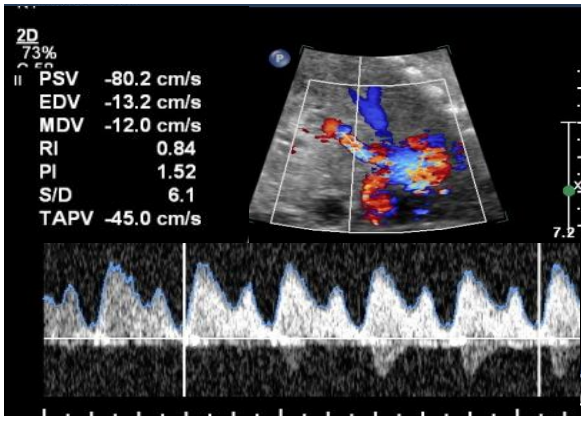

Fig 2. Abnormal ductus venosus showing very small 'a' wave with PI > 2 SD in a case of IUGR at 33weeks+5days of gestation.

The sensitivity, specificity, positive & negative predictive value of DV PI to predict IUGR in the present study was 58.3%, 100%, 100% & 40.5%.

The sensitivity, specificity, positive & negative predictive value of DV PI to predict adverse perinatal outcome in the present study was 59.5%, 71.4%, 71.4% & 59.52%. The incidence of IUD & neonatal mortality was higher in cases with abnormal DV PI (26%, 20%) than in cases with normal DV PI (4%, 4%) (p 0.026, 0.016) as shown in Table 3, Figures 1 and 2.

Table 4: Perinatal outcome in IUGR in relation to Absent/Reversed a-wave in Ductus Venosus (DV) and DV PI

Perinatal outcome	DV a wave Present		DVa wave Absent/ Reversed
Parameters	**DV PI N* (n=25)**	**DV PI Abn* (n=29)**	**DV PI Abn* (n=6)**
a) Fetal distress (n=13)	4	7	2
b) IUD (n=10)	1	5	4
c) AS <7 at 5 min (n=7)	3	3	1
d) Resuscitation (n=7)	2	4	1
e) Respiratory distress at birth (n=28)	14	12	2
f) Acidemia(Cord ph<7.2) (n=25) [Of this Cord ph<7 (n=7)]	10 [2]	13 [3]	2 [2]
g) Increased duration(>7d) of hospital stay (n=12)	5	6	1

h) Early neonatal Mortality (<7d) (n=8)	1	6	1
i) Perinatal Morbidity (n=48)	23	23	2
j) Adverse outcome† (n=42)	17	19	6

** DV PI of > 2 S.D. was taken as abnormal[6]*

†Usually a case had more than one adverse outcome. Postnatal outcomes after exclusion of IUD.

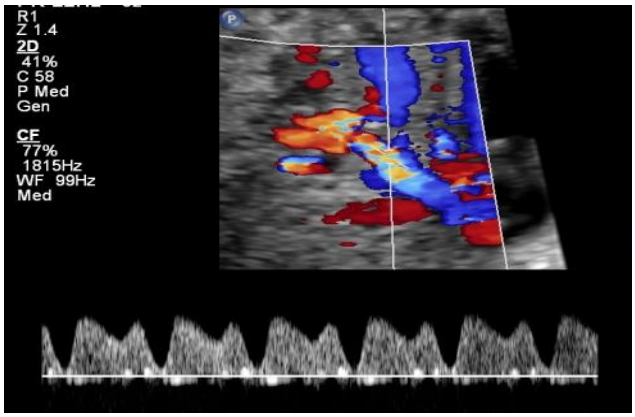

Fig 3. Ductus venosus waveform showing absent 'a' wave.

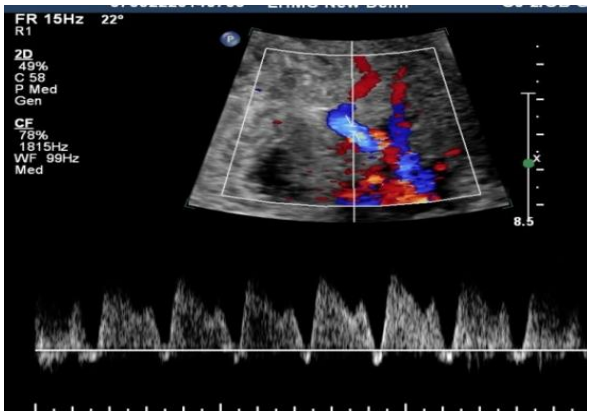

Fig 4. Reversal of 'a' wave in ductus venosus.

Of the cases with abnormal DV PI, there were 6 with absent/ reversed 'a' wave (2+4) (Figures 3 and 4). As shown in Table 4, all 4 cases with reversal of 'a' wave in DV had IUD within 24 hours. The 2 cases with absent 'a' wave were induced subsequently, but had to undergo C.S. for fetal distress. Both had respiratory distress at birth and cord ph <7, and were admitted to NICU. The perinatal morbidity in both these cases was also high in the form of prematurity, low birth weight, need for ventilatory support, HIE, NEC and 1 of them died within 7 days of birth.

Table 5: Perinatal outcome in IUGR in relation to Umbilical Vein velocity

Perinatal outcome	**Umbilical Vein velocity**		***P* value (Chi Square test)**
Parameters	**UV vel N* (n=34)**	**UV vel Abn* (n=26)‡**	
a) Fetal distress (n=13)	6	7	0.029
b) IUD (n=10)	1	9	0.020
c) AS <7 at 5 min (n=7)	1	6	0.011
d) Resuscitation (n=7)	1	6	0.011
e)Respiratory distress at birth (n=28)	11	17	0.003
f) Acidemia(Cord ph<7.2)(n=25) [Of this Cord ph<7 (n=7)]	9 [1]	16 [6]	0.014
g) Increased duration (>7d) of hospital stay (n=12)	2	10	0.001
h) Early neonatal Mortality (<7d) (n=8)	3	5	0.007
i) Adverse outcome† (n=42)	18	24	0.046

** UV vel< 2 S.D. was taken as abnormal,[7] ‡5 cases had pulsatile flow*

†Usually a case had more than one adverse outcome. Postnatal outcomes after exclusion of IUD.

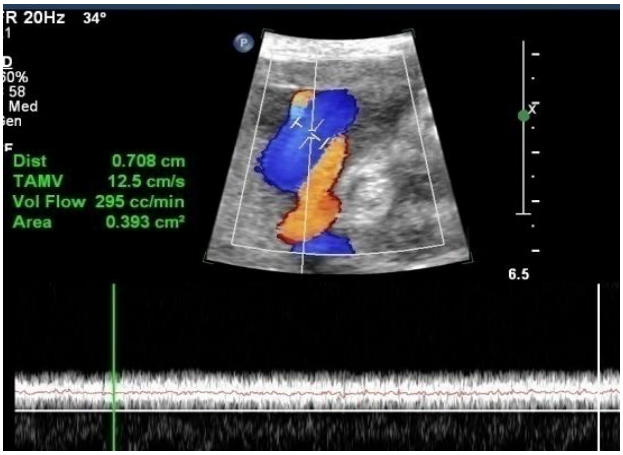

Fig 5. Umbilical vessels on color Doppler imaging with umbilical vein waveform showing continuous, nonpulsatile flow and normal velocity (12.5cm/s), in a case of IUGR with gestational age of 35weeks+4days.

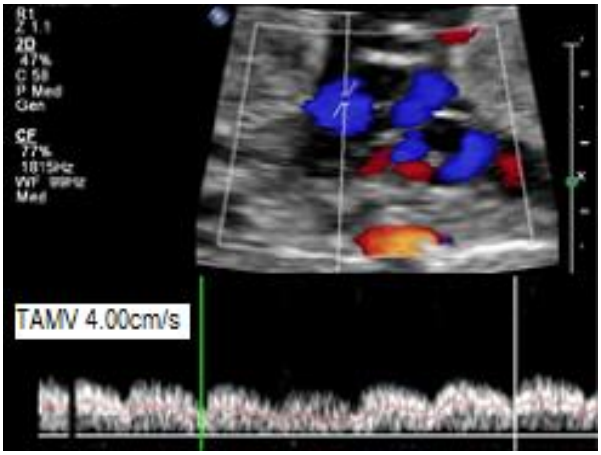

Fig 6. Umbilical vein Doppler velocimetry showing reduction in mean average velocity (4cm/s) with pulsatile flow in a case of IUGR at 34weeks+2days of gestation.

Out of 60 cases of IUGR, 34 cases (56.7%) had normal UV velocity and 26 cases (43.3%) had abnormal UV velocity (<2 S.D.) as shown in Table 5. Complications like fetal distress, low Apgar score, respiratory distress at birth, academia, & increased duration of hospital stay were more commonly seen in cases with abnormal UV velocity (26.9%, 35.3%, 100%, 94.1%, 38.5% respectively) than with normal UV velocity (17.6%, 3%, 33%,27%, 5.9% respectively). Perinatal mortality was also higher in group with abnormal (53.8%) than in the group with normal (11.8%) UV velocity. Of the 26 cases with low umbilical vein velocity, 5 had pulsatile flow and were premature (Figure 6). Of these, 4 had intrauterine demise, while 1 had respiratory distress at birth, low Apgar score, academia (cord pH<7), need for ventilator support, NEC & died early in the neonatal period, suggesting that the appearance of pulsations in UV is foreboding.

Table 6: Perinatal outcome in IUGR (n=60) in relation to Cerebro-Umbilical Ratio and Ductus Venosus PI

Perinatal outcome	**CU Ratio (CPR) & DV PI Doppler velocimetry**			
Parameters	**Group 1 CPR N* DV PI N (n=6, 10%)**	**Group 2 CPR N* DV PI Abn (n=5, 8%)‡**	**Group 3 CPR Abn* DV PI N (n=19, 32%)**	**Group 4 CPR Abn* DV PI Abn (n=30,§ 50%)**
a) Fetal distress (n=13)	1	0	6	6
b) IUD (n=10)	0	0	1	9
c) AS <7 at 5 min (n=7)	0	0	3	4
d) Resuscitation (n=7)	0	0	2	5
e)Respiratory distress at birth (n=28)	3	2	11	12
f) Acidemia(Cord ph<7.2)(n=25) [Of this Cord ph<7 (n=7)]	0 [0]	2 [0]	10 [2]	13 [5]
g) Increased hospital stay (>7day) (n=12)	1	1	4	6
h) Early neonatal mortality (<7d) (n=8)	0	0	3	5
i) Perinatal Morbidity (n=48)	6	4	17	21
j) Adverse outcome† (n=42)	1	1	15	25

**CPR of < 1.08[8] & DV PI > 2 S.D.[6] was taken as abnormal.*
‡No absent/reversed a wave.
§2 cases had absent and 4 cases had reversed a wave.
†Usually a case had more than one adverse outcome. Postnatal outcomes after exclusion of IUD.

As shown in Table 6, incidence of low Apgar score, academia, increased duration of hospital stay, early neonatal mortality & adverse perinatal outcome were more in group 4 (19%, 62%, 28.6%, 29%, 83%) with both CPR and DV PI abnormal than in group 3 (16%, 55%, 22%, 22%, 79%) where CPR was abnormal while DV PI remained normal. Out of 10 IUD cases, 9 cases (90%) were seen in group 4 and 1 case (10%) in group 3, suggesting the need for timely intervention with DV changes. Group 2 with normal CPR & abnormal DV PI and group 1 with both CPR and DV PI normal, had better perinatal outcomes, suggesting the need to be cautious about intervention in cases with abnormal DV PI with normal CPR.

DISCUSSION

Diagnostic performance of Ductus venosus PI for IUGR and adverse perinatal outcomes

The sensitivity, specificity, positive & negative predictive value of DV PI to predict IUGR in the present study was 58.3%, 100%, 100% & 40.5%. The sensitivity, specificity, positive & negative predictive value of DV PI to predict perinatal outcome in the present study was 59.5%, 71.4%, 71.4% & 59.52% respectively. These values compare favourably with a study by Odibo et al[9] who found sensitivity of 58.8% and specificity of 44.9%, Wong et al[10] who found sensitivity, specificity, PPV, and NPV of ductus venosus indexes in predicting adverse perinatal outcome in high risk pregnancies as 53.3%, 74.5%, 32% and 87.7% and Del Rio et al[11] who found that absent/reversed DV a wave had sensitivity, specificity, PPV, and NPV of 36.8%, 96.9%, 87.5% and 72.1% for adverse perinatal outcome and 77.8%, 97.6%, 87.5%, 95.3 for perinatal mortality, respectively. Contrastingly, Mishra D et al [12] demonstrated sensitivity and specificity for abnormal Ductus (absent/ reversal) flow to predict perinatal outcome as 88% and 95% respectively.

Mean birth weight was lower in cases with abnormal DV PI (1380±320g) than in cases with normal DV PI (1510±290g). Gestational age at birth in both groups was comparable. It was noted that incidence of some perinatal complications were slightly higher in cases with abnormal DV PI [prematurity (82.8%), acidemia (54%), perinatal mortality (46%)] than in cases with normal DV PI [prematurity (76%), acidemia (41%), perinatal mortality (8%)], with significant difference in IUD & neonatal mortality; 26%, 20%, versus 4%, 4% (p 0.026, 0.016) similar to a study by Bilardo et al [13] who showed that DV PI measurement was the best predictor of perinatal outcome and this measurement may be useful in timing the delivery of early IUGR fetuses and in improving perinatal outcome, even when delivery may be indicated at an earlier gestational age. Other perinatal complications were comparable between the two groups, mainly because most infants showing derangement in DV either died in utero or within 7 days of birth. The disappearance of ductus venosus 'a' wave was an ominous sign and reversal of 'a' wave was a preterminal event [14] as seen in our study mortality and morbidity data.

Diagnostic performance of Umbilical Vein velocity for adverse perinatal outcome

The cases with abnormal Umbilical vein velocity were born at an earlier gestational age (mean-34.2±2.1 weeks) and had a lower mean birth weight (1.34±0.32 kg), than those with normal Umbilical vein velocity (mean gestational age-35.7±1.2) (mean birth weight-1.61±0.26 kg).

The presence of pulsations in umbilical vein was an ominous sign. It was observed in the present study that no case had pulsatile flow if the velocity of umbilical vein was normal and it occurred only if velocity was reduced, suggesting that reduction in UV velocity was an earlier change to occur than the flow becoming pulsatile. Similar findings were reported by Chander et al, [14] Rigano et al[15] and Di Naro et al.[16]

CONCLUSION

1. Doppler velocimetry should be performed in all the cases having low EFW (< 10 centile) to ascertain if they are constitutionally small –SGA (less likely to have adverse perinatal outcome) or IUGR.
2. Apart from arterial Doppler, venous Doppler surveillance is helpful in fetal monitoring and thereby potentially improves the timing of delivery.
3. Typically, arterial Doppler abnormalities precede venous Doppler abnormality. This knowledge allows us to continue certain pregnancies with deranged arterial Doppler and normal venous Doppler in cases where we need to give time for fetal lung maturity or fetal weight gain.
4. Reversal of a wave in Ductus venosus and UV pulsations are preterminal events to be avoided.

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