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Doppler Prediction of Adverse Perinatal Outcome in PIH and IUGR

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Abstract

Purpose : To determine and compare the diagnostic performance of Dopler sonography of fetal middle cerebral artery (MCA), descending abdominal aorta (DAA), umbilical artery (UA), umbilical vein (UV) and inferior vea cava (IVC) for predictoin of adverse perinatal outcome in suspected intrauterine growth retardation (IUGR) and pre-eclampsia (PET).

Materials ad Methods : Fifty-eight Singleton pregnancies beyond 30 weeks of gestation complicated by intrauterine growth restriction and severe pre-eclampsia or both were prospectively examined with Doppler US of the UA, MCA, DAA, UV and IVC.

Results : Thirty-six patients of the 58 included in the study population had at least one major or minor adverse outcome. Major adverse outcome criteria included perinatal deaths - includinag intrauterine and early neonatal deaths, hypoxic ischemic encephalopathy, intraventricular hemorrhage, periventricular leukomalacia, pulmonary hemorrhage and necrotizing enterocolitis. Minor outcomes included cesarean delivery for fetal distress, APGAR score below 7 at 5 minutes, admission to neonatal intensive care unit (NICU) for treatment.

Conclusion

S/D ratio of MCA/UA is the most sensitive and specific index in predicting major perinatal adverse outcome (83% and 75%), while umbilical artery S/D ratio is the most sensitive index (66.6%) in predicting any adverse perinatal outcome i.e. including both major and minor outcome. MCA pulsatility index (P.I) is the most specific index (90.9%) for predicting in any adverse perinatal outcome. The sensitivity of the Doppler studies can be significantly increased by studying multiple vessels (91.6%). Hence we conclude that Doppler studies of multiple vessels in the fetoplacental circulation can help in the monitoring of compromised fetus and can help us predicting neonatal morbidity. This may be helpful in determining the optimal time of delivery in complicated pregnancies.

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Key words : -Umbilical artery, Umbilical vein, Middle cerebral artery, Descending abdominal aorta, Inferior venacava.

Introduction

The development of a good utero-placental circulation is essential for achievement of a normal pregnancy. Intrauterine growth retardation (IUGR) is associated with an increased risk of perinatal mortality, morbidity, and impaired neurodevelopment. The correct detection of the compromised IUGR fetus to allow for timely intervention is a main objective of antenatal care.

The most common methods for evaluating health in fetuses identified as SGA are the biophysical profile (BPP) and the non-stress test (NST). Unfortunately, neither of these tests is particularly sensitive for predicting poor outcome in IUGR pregnancies.

It is here that role of Color Doppler comes to detect these abnormal vascular resistance patterns. The important issue is not the identification of small fetus, but rather the "fetus at risk" for compromise.

Materials and Methods

This is a prospective study conducted between January

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2001 to October 2002, in Department Of Radiodiagnosis and Imaging in Kasturba Medical College. A total of 58 singleton pregnancies constituted the study population.

Pregnancies beyond 30 weeks of gestation complicated by severe pre-eclampsia and intrauterine growth restriction or both were selected. Gestational age determination was based on a best estimate from menstrual history, clinical gestational age or fetal biometry preferably in the first trimester or early second trimester.

Pregnancies with multiple gestations and congenital anomalies were excluded from the study.

Severe pre-eclampsia is defined according to the standard criteria of uncontrolled blood pressure, proteinuria and ultrasound parameters of intrauterine growth restriction. Other pregnancy complications like gestational diabetes mellitus are also included if associated with severe pre-eclampsia or intrauterine growth restriction was diagnosed based on ultrasound parameters with estimated fetal weight being less than 10th percentile for gesatonal age (SGA).

Doppler Vascular Technique

Study of various fetal vessels was performed using pulsed Doppler ultrasound (LOGIQ 700-GE Medical systems, Waukesha, Wisconsin) with 3.5 MHz curvilinear probe with a high pass filter.

The following vessels were studied with the mother in a recumbent position during fetal inactivity and apnea.

1. Umbilical Artery (UA)
2. Middle Cerebral Artery (MCA)
3. Descending Abdominal Aorta (DAA)
4. Umbilical Vein (UV)
5. Inferior Vena Cava (IVC)

The above vessels wee located in the standard plane:

The umbilical artery measurements were made from free loop of cord midway between the placental and abdominal wall insertion.

The middle cerebral artery was located in a transverse plane at the level of the lesser wing of the sphenoid bone with sample gate placed on proximal portion of the vessel.

The descending abdominal aorta was located in the transverse section of abdomen above the level of the bifurcation of the aorta. The inferior vena caval flow is recorded adjacent to it.

Umbilical vein flow was also noted at the time of recording umbilical artery.

Flow velocity waveforms, the resistance index (R.I), pulsatility index (P.I), systolic/diastolic ratio (S/D) of umbilical artery, middle cerebral artery and descending abdominal aorta were noted.

Doppler study was considered abnormal when

1. S/D ratio, Resistance and Pulsatility index of umbilical artery (>2SD), middle cerebral artery (<5th percentile) and descending abdominal aorta (>2SD) for the gestational age according to the standard reference values; Umbilical artery RI reference was according to Kurmanavicius et al (1). The reference value of umbilical artery P.I., descending abdominal aorta P.I., cerebroumbilical ratio are according to Dandolo Gramellini et al (2) and MCA P.I. ratio are according to Giancarlo Mari et al (3). Rajan et al reference values were taken for Umbilical artery S/D ratio (4).

2. The ratios examined were considered abnormal when

S/D of MCA/UA < 1 (5)
P.I. of MCA/UA < 1 (2)
FETAL OUTCOME

Fetal outcome was studied under major and minor adverse outcome (6).

1. Major adverse outcomes were perinatal deaths - including intrauterine and early neonatal deaths. Major complications like hypoxic ischemic encephalopathy, intraventricular hemorrhage, periventricular leukomalacia, pulmonary hemorrhage and necrotizing enterocolitis.
2. Minor outcomes include-cesarean delivery for fetal distress, APGAR score below 7 at 5 minutes, admission to NICU (neonatal intensive care unit) for treatment.

The patients were followed by serial Doppler assessment and non-stress test and the result of the last Doppler examination within 10 days of delivery was considered in the subsequent correlation with perinatal outcomes.

Results

Table 1. Results
Matenal, Fetal and Perinatal characteristics of study population (n=58)

Maternal Characteristics	N	Percentage
Parity		
Primipara	35	60.3
Multipara	23	39.7
Pregnancy complication		
Pre-eclampsia	813.7	
Intrauterine growth restriction	21	36.3
Pre-eclampsia and IUGR	29	50.0
Delivery		
Spontaneous vaginal delivery	3	5.1
Induced	19	32.7
Cesarean section	36	62.0
Indication for cesarean sections		
Fetal distress	14	38.8
Severe pre-eclampsia	4	11.2
Others	18	50.0
Perinatal outcome		
Stillbirth	5	8.6
Survival	46	79.3
Neonatal deaths	7	12.06

Mean maternal age was 27.3 years. Even when the parental resources were poor leading to non-affordability of NICU care, pregnancy was terminated by induction for maternal indications like severe pre eclampsia.

Neonatal characteristics of study population

Table 2. Neonatal characteristics of study population (n=58)

POG at Birth (weeks)	35.8	
Live Births	53	
Stillbirth	5	
Term babies	28	(48.2%)
Preterm babies	30	(51.7%)
Av. Birth weight (gram)	1798.7 grams	
Birth Weight (gm)		
>2,500	6	(10.3%)
1,500-2,500	31	(53.4%)
1,000-1,500	17(29.3%)	
<1,000	4	(6.8%)
Apgar at 5'<7	4	
Admission to NICU	35	(66%)
Neonatal Complications	17	(32.07%)
Duration of stay > 10 days	15	(42.8%)

There were a significant number of preterm babies in our study group - 30 (51.7%). Thirty-five babies were admitted into neonatal intensive care unit for treatment - 6 babies died. Of the remaining, 15 required admission for more than 10 days for various complications. Two babies could not be admitted to NICU because of poor parental resources. Of that one baby died.

Neonatal complications developed

Table 3. Neonatal complications developed

Complications	In 53 Live Births
Hypoglycemia	1
Hypocalcaemia	1
Polycythemia	1
Neonatal hyperbilirubinaemia	14

Table 4. Diagnostic accuracy of Doppler in predicting adverse perinatal outcome (Major and Minor)

Index	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
U.A R.I	44.4	81.8	80	47.3
U.A P.I	50	59	66.6	41.9
U.A S/D	66.6	45.4	66.6	45.4
MCA P.I	41.6	90.9	88.2	48.7
DAA P.I	44.4	59	64	56.5
P.I Of MCA/UA	47.2	86.3	85	50
S/D of MCA/UA	55.5	72.7	76.9	50

Table 5. Efficacy of various Doppler parameters in predicting major adverse perinatal outcome

Abnormal vessels	Sensitivity	Specificity	Positive	Negative predictive value	Accuracy predictive value
UA P.I	58%	56.5%	35%	86.8%	56.8%
UA R.I	58%	71.7%	35%	86.8%	68.9%
UA S/D	75%	41.3%	25%	86.3%	48%
MCA P.I	66.6%	71.7%	47%	90%	77%
DAA P.I	41.6%	56%	20%	78.7%	53.4%
S/D MCA/UA	83%	75%	38.4%	93.7%	68.9%
P/I MCA/UA	66.6%	73.9%	40%	89.4%	72.4%
All Parameters	91.6%	15%	22%	87.5%	31%

In our study, significant neonatal complications like intraventricular hemorrhage, necrotizing enterocolitis did not occur.

Diagnostic accuracy of Doppler in predicting adverse perinatal outcome (major and minor) are shown in Table 4

Statistical analysis showed that umbilical artery S/D ratio is the most sensitive (66.6%) in predicting perinatal morbidity. But the specificity of this index was the least among different parameters (45.4%). The accuracy of the umbilical artery S/D ratio was also less.

Highest specificity and positive predictive value of predicting neonatal morbidity was for middle cerebral artery pulsatility index-90.9% and 88.2% respectively. The different ratios examined show a uniformly high sensitivity for the prediction of the perinatal outcome compared to individual vessels.

Major adverse perinatal outcome

There were a total of 12 perinatal deaths in our study group. Of these seven were neonatal deaths (NND) and five were stillbirths. One patient had normal Doppler parameters but still there was neonatal death.

Efficacy of various Doppler parameters in predicting major advese perinatal outcome are shown inTable 5

As described earlier, the positive predictive value of a test shows its accuracy and this in our study was higher for MCA PI, which was 47%. The sensitivity of the combined Doppler parameters was highest at 91.6% in predicting perinatal outcome when compared with the ratio of the vessels studied which was ratios of the S/D MCA/UA. PI of MCA/UA and PI of MCA/DAA which had 83%, 66.6% and 66.6% of sensitivity respectively.

Absent umbilical artery diastolic flow

Six patients had absent/reverse umbilical artery diastolic flow. All the fetuses had poor perinatal outcome with one intrauterine death (IUD) and five NND. All showed significant brain sparing effect (PI MCA <5th percentile for gestational age, cerebroumbilical ratio < 1). Three patients among this showed changes on the venous side with pulsatile umbilical vein. Two had reversal of flow in the IVC. Two of the babies had low 5 minute APGAR score of 4 and 5 respectively.

In our study also, terminal changes on the venous side of the Doppler i.e. umbilical vein pulsatility was noted in six patients. Perinatal outcome was poor with umbilical vein pulsatility with three deaths (2 IUD and 1 NND). Three babies required cesarean section and two were admitted into NICU for more than 10 days.

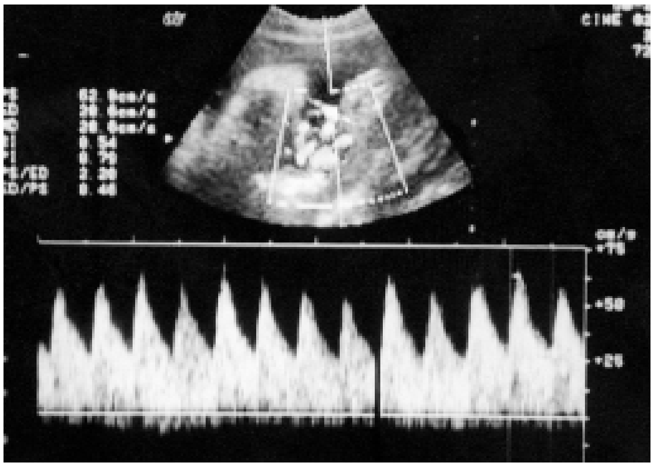

Figure 1. Normal Umbilical artery waveform with good diastolic flow.

Discussion

In normal pregnancy, the three indices; S/D; PI and RI decrease with advancing gestation (7) in Umbilical artery (Figure 1). But in IUGR first there is decreased diastolic flow in the umbilical artery due to increase in the resistance that occurs in small arteries and arterioles of the tertiary villi. This raises the S/D ratio; PI and RI of umbilical artery. As the placental insufficiency worsens, the diastolic flow decreases, then become absent, and later reverses. Some fetuses have decreased diastolic velocity that remains constant with advancing gestation and never become absent or reversed which may be due to a milder form of placental insufficiency. The prevalence of perinatal death in fetuses with absent or reversed end diastolic flow velocity is reported to be oer 40% (8). Yoon et al (9) demonstrated in their study that absent umbilical artery waveform is a strong and independent predictor of adverse perinatal outcome.

Fetal MCA is a low resistance circulation throughout pregnancy and accounts for 7% of fetal cardiac output (10) (Figure 2). The MCA seems to react earlier and more sensitively than CCA to hypoxia and ischemia (11). The MCA impedance varies during gestation according to Mari et al (3), with a parabolic pattern during pregnancy and does not change significantly after delivery. Increase in diastolic flow with decreased pulsatility index shows the brain sparing taking place in compromised fetuses (Figure 3). Arbeille et al (2) found that the cerebral placental ratio is constant during pregnancy especially after 30 weeks and suggested 1 as the cut off value; all values less than 1 are considered abnormal.

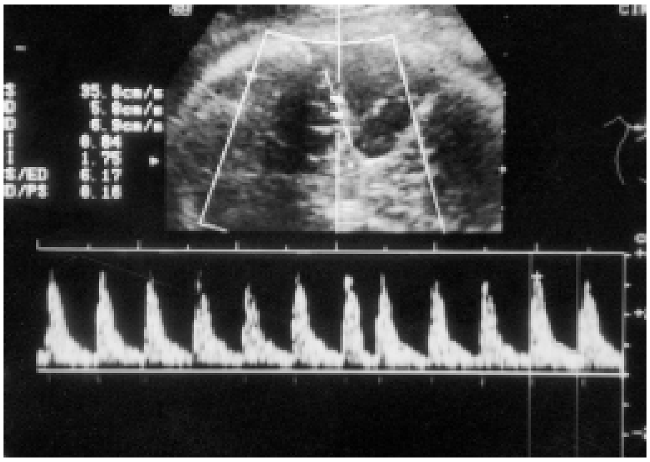

Figure 2. Normal Middle cerebral artery waveform

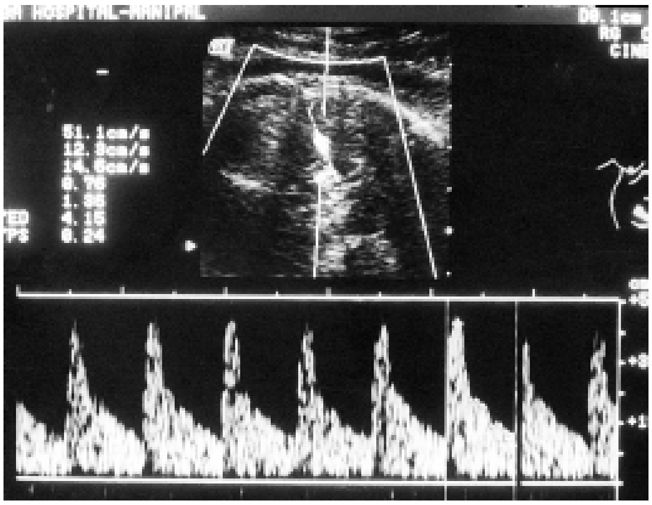

Figure 3. Middle cerebral artery waveform with increased diastolic flow suggestive of Brain sparing effect.

This ratio is shown to have higher sensitivity (100%) when copared with pulsatility index of MCA alone (50%) for 5 min APGAR score according to study by T. Ozcan et al (2).

Normal blood flow in the fetal descending aorta is highly pulsatile with a minimal end diastolic component (13). Wladimiroff et al (14) in their study got a normal pulsatility index of 1.7-1.8 in the descending aorta. A decrease in the aortic blood flow and a high pulsatility index strongly correlates with bad pregnancy outcome, fetal distress and a high cesarean section rate (Figure 4).

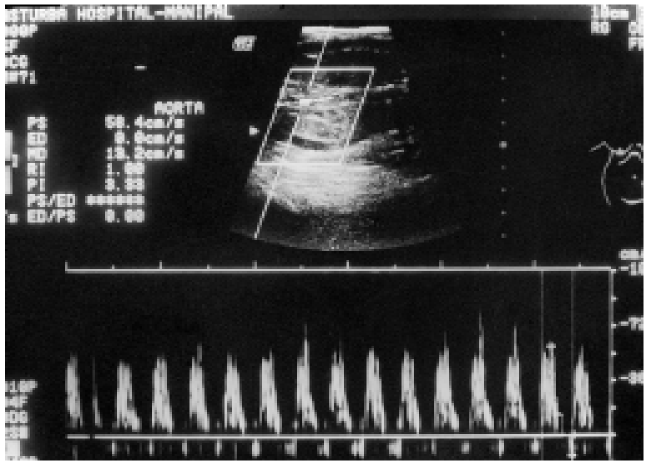

Figure 4. Descending abdominal aortic waveform with reduced diastolic flow.

Venous Doppler is shown to correlate better with academia than those of peripheral arteries according to Rizzo et al (15). Normal blood flow in the umbilical and portal circulation are steady and without pulsations. However physiological pulsatile pattern has been recognized in the first trimester (16). According to S. Gudmundsson et al (17), presence of abnormal and diastolic umbilical cord venous pulsations in fetuses with absent or reversed end diastolic flow in umbilical artery seems to be a sign of a severely compromised fetus with poor perinatal outcome.

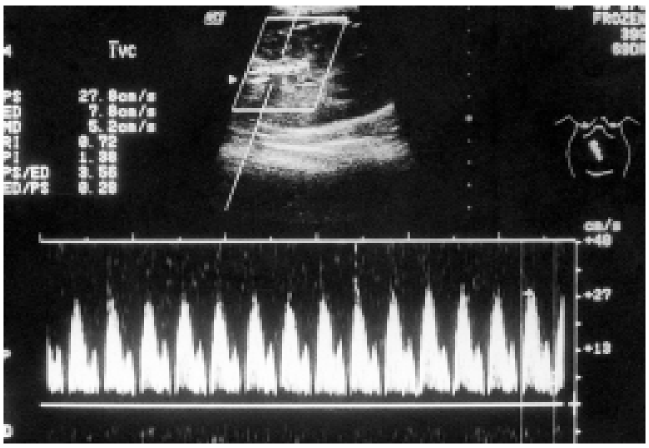

Figure 5. Inferior venecaval waveform

Changes in umbilical vein and Ductus venosus are followed by changes in the inferior venacava. Chiba and associates first reported the flow profile of IVC (17). In humans IVC waveform shows a pulsatile pattern similar to that of animal fetuses or as in adults (Figure 5). Normal inferior vena cava wave form has three components as described by Reed et al (18) - systole-S wave, early diastole-D wave and reverse flow during atrial contration-A wave. According to Rizzo et al (18), the presence of increased reverse flow in the inferior venacava in spite of presence of end-diastolic flow in the umbilical artery may be a warning sign. Rizzo and and co-workers also found that an abnormal PI in the umbilical artery and increased reverse flow in the inferior venacava to be sensitive markers for academia and hypercapnea in IUGR fetuses (15).

In the analysis of adverse perinatal outcome (both major and minor), results of K.W. Fong et al (6) can be compared with our results. The values of umbilical artery sensitivity and specificity in our study (50% and 59%) is comparable to that of K.W. Fong et al (44.7 & 86.6%). We found that ratio of PI of MCA/UA is more sensitive than MCA PI alone in predicting adverse neonatal outcome in contrast to Fong et al. Probably the diference is due to the smaller size of our sample.

Similarly Dandolo Gramellini et al (2) who studied the cerebro-umbilical ratio as a predictor of adverse perinatal outcome gave the sensitivity, specificity, positive predictive value and negative predictive value of P.I of MCA, UA and cerebro-umbilical ratio as depicted in the table.

We obtained a higher sensitivity for MCA PI (41.6%) compared to Gramellini et al (24%) in our study. But in our study we found that umbilical artery PI is more sensitive than cerebroumbilical ratio in predicting adverse perinatal outcome in contrast to Gramellini et al.

Major perinatal adverse outcome

Resulats of K.W. Fong et al can be compared with our results in the following table.

In the study by K.W. Fong et al, they concluded that a normal MCA P.I is helpful to identify the fetuses without a

Table 6

Dandolo Gramellini et al	**MCA**	**UA**	**MCA/UA**
Sensitivity	24.0%	64.0%	68.0%
Specificity	100.0%	90.7%	98.4%
Positive predictive value	100.0%	72.7%	94.4%
Negative predictive value	77.3%	86.7%	88.0%
Our Study	MCA	UA	MCA/UA
Sensitivity	41.6%	50%	47.2%
Specificity	90.9%	59%	86.3%
Positive predictive value	88.2%	66.6%	85%
Negative predictive value	48.7%	45.4%	50%

Table 7

Results of our study for major adverse perinatal outcome

Pulsalitity Index	**Sensitivity (%)**	**Specificity (%)**	**Predictive value**	
			Positive	**Negative**
UA (n=58)	58%	56.5%	35%	86.8%
MCA (n=58)	66.6%	71.7%	47%	90%
MCA/UA (n=58)	66.6%	73.9%	40%	89.4%

Result of the study by Katherine W. Fong et al for major adverse perinatal outcome

Pulsalitity Index	Sensitivity (%)	Specificity (%)	Predictive value	
			Positive	Negative
UA (n=293)	58.3%	81.8%	22.2%	95.7%
MCA (n=293)	91.7%	53.9%	15.1%	98.6%
MCA/UA (n=293)	62.5%	75.5%	18.5%	95.8%

major adverse perinatal outcome, hence once the UA P.I I abnormal, it is better to perform the MCA P.I to know the extent of brain sparing, stressing the importance of studying two vessels in the Doppler.

Absent umbilical artery diastolic flow

Six patients had absent/reverse umbilical artery diastolic flow (Figure 6). All the fetuses had poor perinatal outcome with one IUD and five NND. All showed significant brain sparing effect (PI MCA <5th percentile for gestational age, cerebroumbilical ratio <1). Three patients among this showed changes on the venous side with pulsatile umbilical vein. Two had reversal of flow in the IVC Two of the babies had low 5 min APGAR score of 4 and 5 respectively.

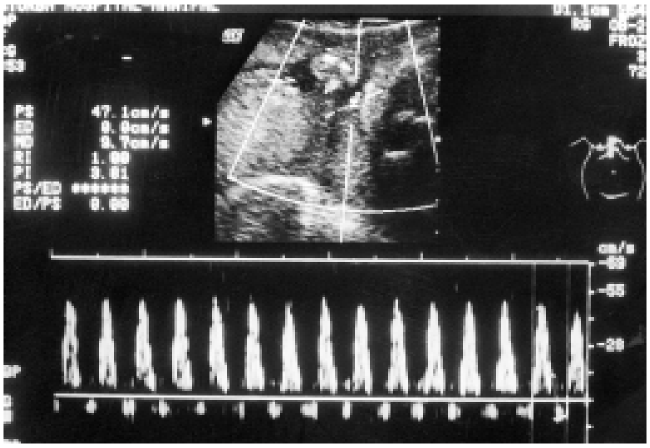

Figure 6. Reversed diastolic flow in the Umbilical artery

In our study also, terminal changes on the venous side of the Doppler i.e. umbilical vein pulsatility was noted in six patients (Figure 7). Perinatal outcome was poor with umbilical vein pulsatility with three deaths (2 IUD and 1 NND). Three babies required cesarean section and two were admitted into NICU or more than 10 days.

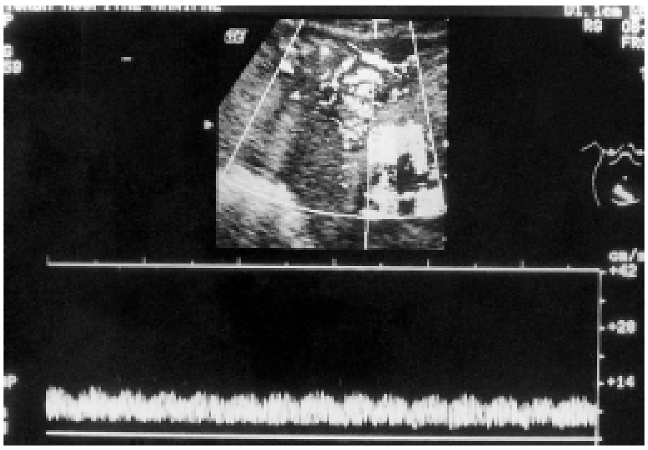

Figure 7. Pulsatile flow in the Umbilical vein.

Conclusion

The introduction of Doppler technology has provided the first opportunity for repetitive noninvasive haemodynamic monitoring in human pregnancy. There is ample evidence that Doppler indices from the fetal circulation can reliably predict adverse perinatal outcome in an obstetric patient population with a high prevalence of complications such as fetal growth restriction. Compared to other methods of fetal monitoring Doppler has proved to be more sensitive in detecting fetal compromises early and aids in the appropriate timing of delivery.

The Doppler patterns follow a longitudinal trend with early changes in the umbilical artery followed by middle cerebral artery and other peripheral arteries. Venous changes follow the arterial pattern and occur in severely compromised fetus and predicts poor perinatal outcome.

Therefore, Doppler investigation of the fetal circulation may play an important role in monitoring the residstributing growth restricted fetus and thereby may help to determine the optimal time for delivery. Fetal Doppler indices, in particular ratios that include measurements obtained from the cerebral circulation, help in the prediction of neonatal morbidity. Hence, the use of Doppler provides information that is not readily obtained from more conventional tests of fetal well being. It therefore has an important role to play in the management of the growth-restricted fetus.

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