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Role of colour doppler in evaluation of intra uterine growth restriction with clinical correlation

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Abstract
Background: Ductus venosus flow deteriorates earlier than does umbilical artery and uterine artery and could be a more sensitive parameter for the prediction of perinatal mortality in IUGR cases. However, not much attempt has been made to estimate the potential contribution of this parameter alone or in combination with other Doppler indices as predictors of adverse perinatal outcome. Therefore, the present study was undertaken to evaluate the correlation of fetal adverse perinatal outcome with changes of the umbilical artery, uterine artery, fetal middle cerebral artery and ductus venosus flow pattern. **Method:** The study was conducted over a period of nine months. Data for the study was collected from patients attending the Department of Radiology, referred by Department of Obstetrics and Gynaecology at our hospital. The study included 50 antenatal women who were diagnosed as having a fetus with intra uterine growth restriction based on grey scale ultrasound findings and referred for obstetric Doppler ultrasound. **Result:** The sensitivity of uterine artery Doppler study to detect adverse perinatal outcome was 84.37% and 81.25% when UA Rl and UA diastolic notch respectively were considered as Doppler parameters. The sensitivity of Doppler examination of the umbilical artery using Pl in predicting perinatal outcome was 81%. The cerebral umbilical ratio provided a better predictor of intrauterine growth restriction and adverse perinatal outcome than either the middle cerebral artery or umbilical artery alone. **Conclusion:** Doppler imaging is of value for monitoring the pregnancy because it can provide indirect evidence of fetal compromise and is known to improve outcomes of high risk pregnancies with Intrauterine growth restriction.
Keywords: Colour Doppler, Intra uterine growth restriction, adverse preinatal outcome, umbilical artery

Introduction

Intrauterine growth restriction (IUGR) is a term used to describe the condition of a fetus whose size or growth is subnormal. The most common definition of intrauterine growth restriction is that "a fetus is growth restricted if its weight is less than the tenth percentile for it's gestational age [1].

The incidence of IUGR in a population where the mothers are generally healthy and well – nourished is estimated to be about 3-5%. In a population of women with hypertension or previous growth restricted fetus however the incidence increases to 15-20% or higher[2]. The incidence of IUGR varies from region to region and even in the same region, it varies in different sub populations. In India, according to recent UNICEF surveys, the incidence of IUGR is 25-30%[3]. IUGR has many causes; maternal causes include hypertension, collagen vascular disease, renal disease, poor nutrition and drug or alcohol abuse which causes placental insufficiency. Fetal infections such as cytomegalovirus, toxoplasmosis and chromosomal anomalies such as triplody and trisomies 13 and 18 also result in IUGR[4].

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Growth retarded fetuses have eight to ten fold increase in perinatal mortality and 50-75% morbidity compared to appropriately sized fetuses[5]. Those fetuses who have suffered from IUGR were prone to develop still birth, intrapartum fetal acidosis, perinatal asphyxia, Meconium aspiration syndrome, Hypoglycemia, Hypocalcaemia, Hypothermia and Hypoxic ischemic encephalopathy etc.

With the introduction of Doppler Ultrasound examination it became possible to assess the uteroplacental blood flow, fetoplacental blood flow and to assess the fetal blood circulation. The uteroplacental and fetoplacental circulation give information on the placental resistance whereas evaluating the fetal circulation using Doppler ultrasound could non – invasively assess the fetal response to hypoxia. Thus it became possible to identify those small fetuses that were at increased risk of perinatal morbidity and mortality due to impaired uteroplacental and fetoplacental circulations. Umbilical arterial (Umb A) Doppler velocimetry is the most rigorously evaluated tests of fetal well – being[6]. Doppler ultrasound studies of the human fetal circulation have shown that in fetuses with IUGR there is a significant reduction of middle cerebral anterial (MCA) pulsatility index when compared with those in normal fetuses[7]. AT Cordocentesis, a significant correlation has been observed between hypoxemia in fetuses with IUGR and an abnormal MCA pulsatality index[8]. The human fetal ductus venosus (DV) plays a major role in the regulation of the circulation of oxygenated blood from the placenta. In normal circumstances 20-30% of the well – oxygenated blood from the placenta gets shunted through the DV to the left side of the heart. The other 70-80% flows through the liver, mainly into the right heart and via the ductus arteriosus and the descending aorta back to the placenta. In fetal compromise up to 70% of the umbilical venous blood gets shunted through the DV to maintain a high oxygen supply

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to essential organs such as the brain, heart and adrenal glands, and liver perfusion is reduced to 30% as shown in studies in animals and in the human fetus. This diversion of oxygenated blood and reduced flow to less important organs like muscles, bowel and kidney, enables the fetus to survive for a considerable period of time, especially if the fetus is under 30 completed weeks of gestation. If the oxygen supply to the myocardium reaches its limit, the myocardium stiffens and the central venous pressure increases. This can be reflected in the blood velocity pattern in the inferior vena cava, hepatic veins, and the DV.

Longitudinal studies have documented that ductus venosus (DV) flow deteriorates earlier than does umbilical artery and uterine artery and could be a more sensitive parameter for the prediction of perinatal mortality in IUGR cases. However, not much attempt has been made to estimate the potential contribution of this parameter alone or in combination with other Doppler indices as predictors of adverse perinatal outcome. Therefore, the present study was undertaken to evaluate the correlation of fetal adverse perinatal outcome with changes of the umbilical artery, uterine artery, fetal middle cerebral artery and ductus venosus flow pattern, as isolated parameters and in a combined model in IUGR fetuses and thus be helpful in deciding the optimal time for delivery in complicated pregnancies.

Material and methods

The study was conducted over a period of nine months. Data for the study was collected from patients attending the Department of Radiology, referred by Department of Obstetrics and Gynaecology at our hospital. The study included 50 antenatal women who were diagnosed as having a fetus with intra uterine growth restriction based on grey scale ultrasound findings and referred for obstetric Doppler ultrasound if the following inclusion criteria were met:

Inclusion criteria

1. Singletion pregnancy with age more than 28 weeks and diagnosed as having a fetus with intrauterine growth restriction based on grey scale ultrasound findings.
2. Women with reliable dating of pregnancy confirmed by and early first trimester ultrasound examination using CRL or BPD or with known LMP will be selected.
3. Pregnant women having registration and / or delivery at this institute.
4. Mothers without pregnancy related risk factors or disorders.

Exclusion criteria

1. Patient not willing for the study.
2. Antenatal women where IUGR was a clinical suspicion only and no grey scale ultrasound assessment was done.
3. Gestational age less than 28 wks.

Results

48% of patients had pregnancy – induced hypertension which is the most common cause for IUGR in our series. Only IUGR as the indication for the Doppler study was seen in 26%. IUGR with anemia complicating pregnancy was present in 18% of cases. Bad obstetric history was seen in 8%.

4. All subjects with history of rupture of membranes, active labour, multiple pregnancies and fetuses with congenital anomalies.

Data collection procedure

The examination procedure was explained to the patient. Ultrasound examined included a complete morphological examination and fetal weight and amniotic fluid index calculations. During each examination Doppler measurements were obtained from the umbilical artery (UA) and from both uterine arteries. Fetal middle cerebral artery Pl was taken close to it's origin with angle of isonation close to zero and on the side close to transducer. Ductus venosus flow during atrial systole was obtained from a mid – sagittal or transverse section of the fetal abdomen.

Color Doppler imaging was used to optimize placement of the pulsed wave. Measurements were taken from the frozen image after at least three consecutive uniform flow velocity waveforms with a high signal to noise ratio.

Follow up Doppler studies were performed, if clinically indicated to determine a favorable or a worsening trend in the Doppler indices. However only the results of the last Doppler ultrasound performed within 72 hrs of delivery were used for analysis of perinatal outcome. Pregnancy was considered to have "Adverse outcome" when any of the complications were present such as Perinatal death, Emergency CS for fetal distress, 5 minute APGAR score of less than 7, Admission to NICU for complications of low birth weight. Pregnancy outcome was considered to be "Uneventful or Favorable" when the above complications were absent.The uterine artery Rl > 0.58 and presence of diastolic notch were considered abnormal. The Umb A Pulsatility index ratios were considered abnormal if the value was above the 95th percentile for the gestational age. The MCA pulsatility index was considered abnormal if the value was below the 5th percentile for the gestational age, according to reference values of D Gramellini et al[9].The MCA Pl / Umb A Pl ratio was calculated. In our study a single cutoff value of 1.08 for MCA / Umb A Pl ratio (cerebral – umbilical ratio) was used, above which velocimetry was considered normal and below which it was considered abnormal, according to reference values of D Gramellini et al[9].

Statistical methods

Descriptive statistics such as mean, SD and percentage was used to present the data. The diagnostic statistics were used to find the diagnostic value of Umb A Pl, MCA Pl and MCA / Umb A Pl in relation to perinatal outcome. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were determined for all Doppler measurements. Statistical analysis was performed by using software SPSS v20.0

Table 1: Distribution of gestational age at doppler examination

Gestational Age	Number	Percentage
26 – 30	4	8.0
31 – 35	32	64.0
36 – 40	14	28.0
Total	50	100.0

64% of the antenatal mothers examined were between 31 – 35 weeks of gestation, 8% between 26 – 30 weeks gestation, and 28% with gestational age between 36 – 40 weeks. None of the antenatal mothers were examined before 29 weeks of gestational age.

Table 2: Changes in uterine artery resistance index (RI), diastolic notch and both parameters by doppler studies

Rl	Number	Percentage
Elevated	36	72
Normal	14	28
Diastolic Notch		
Present	32	64
Absent	18	36
FLOW VELOCITY PROFILE (Both Parameters)		
Abnormal	38	76
Normal	12	24

36 mothers (72%) had an elevated uterine artery Rl and 12 patients (24%) had normal uterine artery Rl.

32 antenatal mothers (64%) had a persistent early diastolic notch in the uterine artery whereas 18 patients (36%) had normal uterine artery flow waveform.

38 of the 50 antenatal mothers (76%) with IUGR showed an abnormal uterine artery flow velocity profile, when two parameters (Rl presence of persistent early diastolic notch) were considered).

Table 3: Findings of umbilical artery doppler examination

Umbilical Artery Pl	Number	Percentage
Elevated	30	60
Normal	20	40
End Diastolic Flow In Umbilical Artery		
Positive	40	80
Absent	8	16
Reversal	2	4

Umbilical artery Pl was elevated in 30 patients (60%) and was normal in 20 (40%) patients. Eight fetuses (16%) showed absence and 2 fetus (4%) had reversal of end diastolic umbilical artery flow with the total of 10 fetuses (20.2%) having abnormal waveforms.

Table 4: Analysis of both uterine and umbilical arteries

Doppler Parameter	Number	Percentage
Both Uterine & Umbilical Changes	42	84.0
Only Uterine A Changes	38	76.0
Only Umbilical A Changes	30	60

84% of the study group (42 mothers) showed abnormalities in either the uterine or umbilical arteries when both were assessed together. When individual arteries were considered, uttering arteries showed better pick up rates (76.0%) than the umbilical arteries (60%).

Table 5: Analysis of perinatal outcome

Perinatal Outcome	Number	Percentage
Adverse	32	64
Uneventful	18	36

There were 5 perinatal deaths. Of the remaining 45, 10 neonates were admitted to NICU, 12 neonates had 5 min APGAR score of less than 7 and 11 babies were born by emergency caesarian section. Mean birth weight at delivery was 2.08 + 0.40 kg (2SD). There were 38 neonates with birth weight less than 2.5 kg. 32 fetuses had at least one adverse perinatal outcome. Remaining 18 fetuses had favorable outcome.

Table 6: Comparison of doppler indices with adverse perinatal outcome

DOPPLER INDEX	TP	TN	FP	FN	SENSITIVITY	SPECIFICITY	PPV	NPV	DIAGNOSTIC ACCURACY
UA Diastolic Notch	26	12	6	6	81.2%	66.6%	81.2%	66.6%	76%
UA Rl	27	9	9	5	84.3%	50%	75%	64.3%	72%
Umb Pl	26	14	4	6	81%	77%	86.6%	70%	80%
MCA Pl	19	15	3	13	59%	83%	86.3%	53%	68%
MCA / Umb Pl	28	14	4	4	87.5%	77.7%	87.5%	77.5%	84%

Discussion

Distribution of gestational age

In this study all patients underwent Doppler study in the third trimester of their pregnancy with 64% being investigated between 31-35 weeks of gestation. The earliest study was done at 29th week of gestation. Hence most pregnancies were monitored between 31-35 weeks, when the fetus would have begun developing sufficient lung maturity to survive outside the uterus. Symmetrical IUGR accounts for 20-30% and asymmetrical IUGR accounts for 70-80%. In asymmetrical IUGR insult begins later than symmetrical IUGR, usually after 28 weeks of gestation. Hence 31-35 weeks of gestation probably could be more common.

Uterine artery

In the present study, the persistent early diastolic notch beyond 26 weeks of gestation showed a sensitivity of 81.25%. This is slightly higher than the study by Colemann et al who showed sensitivity of the uterine artery notch as 76% for adverse perinatal outcome[10]. This may be because of the included women was with bilateral notches in Colemann study, whereas in present study presence of diastolic notch either left or right nor both were included. However, the analysis done by Farrell et al for reliability of early diastolic notch in uterine artery as predictor for uteroplacental insufficiency revealed a sensitivity of 88%[11].

Umbilical artery

In the present study the umbilical artery Pl had a sensitivity of 81%. According to D. Gramellini et al, the sensitivity of Pl in the umbilical artery in predicting perinatal outcome was 64%. Umbilical artery was the main vessel used for monitoring high risk pregnancies[9]. This is because umbilical artery represents fetoplacental system and primarily reflects placental resistance. In present study as there is more number of PIH cases probably this can be attributed for difference in the studies. Another study by K W Fong et al showed the sensitivity of Pl in the umbilical artery as 58.3%[12].

Absence or reversal of the end diastolic flow velocity was seen in 20% fetuses in our study compared with that of 37% in the study by Benson and Doubil et al[13].

Fetal blood circulation and redistribution

The pulsatility index of the fetal MCA was decreased in 44% of fetuses. In the present study fetal middle cerebral artery Pl had a sensitivity of 59%. In Arduini and Rizzo study the sensitivity of MCA in predicting perinatal outcome was 68%[14]. Obviously the present study cannot be compared with the above study in view of difference in considering intra cranial artery as it is clearly established that Pl varies in relation to the intra cranial artery considered. So it is important that the artery be identified precisely and with certainty[15].

Prediction of perinatal outcome

64% (n=32) fetuses had at least one adverse outcome. Remaining 36% (n=18) fetuses had favorable outcome. There were 5 perinatal deaths, three had absent diastolic flow and two had reversal of

diastolic flow in umbilical artery. The mortality in cases of reversed and absent end diastolic flow was 100% and 37.5% respectively, indicating grave prognosis. Of the remaining 45, 10 neonates were admitted to NICU, 12 neonates had 5 min APGAR score less than 7, and 11 babies were born by emergency caesarian section. These results are slightly higher in Gramellini et al study[9]. This can be contributed to difference in perinatal mortality and morbidity rates from western standards to Indian standards.

By using Doppler ultrasound results for analysis, the MCA / Umb A pulsatility index ratio had a higher sensitivity and positive predictive value for predicting the adverse perinatal outcome than the MCA and the Umb A pulsatility indices. Our findings agree with the results of the studies that have shown MCA / Umb A Pl Doppler ratio to be more useful than Umb A Pl or MCA Pl in predicting adverse outcome.

Comparison of mca pl / umb a pl in predicting adverse perinatal outcome

Our studies of sensitivity 87.5%, specificity 77.7%, PPV 87.5%, NPV 77.7%, confirmed with those of Gramellini et al study [9] (sensitivity 68%, specificity 98.4%, PPV 94.4%, NPV 88.8%,) that best results are obtained when we used MCA / Umb A Pl ratio.

Comparison of ua rl in predicting perinatal outcome

Our studies of sensitivity 84.3%, specificity 50%, PPV 75%, NPV 64.28%, confirmed with those of Colemann et al [10] (sensitivity 83%, specificity 47%, PPV 58%) that results are obtained when we used UA RI in predicting perinatal outcome.

Comparison of umb a pl in predicting adverse perinatal outcome

Our studies of sensitivity 81%, specificity 77%, PPV 86.6%, NPV 70%, confirmed with those of D. Gramellini et al study[9] (sensitivity 64%, specificity 90.7%, PPV 72.7% , NPV 86.7%) , BN Lakhkar et al[16] (sensitivity 50%, specificity 59%, PPV 66.6% , NPV 45%), Fong K W et al[12] (sensitivity 44.7%, specificity 86.8%, PPV 54% , NPV 81.7%) that results are obtained when we used UMB A PI in predicting adverse perinatal outcome.

Comparison of mca pl in predicting adverse perinatal outcome

Our studies of sensitivity 59%, specificity 83%, PPV 87.5%, NPV 77.77%, confirmed with those of BN Lakhkar et al[16] (sensitivity 41.6%, specificity 90.9%, PPV 88.2% , NPV 48.7%) and D. Gramellini et al[9] (sensitivity 24%, specificity 100%, PPV 100% , NPV 77.3%) , whereas Fong K W et al[12] (sensitivity 72.4%, specificity 58.1%, PPV 37.7% , NPV 85.7%) shown variation in results when we used MCA PI in predicting adverse perinatal outcome.

Comparison of diagnostic accuracies

Our studies diagnostic accuracy result of MAC/Umb PI ratio 84%, Umb PI 80%, MCA PI 68% confirmed with those of Gramellini et al[9] findings viz. MAC/Umb PI ratio 90%, Umb PI 83.3%, MCA PI 78.6% .

Conclusion

Doppler imaging is of value for monitoring the pregnancy because it can provide indirect evidence of fetal compromise and is known to improve outcomes of high risk pregnancies with Intrauterine growth restriction. Hence Doppler evaluation is complementary to all other surveillance modalities.

Conflict of Interest: Nil
Source of support: Nil

References
1. Lugo G. Cassady. Intrauterine growth retardation clinico pathological findings in 233 conceptive infants. Am J Obstest Gynecol 1971; 109: 615–22.
2. Galbraith RS, Kershmar EJ, Peircy wN, Low JA. The clinical prediction of intrauterine growth retardation. Am J ObstetGynecol 1979; 133: 281 – 286.
3. Devi PIC, Krishan menon MK, Bhaskar Rao K. Post graduate obstetrics and gynecology. Orient long man; 3rd Edn 1986: 219.
4. Seeds J.W. Impaired fetal growth: definition and clinical diagnosis Obstet Gynecol 1984; 64: 303 – 310.
5. Sendhi Jain, Manju Puri, Diagnosis of intrauterine growth retardation – A review. Obstet and Gynae today 2001; 11: 670 – 673.
6. Kok JH, Devi Ouden AL, Verloove – Venhorick SP, Brand R. Outcome of very preterm small for gestational age infants: the first nine years of life. Br. J Obstet and genecol 1989; 105: 162 – 168.
7. Neilson JP, Alfirevic Z. Doppler Ultrasound in high risk pregnancies. Available in Cochrane library [data base on disk and CD rom]. Issue 3, Oxford, England: Cochrane collaboration. 1998
8. Ven den Wijngard JW, Groenenberg IL, Wladimirolb, JW, et al. Cerebral Doppler Ultrasound of the fetus. Br. J obstet Gynaecol 1989; 86: 845 – 849.
9. Gramellini D, Folli MC, Raboni S, et al Cerebral – umbilical Doppler ratio as a predictor of adverse perinatal outcome. Obstet Gynecol. 1992; 79: 416 – 420.
10. Coleman MA, McCowan LM, North RA. Mid – trimester uterine artery Doppler screening as a predictor of adverse pregnancy outcome in high – risk women. Ultrasoud Obstet Gynecol 2000 ; 15 (1): 4 – 6.
11. Farrel T, Chien PF, Mires GJ. The reliability of the detection of an early diastolic notch with uterine artery Doppler velometry. Br J Obstet Gynaecol. 1998 ; (12) 1308 – 11.
12. Fong KW, Ohisson A, Hannah ME, Grisaru S, Kingdon J, Ryan M, et al. Prediction of Perinatal Outcome in Fetuses Suspected to have intrauterine Growth Restriction: Doppler US Study of Fetal Cerebral, Renal and Umbilical Arteries. Radiology. 1999; 213: 681 – 689.
13. Benson CB, Doubilet PM. Doppler criteria for intrauterine growth retardation: predictive values. J Ultrasound Med. 1988; 7: 655 – 659.
14. Arduini D, Rizzo G, Romanini C, Mancuso S. Fetal blood flow velocity wave forms as predictors of growth retardation. Obstet Gynecol. 1987; 70 (1): 7 – 10.
15. Mari G, Moise KJ, Deter Rl, Kirshon B, Carpener RJ, Huhta JC. Doppler assessment of the pulsatility index in the cerebral circulation of human fetus. Am J Obstet Gynecol 1989; 160; 693 – 703.
16. BN Lakhkar, KV Rajagopal, PT Gourisankar. Doppler prediction of adverse perinatal outcome in PIH and IUGR. Ind J Radiollmag 2006 16: 1: 109 – 116.