

Obstetric Doppler studies in prediction of perinatal outcome in intrauterine growth restriction

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ABSTRACT

Background: Fetal surveillance of the pregnancies that are complicated by IUGR is essential to improve fetal outcome. Colour Doppler studies of uteroplacental and fetoplacental circulation are useful in identification of hypoxemic status of the fetus and allows timely intervention in at risk fetuses. The present study was aimed to know the significance of colour Doppler studies in intrauterine growth restriction cases and to correlate with the perinatal outcome thus to offer better strategies for early diagnosis of compromised fetus and timely intervention.

Methods: This was a prospective study of 125 singleton pregnancies in the third trimester with IUGR. The results of last Doppler ultrasound within one week of delivery were used for analysis. Adverse perinatal outcome was studied in the form of emergency cesarean section for fetal distress, meconium stained amniotic fluid, Apgar at 5 min <7, NICU admission and perinatal mortality (stillbirths and neonatal death). Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and Diagnostic accuracy of various Doppler parameters were calculated after comparing with standard.

Results: In the present study 63 patients had one or more adverse perinatal outcome parameter. The diagnostic accuracy of umbilical artery was more (71.20%) than other parameters in predicting adverse perinatal outcome. Middle cerebral artery RI was having highest specificity and positive predictive value of 100% than any other parameter in predicting adverse perinatal outcome. Patients with AEDF and REDF had 33.3% and 50% perinatal deaths respectively.

Conclusions: Middle cerebral artery Doppler studies shown more specificity and positive predictive value than umbilical artery Doppler in prediction of adverse perinatal outcome.

Keywords: Cerebroplacental ratio, Color Doppler, Intrauterine growth restriction, Perinatal outcome

INTRODUCTION

Intrauterine growth restriction (IUGR) syndrome is characterised by failure of the fetus to attain its normal growth potential and is defined as sonographic estimated fetal weight <10th percentile of gestational age.¹ IUGR is one of the most common and complex problems in modern obstetrics and is associated with significant perinatal morbidity and mortality. Suboptimal growth at birth is linked with impaired intellectual performance and diseases such as hypertension and obesity in adulthood.²

Intrauterine growth restriction (IUGR) affects 3 to 10% of pregnancies. Approximately 30 million infants suffer from IUGR every year.³ National Neonatal Perinatal Database of India reported the incidence of IUGR to be 9.65% among hospital born live birth infants.⁴

Fetal surveillance of the pregnancies that are complicated by IUGR is essential to improve fetal outcome. This includes various tests like cardiotocography, serial measurements of fetal biometry with fetal biophysical profile and colour Doppler studies of uteroplacental and

fetoplacental circulation. They are useful in identification of hypoxic status of the fetus and allows timely intervention in at risk fetuses. Colour Doppler studies have proved to be more sensitive in detecting fetal compromise at the earliest so as to make the timely decision of termination of pregnancy.⁵

The purpose of this study was to know the significance of colour Doppler studies in intrauterine growth restriction cases and to correlate with the perinatal outcome thus to offer better strategies for early diagnosis of compromised fetus and timely intervention.

METHODS

Patients attending antenatal care outpatient department and with pregnancies beyond 28 weeks gestation with IUGR during two years period were selected.

Gestational age determination was based on menstrual history (first day of last menstrual period-LMP), clinical examination and fetal biometry preferably in the first or early second trimester. The diagnosis was made by serial measurements instead of single measurement of fetal parameters. The cases admitted with the diagnosis of IUGR was subjected for various investigations to find out the cause. Inclusion criteria were singleton pregnancy at or more than 28 weeks, clinically and sonologically evaluated cases of IUGR. Exclusion criteria were diagnosed cases of congenital anomalies, multiple pregnancies and intrauterine death.

Serial ultrasonography for assessment of fetal biophysical profile and colour Doppler studies was done. Other investigations pertaining to case were carried out simultaneously.

We used G E LOGIQ P3 C5-2E and MINDRAY DC8 ultrasound machines with curvilinear probe of transducer frequency 2-5 MHz for doing Doppler waveform analysis in this study.

After the rest for 10 to 15 minutes in a semi-recumbent position patient were screened for various Doppler studies. Ultrasound evaluation for fetal biometry was done initially to assess fetal growth and estimation of fetal weight. Doppler waveform analysis of umbilical artery and middle cerebral artery were done. During the phase of fetal inactivity and apnoea the waveforms were studied. Doppler indices were automatically computed by the program after obtaining the values of systolic flow (S) and diastolic flow (D) for these vessels.

Umbilical artery Doppler flow velocity waveforms measurements were taken from a free loop of cord after optimizing the angle of insonation. Umbilical artery S/D ratio of more than 3 after 30 weeks gestational age was considered abnormal. Umbilical artery Resistance Index (RI) and Pulsatility Index (PI) of more than the 95th percentile of the range of reference were considered

abnormal. Absent and reverse end diastolic flow were considered ab-normal.

Middle cerebral artery is the largest terminal branch of the internal carotid artery. It was insonated at the level of the greater wing of sphenoid. The angle of insonation can easily be kept at 0 degree for this vessel. MCA S/D was considered abnormal when it is less than 4. MCA RI and PI were considered abnormal when it was more than the 95th percentile of the range of reference.

Cerebroplacental ratio or MCA / UA PI Ratio is a Doppler index useful in identifying fetuses with increased placental and/ or decreased cerebral resistance. It is the ratio of MCA P.I. to Umbilical artery P.I. A single cut off value 1.08 is used above which it is considered as normal and below which it is considered as abnormal.

Further management of the cases were decided depending on the clinical status of the patient and the Doppler report. Those who continued their pregnancies after the initial Doppler examination, Doppler was repeated at appropriate intervals. The pregnancies were terminated depending upon various fetomaternal factors. Findings of the Doppler study done within one week prior to termination/ spontaneous delivery were taken into consideration for the study.

At the time of delivery detail monitoring of the fetus was done and adverse perinatal outcome was calculated based on the following parameters such as

- Emergency cesarean section for fetal distress characterized by abnormal heart rate pattern (e.g. late decelerations, severe variable decelerations or prolonged bradycardia)
- Meconium stained liquor.
- Apgar score at 5 min <7
- NICU Admission
- Perinatal mortality (stillbirths and neonatal death)

Data was statistically analysed with the help of SPSS software version 15 and open epi software. Qualitative data is presented with the help of frequency and percentage table. Sensitivity, Specificity, PPV, NPV and Diagnostic Accuracy is calculated for study variables after comparing with standard. P value of less than 0.05 was considered as statistically significant.

RESULTS

The study comprised of 125 patients with Intra Uterine Growth Restriction out of which 79.2% were moderate and 20.8% were classified as severe IUGR.

Age of the patients ranged from 19 to 35 years while mean was calculated as 26.73 years. Out of 125 patients 56.8% were primigravidas and rest were multigravidas. Gestational age above 28 weeks were taken into consideration and the mean gestational age was found to

be 37.11 weeks. Out of the total 125 babies, 80.8% babies were low birth weight (< 2.5 kg). Mean birth weight was found to be 2.12 kg (Table 1).

Table 1: Maternal and fetal characteristics of study population (n=125).

Characteristics	Number	Percentage
Parity		
Primi	71	56.8
Multi	54	43.2
Gestational age		
28-32 weeks	08	6.4
33-36 weeks	24	19.2
>37 weeks	93	74.4
Lag in weeks-severity of IUGR		
< 6 weeks (moderate)	99	79.2
6 weeks (severe)	26	20.8
Mode of delivery		
Vaginal	70	56.0
Cesarean section	55	44.0
Birth weight (grams)		
< 1500 gm	16	12.8
1500-2499 gm	85	68.0
≥ 2500 gm	24	19.2

Adverse Perinatal outcome was seen in 63 (50.4%) patients. Amongst these cases 71.4% babies had meconium stained amniotic fluid and 61.9% of cases had low Apgar score. NICU admission was required in 88.8% of the babies for various reasons like asphyxia, low birth weight, prematurity etc. There were 6 (9.52%) perinatal deaths, three were stillbirths and three babies died in NICU due to prematurity (Table 2).

Table 2: Adverse Perinatal Outcome (n=63).

Outcome parameter	Number	Percentage
LSCS for fetal distress	27	42.8
Meconium stained liquor	45	71.4
Apgar at 5 minutes <7	39	61.9
NICU admission	56	88.8
Perinatal death	6	9.52

Umbilical artery Doppler studies revealed that umbilical artery S/D, umbilical artery RI and umbilical artery PI waveforms were found to be abnormal in 39.2%, 21.6% and 22.4% of the patients respectively. Amongst the abnormal UA S/D Ratio cases there were 6 cases each having Absent End Diastolic Flow (AEDF) and Reverse End Diastolic Flow (REDF).

The diagnostic accuracy for predicting adverse perinatal outcome was calculated for all Doppler parameters and was found to be highest (71.2%) for umbilical artery S/D than umbilical artery RI (63.2%) and umbilical artery PI (65.6%). The umbilical artery RI and PI were having high specificity of 91.94% and 93.55% respectively in predicting adverse perinatal out-come. Perinatal mortality

were seen in 2 cases having AEDF (33.33%) and in 3 cases having REDF (50%). One baby with normal UA S/D Ratio died on 9th day due to prematurity (Table 3, 4 and 5).

Table 3: Distribution of various color doppler findings (n=125).

Doppler parameter	Normal	Abnormal
UA S/D Ratio	76	49
UA R.I.	98	27
UA P.I.	97	28
MCA S/D ratio	93	32
MCA R.I.	122	03
MCA P.I.	112	13
P.I. of MCA/UA	89	36

Fetal middle cerebral artery was also subjected to Doppler studies and MCA S/D, MCA RI and MCA PI was found to be abnormal in 25.6%, 2.4% and 10.4% patients respectively.

Table 4: Association of doppler parameter with perinatal outcome.

Parameter		Adverse Outcome	Good Outcome
UA S/D Ratio	Abnormal (n=49)	38 (True positive)	11 (False positive)
	Normal (n=76)	25 (False negative)	51 (True negative)
UA R.I.	Abnormal (n= 27)	22 (True positive)	5 (False positive)
	Normal (n=98)	41 (False negative)	57 (True negative)
UA P.I.	Abnormal (n=28)	24 (True positive)	4 (False positive)
	Normal (n=97)	39 (False negative)	58 (True negative)
MCI S/D Ratio	Abnormal (n=32)	28 (True positive)	4 (False positive)
	Normal (n=93)	35 (False negative)	58 (True negative)
MCA R.I.	Abnormal (n=03)	3 (True positive)	0 (False positive)
	Normal (n=122)	60 (False negative)	62 (True negative)
MCA P.I.	Abnormal (n=13)	12 (True positive)	1 (False positive)
	Normal (n=112)	51 (False negative)	61 (True negative)
MCA/UA P.I. Ratio	Abnormal (n=36)	30 (True positive)	6 (False positive)
	Normal (n=89)	33 (False negative)	56 (True negative)

MCA RI and MCA PI was found to be having highest specificity of 100% and 98.39% respectively for predicting adverse perinatal outcome. MCA RI was also

found to have highest PPV (100%) in predicting adverse perinatal outcome. Cerebroplacental ratio incorporates both placental status (umbilical artery) and fetal response (MCA) in the prediction of adverse outcomes.

Cerebroplacental index has the highest specificity and positive predictive value of 90.32% and 83.33% respectively in predicting adverse perinatal outcome.

Table 5: Efficacy of various doppler parameters in predicting adverse perinatal outcome.

Doppler findings	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic accuracy (%)
UA S/D	60.32	82.26	77.55	67.11	71.20
UA RI	34.92	91.94	81.48	58.16	63.20
UA PI	38.10	93.55	85.71	59.79	65.60
MCA S/D	44.44	93.55	87.50	62.37	68.80
MCA RI	4.76	100	100	50.82	52.00
MCA PI	19.05	98.39	92.31	54.46	58.40
MCA/UA PI	47.62	90.32	83.33	62.92	68.80

DISCUSSION

Fetal hypoxia activates a range of biophysical, cardiovascular, endocrine and metabolic responses.

Fetal cardiovascular responses to hypoxia which include variation in heart rate and redistribution of the cardiac output towards vital organs are probably the most important adaptive reactions responsible for maintaining fetal hemostasis.

The redistribution of blood flow towards the fetal brain is known as brain sparing effect.

Perinatal Doppler velocimetry studies can identify fetus at risk of adverse perinatal outcome so that timely intervention can be done.

Since the definition of adverse perinatal outcomes is not fixed it is difficult to compare each parameter separately with different studies.

Since in the present study the Doppler findings along with other clinical parameters were considered for management of the patients, it is possible that the perinatal outcome may vary in comparison with other studies.

In the present study 56.8% of the patients were primigravida. Yash et al, Lakshmi et al and BN Lakhkar et al in their studies reported 54%, 69% and 77.7% primigravida patients respectively.⁶⁻⁸

The present study reveals that maximum patients are found above 37 weeks with the mean gestational age of 37.11 weeks. In similar studies done by Odibo et al and Ulkumen et al mean gestational age was found to be 35.6 and 34.82 weeks respectively.^{9,10} Yash et al reported 34% of the patients were above 36 weeks, 24% were above 32 weeks and 42% above 30 weeks.⁶

Lakshmi et al found out that 60% of the patients were above 37 weeks, 29% were above 32 weeks and 11% were above 28 weeks.⁷

The mean birth weight in the present study is 2.12 kg, whereas in the studies done by B N Lakhkar et al, Kumbhar et al and Odibo et al the mean birth weight was reported as 2356 grams, 2 kg and 1770 grams respectively.^{8,9,11}

Umbilical artery waveforms

Umbilical artery S/D ratio

Umbilical artery Doppler provides an index of resistance to flow in the fetal side of placenta especially in response to placental insufficiency as seen in pregnancy induced hyper-tension and IUGR.

In present study UA S/D ratio showed a higher specificity, positive predictive value and diagnostic accuracy of 82.69%, 77.55% and 71.20% respectively in predicting adverse perinatal outcome.

The comparison of UA S/D Ratio in predicting adverse perinatal outcome with various studies is shown. In the present study diagnostic accuracy is comparable with the studies by Lakshmi et al and Netam et al which is 79.3 % and 75% respectively.^{7,12} (Table 6)

In the present study the association between Umbilical artery S/D with adverse pregnancy outcome was found to be statistically significant. ($p < 0.05$)

Umbilical artery RI

Umbilical Artery RI had a higher specificity and PPV of 91.94% and 81.48% in predicting the adverse perinatal outcome in the present study which is comparable to the study done by B N Lakhkar et al. (Table 7). Lakshmi et al

studied the significance of Doppler in IUGR and pregnancy induced hypertension using umbilical artery and middle cerebral artery blood flow and their study concluded that umbilical artery RI also had a 100%

sensitivity in predicting Apgar <7 at 5 min.⁷ In present study correlation between Umbilical artery RI and pregnancy outcome was found to be statistically significant. (p<0.05).

Table 6: Comparison of UA S/D Ratio in predicting adverse perinatal outcome.

Study	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Lakshmi et al ⁷	83.6%	74.4%	78.8%	80%	79.3%
Lakhkar et al ⁸	66.6%	45.4%	66.6%	45.4%	-
Netam et al ¹²	86.96%	71%	51.28%	94%	75%
Purushotham et al ¹³	83.3%	93.7%	88.2%	90.9%	-
Present study	60.32%	82.26%	77.55%	67.11%	71.20%

Table 7: Comparison of UA RI Ratio in predicting adverse perinatal outcome.

Study	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Lakshmi et al ⁷	84.9%	72.3%	77.5%	89%	79%
Lakhkar et al ⁸	44.4%	81.8%	80%	47.3%	-
Present study	34.92%	91.94%	81.48%	58.16%	63.20%

Table 8: Comparison of UA P.I. in predicting adverse perinatal outcome.

Study	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Lakshmi et al ⁷	86.7%	63%	73%	81.8%	76%
Lakhkar et al ⁸	50%	59%	66.6%	41%	-
Kumbar et al ¹¹	89%	85.7%	85%	90%	87.5%
Gramellini et al ¹⁴	64%	90%	72%	86%	-
Yoon et al ¹⁵	89%	86%	86%	89%	-
Bano et al ¹⁶	46.7%	93%	87%	63%	70%
Khanduri et al ¹⁷	73.8%	75.9%	87.7%	55.4%	75%
Present study	38.10%	93.55%	85.71%	59.79%	65.60%

Umbilical artery PI

In the present study, Umbilical artery PI was found to be less sensitive and highly specific. The high specificity (93.55%) is comparable with the studies of Kumbar et al, Gramellini et al, Yoon et al and Bano et al. (Table 8).^{11,14,15,16}

Absent and Reverse End Diastolic Flow (AEDF/REDF)

Fetuses with absent and reverse end diastolic flow were at a significantly increased risk for delivery at low gestation, IUGR, low birth weight and perinatal deaths. In patients of IUGR there is an increased risk of serious diseases affecting the infants' central nervous system, lung or intestine. Kumbar et al evaluated the role of Doppler parameters in IUGR babies and found out that 50% perinatal deaths were seen in cases having absent of diastolic flow and 100% in cases having reverse end diastolic flow. In the present study 33.33% mortality was seen in cases with AEDF and 50% mortality in cases of REDF (Table 9).¹¹

Middle Cerebral Artery (MCA) Doppler waveforms

Fetal MCA is a low resistance circulation throughout pregnancy. The mean values of all indices showed a decline with gestational age.

Table 9: Perinatal mortality with AEDF and REDF.

Study	AEDF		REDF	
	No. of cases	Perinatal deaths	No. of cases	Perinatal deaths
Kumbar et al ¹¹	04	02 (50%)	02	02 (100%)
Present study	06	02 (33.33%)	06	03 (50%)

MCA PI

The decrease in MCA PI value shows the hypoxia which is caused by placental insufficiency but would not directly demonstrate placental vascular resistance. Thus, its efficacy in predicting fetal distress is found to be lower than that of umbilical artery Doppler indices. Hence in predicting severe perinatal hypoxia it is better to

correlate MCA PI with umbilical artery Doppler indices or CPR.

MCA PI correlation with adverse perinatal outcome was compared with other studies. In the present study the correlation of MCA PI and pregnancy outcome was

found to be statistically significant ($p < 0.05$). The specificity and PPV of MCA PI in the present study is 98.39% and 92.31% respectively in predicting adverse perinatal outcome which is comparable with the studies done by Gramellini et al, Bano et al, and Khanduri et al. (Table 10).^{14,16,17}

Table 10: Comparison of MCA P.I. in predicting adverse perinatal outcome.

Study	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Yash et al ⁶	76%	78%	-	-	52%
Lakshmi et al ⁷	62.2%	78.7%	76.7%	64.9%	63%
Kumbar et al ⁸	78.9%	68.4%	65.2%	76.4%	70%
Netam et al ¹²	47.06%	81.81%	57.14%	75%	70%
Gramellini et al ¹⁴	24%	100%	100%	77.3%	-
Bano et al ¹⁶	8.9%	100%	100%	-	-
Khanduri et al ¹⁷	35.7%	92.6%	91.8%	38.2%	-
Arduini & Rizzo et al ¹⁸	68%	91%	-	-	-
Fong et al ¹⁹	72.4%	58.1%	37.7%	85.7%	-
Present study	19.5%	98.39%	92.31%	54.46%	58.40%

Table 11: Comparison of Cerebroplacental Index in predicting adverse perinatal outcome.

Study	Sensitivity	Specificity	PPV	NPV
Lakshmi et al ⁷	90%	86%	94%	92.5%
Odibo et al ⁹	72%	62%	68%	67%
Kumbar et al ¹¹	94.7%	90.4%	90%	95%
Gramellini et al ¹⁴	68%	98.4%	94.4%	88.8%
Fong et al ¹⁹	51.3%	80.6%	48.1%	82.5%
Present study	47.62%	90.32%	83.33%	62.92%

Cerebroplacental ratio

In the present study the cerebroplacental index has the highest specificity and positive predictive value of 90.32% and 83.33% respectively in predicting adverse perinatal outcome. The present study results of specificity and PPV are comparable with the studies done by, Lakshmi et al, Kumbar et al. and Gramellini et al. (Table 11).^{3,11,14}

CONCLUSION

The present study noted the significance of Doppler ultrasound studies in patients with IUGR to identify compromised fetuses in utero and to take timely appropriate action. The diagnostic accuracy of umbilical artery S/D ratio in prediction of adverse perinatal outcome in the present study was found to be high compared to UA RI and UA PI. Middle cerebral artery RI and PI were found to be having highest specificity and positive predictive value in predicting adverse outcome. Cerebroplacental index is having high specificity and positive predictive value in predicting adverse perinatal outcome. The AEDF and REDF were associated with significant perinatal morbidity and mortality. Hence

AEDF and REDF are ominous signs in Doppler study and helps the obstetricians to take a prompt action to rescue the baby. The middle cerebral artery Doppler indices were a better predictor of fetal outcome in IUGR compared to umbilical artery in terms of specificity and positive predictive value.

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