

A study to evaluate umbilical artery and middle cerebral artery doppler indices as predictors of adverse perinatal out come in clinically suspected IUGR pregnancies

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Abstract

Background and Objectives: Objective of our study was to evaluate the usefulness of middle cerebral artery and umbilical artery Doppler indices as predictors of adverse perinatal out come in clinically suspected IUGR pregnancies and to establish the role of Doppler ultrasound in the management of IUGR pregnancy. **Materials and Methods:** We studied Doppler Velocimetry of umbilical artery and Middle cerebral artery in 40 cases with clinical suspicion of IUGR between 31 to 40 weeks of gestation .Pulsatility Index was used as the Doppler index. Pregnancies with documented major congenital abnormality, multiple gestations and intrauterine death at the time of first Doppler examination were excluded from the study. **Results:** Cerebroplacental ratio (MCA/UA PI Ratio) was most sensitive (sensitivity 95%). It was more sensitive than either UA PI (sensitivity 90%) or MCA PI (sensitivity 76.19%) alone in predicting any adverse outcome. Diagnostic accuracy of Cerebroplacental ratio (Accuracy=92.50%) was better than UA PI (Accuracy=80%) and MCA PI (Accuracy=62.5%) in predicting adverse outcomes **Conclusion:** Fetal Doppler indices, in particular ratios that include measurements obtained from the cerebral circulation, help in the recognition of the compromised growth-retarded fetus.

Key Words: Umbilical artery Doppler, Middle cerebral artery Doppler; Fetal Doppler; Cerebro-placental Ratio

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INTRODUCTION

Intrauterine growth restriction (IUGR) is associated with an increased risk of perinatal mortality, morbidity, and impaired neurodevelopment^{1, 2, 3}. Ultrasonographic (US) biometry helps to identify a heterogeneous group of small-for-gestational age fetuses that include fetuses

with IUGR, fetuses with small constitution, and fetuses with appropriate growth (misdiagnosed as small). The correct detection of the compromised IUGR fetus to allow for timely intervention is a main objective of antenatal care. Umbilical arterial (UA) Doppler velocimetry is the most rigorously evaluated test among noninvasive tests of fetal well-being⁴. A meta-analysis of randomized controlled trials of UA Doppler velocimetry in high-risk pregnancies (mainly pregnancies with associated hypertension and suspected IUGR) demonstrated that its use was associated with a trend toward reduction of perinatal mortality, although there was no effect on neonatal morbidity⁴. Animal studies have documented redistribution of cardiac output in response to hypoxemia, with increased flow to the brain and decreased flow to other organs⁵. Doppler US studies of the human fetal circulation have shown that in fetuses

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with IUGR there is a significant reduction of middle cerebral arterial (MCA) pulsatility index when compared with those in normal fetuses⁶. At cordocentesis, a significant correlation has been observed between hypoxemia in fetuses with IUGR and an abnormal MCA pulsatility index^{8,9}. Results of several studies suggest that the MCAP/UA Doppler ratio is more accurate in the prediction of adverse perinatal outcome than UA Doppler US alone^{10,11,12}. Differences in study design, including the criteria for patient selection, the definition of adverse outcomes, different cutoff levels between normal and abnormal test results, and the small number of patients studied, make direct comparison of the studies difficult. Our study was an effort at establishing the role of UA and MCA Doppler ultrasound in predicting adverse perinatal outcome in clinically suspected IUGR pregnancies, and to determine the role of Doppler velocimetry in clinical management of such pregnancies.

MATERIALS AND METHODS

Study setting: - Department of radiology, Sri Siddhartha medical college, Tumkur, Karnataka department of radiology

Study design: - Prospective cross sectional study

Source of data: - Data for the study was collected from patients attending the department of Radio diagnosis Sri Siddhartha medical college, Tumkur.

Women referred for antenatal Doppler were included in the study if the following

Inclusion criteria were met:

Singleton pregnancy.

Fetal gestational age of 31 to 40 weeks with clinically suspected intrauterine growth retardation. (Estimated fetal weight <10th percentile for gestation)

‘The gestational age was based on ultrasound biometry performed before the 20th gestational week, when the LMP is uncertain or not known and early ultrasound before 13 weeks has not been performed’.

Exclusion criteria for the study included any pregnancy with Documented major congenital abnormality Multiple gestations Intrauterine death at the time of first Doppler examination. Present study included a total number of 40 cases meeting the inclusion criteria. Doppler US evaluation was performed following a detailed clinical history, US biometry, and assessment of amniotic fluid and placental maturity. 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 first Doppler ultrasound were used for analysis of perinatal outcome.

Doppler US Technique:

We used PHILIPS ENVISOR MACHINE with the transducer frequency of 3.5–5.0 MHZ. The patients were

allowed to rest for 10 to 15mins in a semi-recumbent position prior to commencing the ultrasound investigation. Fetal biometry was performed initially. The waveforms were obtained during fetal inactivity and apnoea. Umbilical artery Doppler flow velocity waveforms were obtained from a free loop of cord, and measurements taken when a clear waveform was acquired in the absence of fetal breathing or body movement. The Pulsatility index (PI) was measured, and the presence or absence of end-diastolic frequencies was noted. The PI was used as it continues to reflect changes in resistance with progressive absence of end-diastolic frequencies or reverse flow, and the values are normally distributed in the third trimester¹³. For MCA Doppler US, a transverse image of the fetal head was obtained at the level of the sphenoid bones. Color flow imaging was used to display the circle of Willis. The MCA in the near field was insonated about 1 cm distal to its origin from the internal carotid artery.

Outcome Criteria

Doppler US results were analyzed for prediction of perinatal outcome. Outcome variables included, Birth Weight, Perinatal death, Emergency CS for fetal distress, Low Apgar score (5 min Apgar score less than 7), Admission to NICU for complications of Low Birth Weight. Pregnancy was considered to have ‘‘Adverse outcome’’ when any of the following complications were present 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 Favourable when the above complications were absent. The outcome for each pregnancy was obtained by examining the labor ward records and neonatal intensive care unit records wherever appropriate. The UA Pulsatility index ratios were considered abnormal if the value was above the 95th percentile of previously published values for gestational age¹⁴. The MCA pulsatility index was considered abnormal if the value was below the 5th percentile of previously published values for gestational age¹⁴. The MCA/UA PI ratio (cerebro-placental ratio) is usually constant during the last 10 weeks of gestation. It is possible to use a single cut off value after 30th week because cerebral-umbilical Doppler ratio does not vary significantly between 30th and 40th weeks as reported by Wladimiroff *et al*¹⁵ who observed a significant differences in cerebroplacental ratio only between weeks 26-38. After 26th week, the statistical comparison showed no significant differences between the intervals considered. Arbeille *et al*¹⁶ also found the cerebral-placental ratio constant during the pregnancy and suggested 1 as the cut off value; all values below 1 were considered abnormal. Gramellini *et al*¹¹

also used a single cut off value of 1.08. Therefore, in our study a single cutoff value (1.08) was used, above which velocimetry was considered normal and below which it was considered abnormal.

Statistical analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Continuous data was represented as mean and standard deviation. The sensitivity, specificity, positive predictive value, negative predictive Value and diagnostic accuracy were determined for all Doppler measurements

RESULTS

Of the 40 pregnancies studied acceptable wave forms were obtained from all the 40 cases. 6 cases were

followed up with repeat Doppler. 52.5 % of the mothers had Pregnancy Induced Hypertension, 30% had anemia, 2 patient had Diagnosed Diabetes Mellitus at first Doppler examination. 27.5% had normal liquor and 72.5% had Oligohydramnios at first Doppler examination. 70% of cases had Grade III Placental maturity at the time of first Doppler Examination and 30 %had Grade II Placental maturity. Mean gestational age at the first Doppler US examination was 34.9 weeks \pm 3.57 weeks (2SD). 45% (n=18) fetuses had at least one abnormal outcome, of those; some (n=8) had more than one abnormal outcome. Remaining 22 fetuses had normal outcome. Of the 6 IUDs 4 cases had reversal of diastolic flow and 2 had absent diastolic flow. In all cases with reversal of diastolic flow, IUD of the fetus occurred within one week of diagnosis. And all the 4 cases were less than 32 weeks.

Table 1: Performance Characteristics of Doppler Indices

Doppler index	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
UA PI	90%	70%	75%	87.50%	80%
MCA PI	76.19%	47.37%	61.54%	64.29%	62.5%
MCAPI/UAPI RATIO	95%	90%	90.48%	94.74%	92.50%

Cerebroplacental ratio (MCA/UA PI Ratio) was most sensitive (sensitivity 95%). It was more sensitive than either UA PI (sensitivity 90%) or MCA PI (sensitivity 76.19%) alone in predicting any adverse outcome. Cerebroplacental ratio (MCA/UA PI Ratio) was most specific (Specificity 90%). It was more specific than either UA PI (Specificity 70%) or MCA PI (Specificity 47.37%). Cerebroplacental Ratio had highest Positive Predictive Value (PPV=90.48%) followed by UAPI (PPV=75%) and MCA PI (PPV=61.54%). Negative Predictive Value of Cerebroplacental Ratio was 94.74% when compared to 87.50% for UA PI followed by MCA PI (NPV=64.29%). Diagnostic accuracy of Cerebroplacental ratio (Accuracy=92.50%) was better than UA PI (Accuracy=80%) and MCA PI (Accuracy=62.5%) in predicting adverse outcomes.

DISCUSSION

When fetal growth retardation is diagnosed during the third trimester of pregnancy, the obstetrician must decide whether the fetus is "constitutionally" small or small as a consequence of impaired placental perfusion. Doppler flow velocity analysis can be valuable in resolving this question. The umbilical-placental and cerebral vascular beds are directly involved in the haemodynamic adjustments of fetal growth retardation. A Doppler index that reflects both of these areas can be useful for identifying fetuses with increased placental and/or decreased cerebral resistance. PI varies in relation to the intracranial artery considered, so it is important that the

artery be identified precisely and with certainty.¹⁷ In the evaluation of the fetal cerebral circulation, the MCA is the most accessible vessel and it can be easily located on colour dopler therefore the vessel of choice. It is the main branch of the circle of Willis and carries 80% of the blood flow to the ipsilateral cerebral hemisphere, a constant 3%–7% of cardiac output throughout gestation. Hence we used middle cerebral artery for the evaluation of fetal cerebral circulation. We studied the Doppler index of umbilical artery only after 30th week, because in agreement with Schulman¹⁸, Gramellini¹¹ we believe that it is difficult to define normal or abnormal umbilical flow velocity before 30th week, with the exception of absent end diastolic flow velocity after 20th week. Further more in most cases clinical issues concerning asymmetrical growth retardation (placental insufficiency) arise after the 30th week. It is possible to use a single cut off value for cerebroplacental ratio after 30th week because cerebral-umbilical Doppler ratio does not vary significantly between 30th and 40th weeks as reported by Wladimiroff *et al*¹⁵ who observed a significant differences in cerebroplacental ratio only between weeks²⁶⁻³⁸. After 26th week, the statistical comparison showed no significant differences between the intervals considered. Arbeille¹⁶ *et al* also found the cerebral-placental ratio constant during the pregnancy and suggested 1 as the cut off value; all values below 1 were considered abnormal. Several observational studies have explored cerebral redistribution (abnormal MCA Doppler US result and/or abnormal MCA/UA Doppler ratio for the prediction of

perinatal outcome in high-risk pregnancies^{10,11,15}. We chose incidences of perinatal death, emergency section for fetal distress, NICU admission for complication of low birth weight and low Apgar score as outcome variables in concurrence with previous studies done. However the choice of “Low 5 min Apgar score” could be debated as only about 15 % of newborns affected by cerebral palsy have low apgar scores³². Arduini and Rizzo¹⁰ studied the test characteristics of the pulsatility index from the UA, MCA, and RA to predict adverse perinatal outcome in 120 small-for-gestational age fetuses. In 46.7% (56 of 120) of fetuses, there was at least one of the following. Adverse outcomes: perinatal death, cesarean section for fetal distress, 5-minute Apgar score below 7, and asphyxia that necessitated admission to the neonatal intensive care unit for more than 48 hours. By using the first Doppler US result for analysis, the authors found that the UA/MCA pulsatility index ratio was the best test when compared with MCA, UA, and RA pulsatility indices (sensitivity, 89% vs 68%, 66%, and 43%; specificity, 94% vs 91%, 88%, and 91%). Gramellini D, Folli MC, *et al*¹¹ concluded that the cerebral-umbilical Doppler ratio provided a better predictor of small for gestational age newborns and adverse perinatal outcome than either the middle cerebral artery or umbilical artery alone. In fact, in predicting those newborns that were small for gestational age, the cerebral-umbilical ratio had a 70% diagnostic accuracy compared with 54.4% for the middle cerebral artery and 65.5% for the umbilical artery. The results were more encouraging for prediction of adverse perinatal outcome; diagnostic accuracy for the cerebral-umbilical ratio was 90%, compared with 78.8% for the middle cerebral artery and 83.3% for the umbilical artery. Fong KW *et al*³ studied Two hundred ninety-three small-for-gestational age fetuses (24–39 weeks at recruitment and US-estimated weight or abdominal circumference below 10th percentile) with Doppler US of the UA, MCA, and RA. They concluded that The MCA pulsatility index (PI), compared with the UA PI and RA PI, was more sensitive (72.4% vs 44.7% and 8.3%) but less specific (58.1% vs 86.6% and 92.6%) in predicting adverse outcome. Chan *et al*³³ studied 71 high-risk fetuses with weekly UA and MCA Doppler US examinations until delivery. In 15.5% (11 of 71) of fetuses, there was perinatal mortality or major morbidity, including major intracranial hemorrhage, periventricular leukomalacia, necrotizing enterocolitis, and major neurological handicap (follow-up data in 24 cases and up to only 2 years of age). By using the last Doppler US result for analysis, the UA/MCA resistance index ratio, compared with the UA systolic-to-diastolic ratio, was more sensitive (75% vs 64%) but less specific (60% vs 74%). UA Doppler US was a better

predictor for each of the individual adverse outcomes when separate analyses were performed. By using the first Doppler US results for analysis, the MCA/UA pulsatility index ratio had a higher Sensitivity, Positive predictive value for adverse perinatal outcome than did the MCA pulsatility index and the UA PI. Our findings agree with the results of the studies that have shown MCA/UA PI Doppler ratio to be more useful than UA PI or MCA PI in predicting adverse outcome^{10,11}.

In the literature, the criteria for cerebral redistribution vary, including an MCA pulsatility index below the 5th percentile¹⁰, MCA pulsatility index below 2 SD (26), UA/MCA pulsatility index ratio greater than 0.72³⁴, UA/MCA pulsatility index ratio above the 95th percentile¹⁰, UA/MCA resistance index ratio above 1.0³³, MCA/UA resistance index ratio below 1.0¹² and MCA/UA PI Ratio of less than 1.08¹¹.

CONCLUSION

Fetal Doppler indices, in particular ratios that include measurements obtained from the umbilical and cerebral circulation, help in the recognition of the compromised growthretarded fetus. In suspected IUGR, cerebroplacental Ratio (MCA/UA PI) is a better predictor of adverse perinatal outcome than an abnormal MCA PI or UAPI. Best results are obtained when we use MCA/UA PI Ratio, rather than PIs of middle cerebral artery and Umbilical artery separately. Presence of Absent/Reversal of diastolic flow in Umbilical artery is an ominous sign since it carries a grave prognosis and high mortality. Fetal Doppler indices provide information that is not readily obtained from more conventional tests of fetal well-being. Fetal Doppler velocimetry helps in the recognition of compromised growth retarded fetus thus allowing for timely interventions. It therefore has an important role to play in the management of the growth-retarded fetus.

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