

Intrauterine Growth Restriction and Doppler Waveform

Abstract

Background: Fetal growth restriction is defined as the estimated fetal weight less than 10th percentile for that gestational age on ultrasound study. There is no cure; management is reliant on a structured antenatal surveillance programme. Recent advances in ultrasound and Doppler have elucidated several mechanisms of growth restriction. Prediction of intrauterine hypoxia and acidemia can be done by Doppler study of fetal cardiovascular system.

Objectives: To analyze the uteroplacental and fetoplacental blood flow using Doppler ultrasound in FGR fetuses with reference to flow velocity and waveform indices.

Materials and Methods: This prospective study involved Doppler ultrasound examination of fetal cardiovascular system after 28 weeks gestation in 32 singleton pregnancies with fetal growth restriction.

Results: In the present study preeclampsia and maternal anemia were found to be the most important cause of FGR. Abnormal Doppler indices in umbilical and middle cerebral artery correlated statistically with lower birth weights, higher rate of caesarean delivery, oligohydramnios, low Apgar scores, perinatal death and higher admission to NICU. Absent and reduced end diastolic flow in the umbilical artery is associated with poor perinatal outcome. Cerebroplacental Ratio (pulsatility index of middle cerebral artery/pulsatility index of umbilical artery) < 1 is a very sensitive and specific sign of fetal compromise.

Conclusion: Abnormal Doppler waveforms within the umbilical and middle cerebral arteries are indicative of redistribution of cerebral blood flow in fetal hypoxia. If there is reduced or low blood flow during diastole in umbilical arteries, the fetal perfusion becomes intermittent and fetal hypoxia develops. The fetus redistributes the blood flow to vital organs like brain and kidneys and the pulsatility index of middle cerebral artery falls. The plausible explanation is sympathetic activation in a hypoxemic fetus leading to increased cerebral perfusion. With continued hypoxia the ductus venosus flow is also reduced and reversed.

Key words: Fetal Growth Restriction, Doppler, Middle cerebral artery, Ultrasonography and Umbilical Artery

Background

Fetal Growth Restriction (FGR) is defined by international fetal medicine experts with consensus on solitary parameters either Estimated Fetal Weight <3rd percentile for that gestational age, Abdominal Circumference <3rd percentile for that gestational age or absent umbilical artery end diastolic flow (1). FGR is the result of numerous pathologies that reduce fetal cell size and when these pathologies are very early and severe occurring before 20

weeks, there is also reduction in fetal cell number that is hypoplasia (early onset FGR). When these pathologies are late the cell number is normal but the cell size is small resulting in small babies whose cell number is normal but cell size is small (late onset FGR)(2).

Thus there are two types of fetal growth restriction-the early and the late onset FGR (2). In the first type there is suboptimal number of fetal cells and there is intrinsic or symmetrical fetal growth restriction. Intrinsic FGR arises from fetal conditions such as infections or chromosomal abnormalities. These fetuses grow slowly because their growth potential has been permanently affected by a severe insult in the first trimester and tend to grow in a low percentile in the gravidogram. Medical interventions like NO donors to improve the fetoplacental flow have little or no effect. Furthermore the fetal sympathetic system is immature before 20 weeks and is unable to employ any adaptive mechanisms.

In the late onset FGR the cause is usually extrinsic and the growth failure is due to an element outside the fetus-such as placental insufficiency, maternal malnutrition, preeclampsia, chronic maternal medical diseases. The fetal sympathetic system is mature and various adaptive mechanisms and redistribution of nutrients are employed at the fetomaternal interphase and subsequently a sonologically evident asymmetrical FGR develops.

According to recent UNICEF survey the incidence of FGR in developing countries is 25-30 %. Current challenges in the clinical management of FGR include accurate diagnosis of truly growth-restricted fetuses, selection of appropriate fetomaternal surveillance markers and optimizing the time of delivery. Fetal gestational age has to be assessed precisely because of risk of adding the problem of prematurity to growth restriction. If a decision is made to deliver a fetus prematurely because of fetal growth restriction, steroids to prevent acute respiratory distress syndrome of lungs and MgSO₄ for neuroprotection should be given. Trials have shown Doppler interrogation of Umbilical artery and Middle cerebral artery remain the most useful and practical tool in identifying fetuses at risk of adverse perinatal outcome, identifying around 88% of all adverse outcomes (3,4).

Materials and Methods

This prospective study involved Doppler ultrasound examination of the umbilical arteries at 28 weeks gestation in women with singleton pregnancies attending a routine scan. This study was approved by the ethical and research board. All women with no major fetal anomaly were offered the option of uterine artery Doppler evaluation. Written consent was obtained in all cases. A first trimester scan was done to measure Crown Rump Length (CRL) to date the pregnancy in all cases.

Study was carried out on 697 pregnancies in the Department of Radiology and Department

of Obstetrics and Gynecology at Saveetha Medical College and hospital, Chennai, India between 1 April 2015 and 31 December 2016 after getting written informed consent from participants in local language. Multiple Pregnancies and pregnancies with congenital anomalies were excluded. Detailed maternal factors like age, gestational age, parity, pre pregnancy body mass index, previous low birth weight, hemoglobin levels, chronic hypertension, gestational diabetes and previous preeclampsia were recorded. Placental problems like infarcts, retro placental calcifications, small placenta, and premature separation were noted. The ultrasound machines used for the study were PHILIPS HD11XE (Acuson, Mountain View, CA, USA); GE LOGICS7 Expert; Siemens Sonoline Acuson X150 (Siemens).

Pulsatility index rather than resistivity index was considered because PI describes the shape of the velocity waveform much better as it includes the area below the curve into the formula. Presence or absence of an early diastolic notch was recorded. 125 Hz high pass filter was used to eliminate signals from slowly moving tissues. The curved transducer (3.5-or 5-MHz) had spatial peak temporal average intensities $<100 \text{ mW/cm}^2$. Recordings for measurements were obtained in the absence of fetal breathing movements and fetal heart rate between 120 -160 beats per minute. The angle between the ultrasound beam and the direction of blood flow was always less than 30° .

Fetal growth restriction was defined as fetal weight below the expected weight in the customized population fetal growth charts (5). The patients of FGR were followed up by serial scans every weekly after 28 weeks and Doppler velocimetry studies of umbilical artery and middle cerebral arteries were done to identify the severity of uteroplacental insufficiency and brain sparing effect. Umbilical Artery Doppler measurements were obtained in the free loop. Figure 1 depicts the umbilical artery pulsatility Index. The normal flow is high velocity and low pulsatility Index {Figure 1(a)}. With increasing fetoplacental insufficiency the diastolic flow is reduced or absent {Figure 1 (b)}. If the fetoplacental perfusion is further compromised the blood starts flowing back from the fetus to the placenta. This is called as reversed diastolic flow in umbilical artery {Figure 1(c)}.

If there was absent or reduced flow in umbilical artery the fetal MCA Doppler evaluation was made by obtaining a fetal axial section including fetal thalamic nuclei on the scan. Color flow mapping was used to identify the circle of Willis. The measurement was made on the proximal third of the Middle Cerebral Artery where it is close to its origin in the internal carotid artery. Figure 2(a) and 2 (b) show the normal and decreased Pulsatility index of Middle cerebral artery. Ductus Venosus was seen by midsagittal plane of the fetal trunk. Color flow mapping was used to identify the alignment where the high velocity of the vessel can be seen at its narrow entrance. All Doppler waveforms were calculated only after obtaining three consecutive waveforms. Statistical analysis was done using MEDCALC.

Results

Doppler examination was done in 750 pregnancies. Satisfactory waveforms were obtained in 743 pregnancies (99%). During the study period, a follow up was available for a total of 697 pregnancies. A total of 32 (4.59%) pregnancies resulted in intrauterine growth restriction neonates out of total 697 pregnancies. There were no intrauterine deaths. There was a significant association off maternal age >34 with IUGR (Odds Ratio 241.5192, Confidence interval 72.0261 to 809.8671, Z statistic 8.889, p value <0.0001). Out of 32, 7 were early onset (<32 weeks) and 25 were late onset (>32 weeks). Thirteen cases of FGR had pregnancy-induced hypertension. In twelve cases there was severe and very severe anemia. In 4 cases there were placenta praevia. In two cases there was velamentous cord insertion. Out of 32 intrauterine growth restricted newborns, 31 survived beyond four weeks of life. Table 1 summarizes the maternal history variables associated with fetal growth Restriction. In 2 neonates (6.25%) no maternal cause of FGR could be identified

Color Doppler Findings were abnormal in 29/32 IUGR. All 3 pregnant women with normal Doppler study were induced for vaginal labor. One patient delivered vaginally and two had LSCS for Non Reassuring Fetal heart on CTG. Table 2 tells the average birth weight and number of days of Neonatal ICU admission for Normal and Abnormal Doppler study of Neonates.

Gestational age rather than weight was a predictor of neonatal mortality, as all IUGR babies beyond 34 weeks had no neonatal mortality. Table 3 brings up the Abnormal Color Doppler findings in IUGR fetuses (29/32). All these newborns were delivered by Caesarean Section.

Discussion

In our study there were 32 IUGR cases with high abnormal umbilical pulsatility Index in 29/32 pregnancies. Abnormal umbilical artery Doppler is characterized by reduced or absent forward flow in diastole and increased resistance (6). Absent end diastolic flow is noted when 75% of the placental bed has been obliterated (7). Reversed end diastolic flow is an end stage finding when the fetus is severely compromised and a decision to deliver the fetus has to be made.

Other indications of fetal Doppler are fetal anemia, fetal infections, feto-maternal hemorrhage, preeclampsia, fetal cardiac failure and pre and post fetal exchange transfusion in cases of red cell alloimmunisation (8) .The Doppler is done every 2 weekly from 26 weeks onwards. Abnormal umbilical artery Doppler is an indication of further workup of the degree of uteroplacental insufficiency; that is the fetal MCA Doppler assessment (9,10). If the PI of middle cerebral artery is reduced the ductus venosus and umbilical vein flow should also be assessed (11,12).

The fetal head sparing theory has been proposed in asymmetrical intra-uterine growth restriction, where the difference between normal head circumference and decreased

abdominal circumference is attributed to the fetus's ability to preferentially supply the cerebral, coronary, and adrenal and splenic circulations. In a situation of chronic fetal hypoxemia, the fetus redistributes its cardiac output to maximize the oxygen supply to brain by vasodilatation of the cerebral arteries and thus there is reduced pulsatility index of middle cerebral artery. This is to ensure a decreased left ventricular after load. Few recent studies have also emphasized the role of aortic isthmus Doppler study when Umbilical artery pulsatility index is high as this vessel directly measures the cardiac output in a compromised fetus. Aortic isthmus flow index is found to be increased in growth-restricted fetuses. Absolute end-diastolic (EDV) and mean velocities are usually decreased in the IUGR fetuses (13,14,15). Diagnosis of FGR is a challenge in routine obstetric practice. Vigilant surveillance, antenatal treatment with steroids to enhance maturity and optimizing the time of delivery can prevent fetal and neonatal complications(16).

Conclusion

Doppler waveform analysis is a useful biophysical marker. The study concludes that umbilical artery Doppler identifies a subset of FGR with a compromised fetoplacental circulation. When umbilical artery circulation is abnormal, fetal middle cerebral artery study is done. It is a grave situation when the fetus is shunting its flow to vital organs like brain. The fetus manifests as decreased pulsatility index of middle cerebral artery and alteration of cerebroplacental ratio. If middle cerebral pulsatility index is low it becomes an indication to assess the ductus venosus and umbilical vein flow. The Doppler study of IUGR in pregnancy can be useful in identifying fetus that needs increased surveillance to decide the time of delivery (16,17,18). There is an emerging role of ductus venosus and aortic isthmus Doppler study to identify the severely hypoxic fetuses. Strict criteria should be used when performing advanced fetal Doppler. The Doppler findings need to be correlated in context of clinical fetal growth assessment (19).

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Figure Legends

Figure 1 (a): Normal blood flow in umbilical artery

Figure 1(b): Doppler showing absent end diastolic flow in Umbilical artery: Absent end diastolic flow (AEDF): RI = 1

Figure 1(c): Reversed Diastolic flow in umbilical artery

Figure 2(a): Doppler velocimetry of the middle cerebral artery visualized from the circle of Willis and insonated immediately after its origin from the internal carotid artery.

Figure 2(b): Brain sparing effect in middle cerebral artery: An adaptive mechanism to the suboptimal intrauterine environment, in IUGR pregnancies

Table 1: Maternal history variables associated with intrauterine growth Restriction

Table 2: The average birth weight and number of days of Neonatal ICU admission for Normal and Abnormal Doppler study of Neonates.

Table 3: Abnormal Color Doppler findings in IUGR fetuses

272 Table 1

Factor	No of Cases
Preeclampsia	13/32
Maternal Anemia (severe and very severe)	12/32
Gestational Diabetes / Overt Diabetes	9/32
Maternal Age >34	19/32
Placenta Praevia	4/32
Velamentous Cord Insertion	2/32
No Maternal Cause Identified	2/32

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274 Table 2

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Doppler Study	No of Newborns	Average Birth Weight	Average Days In NICU
Normal Umbilical artery and normal Middle cerebral artery	3/32(9.38%)	1800 gms	38
Abnormal Umbilical artery and/or normal Middle cerebral artery	29/32(90.62%)	1760 gms	59

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279 Table 3

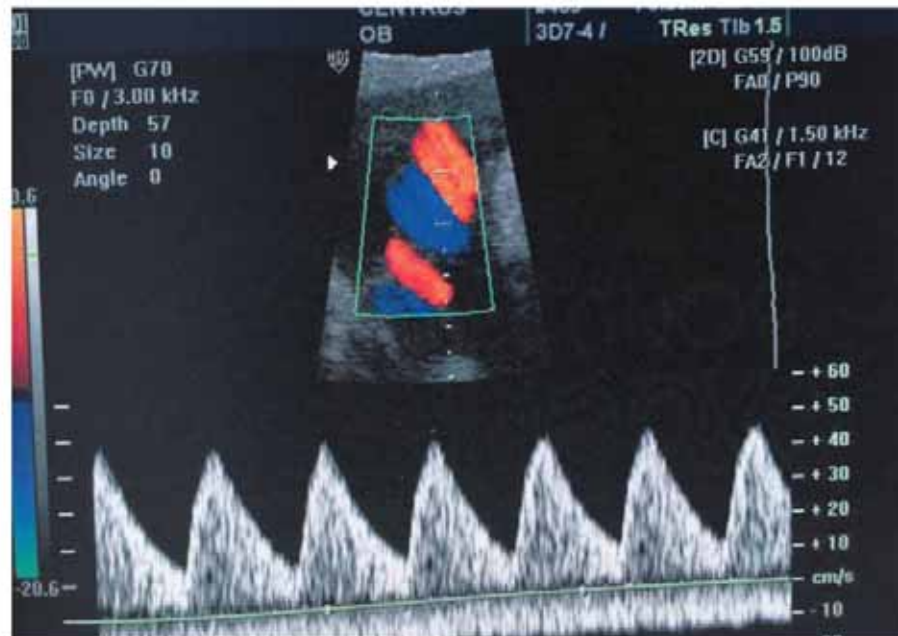
Doppler Derangement	No of Cases	Percentage	Average NICU Admission Days
Decreased End diastolic flow in Umbilical Artery with normal middle cerebral artery (CPR>1)	14/32	43.75%	46
Decreased End Diastolic flow in Umbilical Artery with abnormal Middle Cerebral Artery (CPR<1)	6/32	18.75%	58
Absent/reversed End diastolic flow in Umbilical Artery with Normal Middle Cerebral Artery (CPR >1)	1/32	3.13%	67
Absent/reversed End diastolic flow in Umbilical Artery with Abnormal Middle Cerebral Artery (CPR <1)	7/32	21.87%	66
CPR Ratio <1 with Decreased Flow in Ductus Venosus	1/32 (Early neonatal Death)	3.13%	Died on Day 4 Necrotizing enterocolitis)

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282 Figure 1(a):

Figure 1 (a):Normal blood flow in umbilical artery

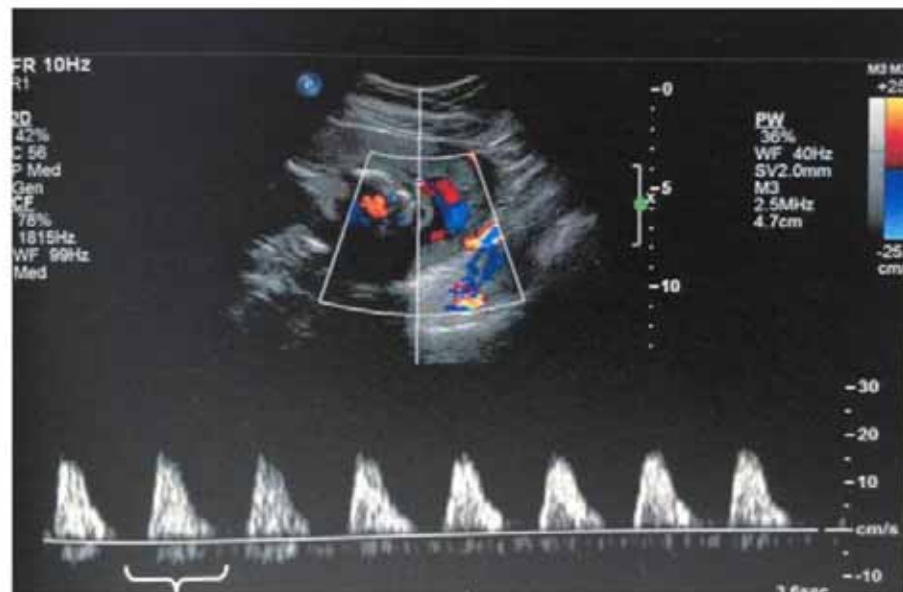


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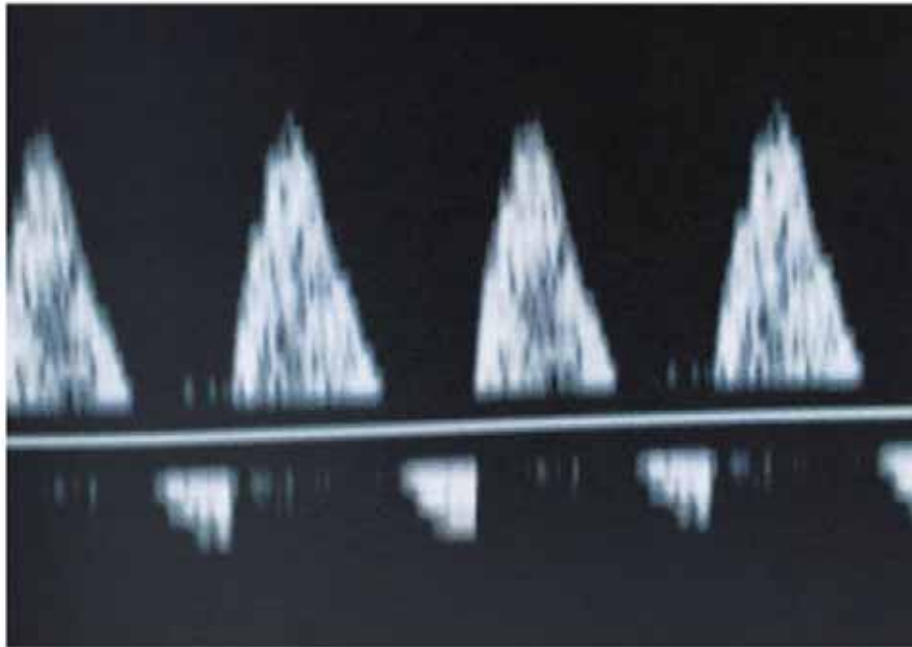
285 Figure 1(b)

Figure 1(b):Doppler showing absent end diastolic flow in Umbilical artery : Absent end diastolic flow (AEDF): RI = 1



288 Figure 1(c):

Figure 1(c):Reversed Diastolic flow in umbilical artery

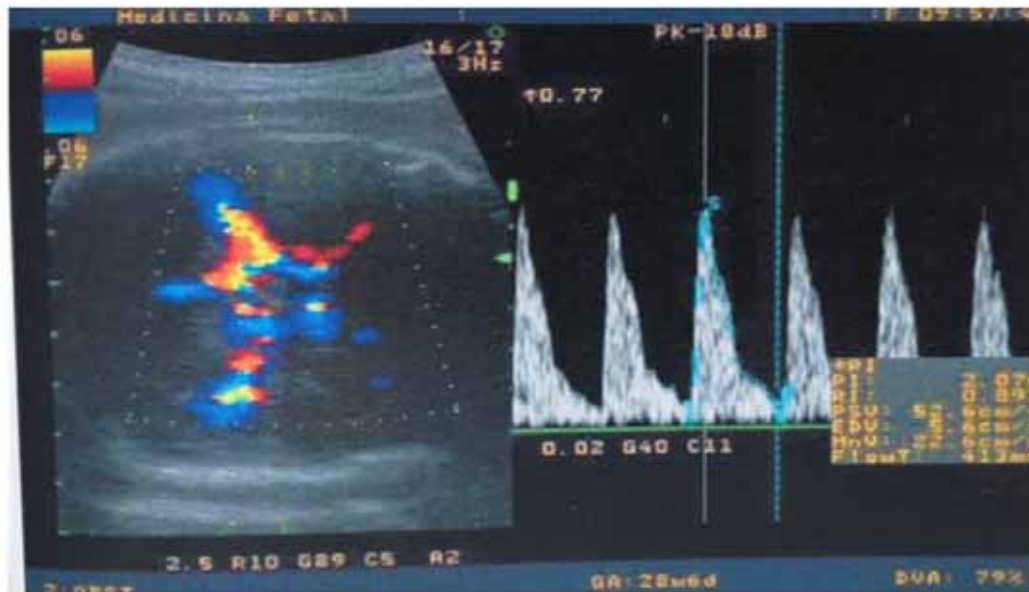


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291 Figure2 (a):

Figure 2(a): Doppler velocimetry of the middle cerebral artery visualized from the circle of Willis and insonated immediately after its origin from the internal carotid artery.



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Figure 2(b): Brain sparing effect in middle cerebral artery: An adaptive mechanism to the suboptimal intrauterine environment, in IUGR pregnancies

