RESEARCH ARTICLE

Umbilical Artery Doppler Flow Velocimetry in Intrauterine Growth Restriction and its Relation to Perinatal Outcome

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Abstract

Materials and methods: A retrospective data analysis was conducted on antenatally detected intrauterine growth restricted (IUGR) fetuses born between 26 and 38 weeks of gestational age with high resistance Doppler flow (HRDF) and absent or reversed end-diastolic flow (AREDF), excluding multiple gestations. The data was collected using an obstetric information management system and evaluated. About 152 cases were identified over a 5-year period in our tertiary referral center. The patients were divided into two groups: those with elevated systolic/diastolic ratio group of 95th or more percentile ($n = 123$, 81%) and those with absent/reversed end-diastolic flow ($n = 38$, 19%). Maternal characteristics and perinatal outcomes of these groups were comparatively analyzed. Results of umbilical artery Doppler showed a significant correlation with the perinatal outcome. The poor perinatal outcome was 26% in those with absent or reversed diastolic flow in Doppler, as compared to only 1% in those with increased Doppler flow. Using Fischer's exact test, the result is statistically significant ($p < 0.05$). Predictors of nonsurvival were the presence of reversed end-diastolic flow and preterm <30 weeks of gestation. Nonsurvivors had a significantly lower gestational age at diagnosis and delivery.

Conclusion: Antenatal umbilical artery Doppler is shown as a significantly efficient marker in predicting perinatal outcomes in IUGR fetuses. Severely abnormal umbilical artery blood flow poses a significant risk for pregnancy, while perinatal mortality is also dominated by gestational age at diagnosis and delivery.

Keywords: Intrauterine growth restricted, Preterm, Ultrasonography, Umbilical Doppler.

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Introduction

Suboptimal intrauterine growth affects up to 10% of pregnancies and confers an increased risk of perinatal morbidity and mortality. Current antenatal detection of IUGR is reported to be between 25 and 36%.[1] The risk of stillbirth in prenatally identified IUGR is 1%. Pregnancies with unidentified IUGR carry over an eightfold increase in the risk of stillbirth when compared to pregnancies without IUGR. So, when IUGR is diagnosed prenatally, increased surveillance and timely delivery aim to improve perinatal outcome in IUGR, balancing the risk of antepartum stillbirth by remaining *in utero* and iatrogenic prematurity potentially causing significant morbidity or neonatal death by too early intervention.

Doppler's velocimetry has been extensively used in the prenatal diagnosis of IUGR. Blood flow in numerous vessels, especially in the umbilical artery, has been investigated to predict fetal condition. The increased placental vascular resistance is reflected as a decreased diastolic phase of umbilical artery waveform (HRDF); the further end-diastolic flow of the umbilical artery vanishes and ultimately reverses in progressively worsened condition (AREDF), which is a strong indication of placental insufficiency. It is a significant risk factor for progression to fetal acidosis, fetal distress, preterm delivery, low appearance, pulse, grimace, activity, and respiration (APGAR) scores, and perinatal death.

Objective

To evaluate the merit of umbilical artery Doppler as a predictor of perinatal outcome in IUGR fetuses.

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Materials and Methods

A retrospective data analysis was conducted on antenatally detected IUGR fetuses born between 26 and 38 weeks of gestation with Doppler changes in the umbilical artery. The data was collected using an obstetric information management system and evaluated. About 143 singleton pregnancies were identified over a 5-year period in our tertiary referral center. IUGR was prenatally defined as an abdominal circumference in ultrasound below the 10th centile or estimated fetal weight below the 10th centile for that gestational age after confirming the dating of pregnancy with first trimester crown-rump length. Multiple gestations, anomalous

fetuses, congenital infections, inborn errors of metabolism, and birth weight above the 10th centile were excluded.

All prenatal ultrasound examinations in this series were performed by a single observer using GE Voluson P8, equipped with a 5 MHz transducer. Written consent was obtained from all the patients before performing ultrasound examinations, which explained clearly the nature of the examination. After fetal biometric measurement and quantitative measurement of amniotic fluid, umbilical artery Doppler measurement was performed on free-floating loops of the umbilical cord, which were recorded from five or more consecutive waveforms with the angle of insonation as close to 0° as possible in the absence of fetal movements and if required, voluntary suspension of maternal breathing for few seconds. The mechanical and thermal indices were maintained below one. The umbilical artery pulsatility index and resistance index were calculated by the ultrasound system using peak systolic and end-diastolic velocities.

Accordingly, the cohort was divided into two groups. Group I with HRDF, which is reflected as a decreased diastolic phase of the umbilical artery, and group II with AREDF, wherein the end-diastolic flow of the umbilical artery vanishes and ultimately reverses in the progressively worsened condition. The data obtained were entered in excel format, and analysis was done using Statistical Package for the Social Sciences software.

The maternal characteristics like age, parity, gestational age, and associated antenatal complications in each group were analyzed and compared. The outcome measures like mode of onset of labor, mode of delivery, birth weight, APGAR scores, and umbilical artery pH were analyzed. The outcome in terms of perinatal mortality, which includes stillbirth and neonatal deaths before the time of first discharge from the hospital, and perinatal morbidity in terms of duration of stay in the neonatal intensive care unit (NICU) and neonatal complications like periventricular leukomalacia (PVL), intraventricular hemorrhage (IVH), bronchopulmonary dysplasia (BPD), respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC), and transient tachypnea of the newborn (TTN) were analyzed. Statistical analysis was done using a *t*-test, and probability values (*p*-values) <0.05 was considered significant.

Observation

A total number of 143 cases of IUGR with Doppler changes that fit into the selection criteria were identified and divided into two groups. Out of the 143 cases, 107 (74.8%) had HRDF and were categorized as group I, and 36 (25.2%) belonged to group II, whose umbilical artery Doppler showed AREDF.

Maternal and obstetric characteristics like age, parity, booking status, and gestational age in each group are shown in Table 1. The antenatal complications and systemic disorders associated were analyzed and compared in both groups and are shown in Table 2.

Intrauterine fetal death occurred in five cases (3.5%). In one case in group I had severe early-onset preeclampsia and induction of labor at 28 weeks (560 gm). Four were in group II (two cases of severe preeclampsia with abruption, one case had severe preeclampsia (660 gm at 26 weeks), and one case was antiphospholipid antibodies (APLA) positive (500 gm at 29 weeks).

Labor was spontaneous in eight cases (5.6%), augmented in seven (4.9%), and induced in 98 (68.5%), which were for maternal and fetal indications. Mode of delivery was by cesarean section in 55 (88%) cases, and 88 (62%) were delivered vaginally, out of which normal delivery was 35 (48%), instrumental in 45 (51%), and eight (0.9%) were assisted breech deliveries. The neonatal data at delivery are summarized in Table 3.

Out of the 143 cases, 127 (88.8%) were live-born. There was a total of 86 admissions to the NICU. About 39 babies were without any morbidity and required no admission to the NICU. There was a total of 11 stillborns, out of which 10 belonged to group II with AREDF, and one was from group I with HRDF. Stillbirths occurred

Table 1: Maternal and obstetric characteristics in group I and group II

Maternal characteristics	*Group I (HRDF)*	*Group II (AREDF)*
Age ≤19	4 (3.7%)	2 (5.5%)
>35	4 (3.7%)	4 (11.1%)
21–26	44 (41%)	14 (39%)
Primipara	71 (66.3%)	30 (83%)
Multigravida	36 (33.6%)	6 (17%)
Gestational age <28 weeks	nil	2 (5.5%)
28–32 weeks	17 (15.8%)	22 (61%)
33–36 weeks	67 (62.6%)	13 (36%)
≥37 weeks	23 (21.4%)	nil
Booked at our center	71 (66%)	3 (11%)
Booked outside	36 (34%)	33 (89%)

Table 2: Comparison of the significant antenatal complications in the two groups

Variable	*Group I*	*Group II*
Severe preeclampsia	35 (33%)	12 (33.3%)
Eclampsia	3 (2.8%)	3 (8.3%)
Hemolysis, elevated liver enzymes, low platelet count syndrome	2 (1.9%)	4 (11.1%)
Gestational hypertension	2 (1.9%)	nil
Abruptio placenta	6 (5.6%)	2 (5.5%)
Severe anemia	1 (0.9%)	1 (2.7%)
Moderate anemia	13 (12.1)	nil
Gestational diabetes	13 (12.1%)	nil
Preexisting type 1 diabetes	nil	1 (2.8%)
Associated cardiac disease	7 (6.5%)	1 (2.8%)
APLA positive	1 (0.9%)	2 (5.5%)

Table 3: Neonatal data at delivery for those in HRDF group and those in AEDF group

Neonatal factors	*Group I*	*Group II*
Still born	1 (0.9%)	10 (28.7%)
Mean birth weight	1.93 kg	1.14 kg
APGAR score <6 in live birth 1 and 5 minutes	13 (12.3%) 3 (2.8%)	8 (36.4%) 3 (13.6%)
Arterial pH ≥7 to <7.2	16 (15.2%)	1 (4.5%)
<7	4 (3.8%)	9 (41%)
Gender male	56 (52.8%)	18 (50%)
Female	51 (47.6%)	18 (50%)

at gestational ages between 29 and 32 weeks, and birth weights ranged from 500 gm to 1.26 kg. In one case, HRDF was detected at 32 weeks and was not willing to any intervention and progressed to REDF and had a stillbirth at 34 weeks.

The average duration of stay in NICU was 8 days. The duration of stay was ≤5 days in 24 babies (29%), 6–10 days in 25 (30%), 11–30 days in 23 (28%), and >30 days in six cases (7.2%). The major contributors to morbidity in relation to gestational age were RDS (22% in group I versus 64% in group II), sepsis (3.8% versus 16%), and extremely low birth weight (3.6%). Relatively infrequent but severe morbidity requiring a longer duration of stay in NICU were NEC (1%), IVH (1%), persistent hypertension (1%), and germinal matrix hemorrhage (1%).

Other minor causes requiring admissions for a shorter period were TTN (13%), hypoglycemia (5%), hypocalcemia (5%), hyperbilirubinemia (4.8%), and 15.6% were admitted for preterm care.

There were five neonatal deaths during the original neonatal admissions. One (0.01%) neonatal death in group I as parents were not willing to further treatment, and the mother had severe preeclampsia. There were four (0.1%) neonatal deaths in group II. The cause of death in case one was RDS with sepsis, and in case two, the baby died of chronic lung disease on the 24th day. Case three was taken to lower-level care, and the baby died after 3 days. In case four, there were REDF changes in Doppler and it weighed 850 gm. No active intervention was done as the parents were not willing for it.

Perinatal mortality, which includes stillbirth and early neonatal deaths in group I, was 1.8%, and in group II was 38.9%, and the difference was found to be statistically significant ($p = 0.0001$), calculated using a proportion test of probability. Perinatal death more commonly occurred in pregnancies with severe growth restriction (estimated fetal weight < 3rd percentile) and in mothers who had preeclampsia with severe features.

Discussion

In our retrospective study of 143 cases of IUGR with Doppler changes, we found that there were 10% of cases in the age group >35 years in the AREDF group compared to 3% of cases in the HRDF group, though the association was not statistically significant. The majority of the cases were young mothers in the age group of 21–26 years (40%), and parity distribution in our study showed a preponderance of IUGR to primipara and age group 21–26 years. A similar observation was observed in the study by Malik and Saxena.[2] Majority of the women in both the group were primipara, 66% in group I and 83% in group II.

The majority of (63%) of the cases in group I belonged to the gestational age of 33–36 weeks, whereas in group II majority (60%) belonged to much earlier gestation of 28–32 weeks. In early onset IUGR, expectant management was done with close monitoring with Doppler till there was absent or reversed flow in the umbilical artery blood flow, so the fetus became salvageable. Early onset IUGR has severe Doppler changes and a poorer prognosis; hence close follow-up is needed.

Preeclampsia in its severe form was the most common antepartum complication associated with both groups. The association was higher (50%) in group II and 40% in group I. A major determinant of adverse perinatal outcomes was maternal hypertension, the presence of which shortened the diagnosis to delivery interval and more preterm deliveries.

Our findings coincide with the European multicenter trial of randomized umbilical and fetal flow in Europe (TRUFFLE) study[3] by Lees et al. Other associated antepartum complications that may have contributed to the IUGR were maternal anemia (13%) and maternal cardiac disease present in eight cases (9%), though the association is not statistically significant. Gestational diabetes was associated with 13% of IUGR, which emphasizes that gestational diabetes can lead to IUGR.

Four out of five antepartum deaths were from group II, which shows that early diagnosis of IUGR, close monitoring with Doppler, and timely intervention can improve the outcome of these fetuses. Growth restriction and intervention trial (GRIT),[4] which comprises 548 women from 13 European centers, showed outcomes for neonatal morbidity and mortality, which were similar between the immediate and deferred delivery groups, but antenatal surveillance was not standardized. Thus, by improving antenatal surveillance, as in TRUFFLE,[3] where babies were born 1 week earlier than GRIT and were approximately 300 gm lighter, a reduction in antenatal mortality was achieved without worsening neonatal outcomes. Also, antepartum deaths were caused either by a decision for nonintervention because the prognosis was considered too poor or unanticipated.[3]

In our study, 90% (10 out of 11) of the stillbirths happened in group II, and most of them were early onset IUGR and were referred to our center after the onset of absent or reversal of umbilical artery Doppler flow in the umbilical artery. The decision to deliver them by cesarean versus vaginal route depended in our setting on the willingness of the parents to continue neonatal care in a high-dependency unit.

Adverse perinatal outcomes in terms of perinatal mortality and severe morbidity were significantly higher in the AREDF group. Lecarpentier et al.[5] showed similar adverse outcomes with the AREDF group.

An increased pulsatility of the ductus venosus (DV) is associated with fetal acidosis and hypoxemia. The DV pulsatility index reflects impaired myocardial relaxation and reduced compliance of the distended venous system. In our study, we did not wait for the changes in DV, as it is associated with the poor perinatal outcome as shown by Lecarpentier et al.[5] AREDF flow pattern itself reflects a more advanced hemodynamic compromise, hence in our center, delivery before DV changes set in was instituted. Thus, overall perinatal mortality was far less (14%) than in other quoted studies. It was much less if delivered before the absence or reversal of diastolic flow in the umbilical artery sets in.

Respiratory distress syndrome (RDS) was the most commonly associated morbidity, which was 22% in group I and 64% in group II, which was statistically significant ($p < 0.05$). Wang et al.[6] analyzed the perinatal complications in AREDF in the umbilical vessel. It showed that the relationship is still controversial. Gonzalez et al.[7] performed a retrospective cohort study of 151 pregnancies and found umbilical artery AREDV was associated with a significantly increased incidence of RDS.

Intraventricular hemorrhage (IVH) is an important cause of morbidity and mortality in very low birth weight infants. A study done by Vergani et al. showed a significant association between IVH and abnormal umbilical artery Doppler. In our study, we report one case of IVH grade III, which belonged to the HRDF group, and there was one case of germinal matrix hemorrhage in the AREDF group that required a longer duration of stay in the NICU.

Pathogenesis of NEC is not well understood, and factors thought to increase the risk include prematurity, intestinal ischemia, enteral feeding, and bacterial colonization. Recent studies have

shown IUGR with abnormal Doppler may be an additional risk factor for NEC. In our study, we had one case of NEC, and the association did not prove to be significant. Hartung et al. found a statistically significant increase in intestinal complications in the AREDV group. Wang et al. concluded that placental insufficiency may predispose to NEC but is not the primary cascade of events leading to NEC.

Periventricular leukomalacia (PVL) is the most important determinant of neurologic morbidity in premature neonates. Several studies failed to find an association between AREDV and PVL. In our study, there were no cases of PVL. Similarly, in our study, there were no cases of BPD, which is the most common respiratory complication in premature infants. Hartung et al. and Eronen et al. found a statistically significant increase in BPD in neonates with AREDV compared to control groups. In our study, we found that sepsis and RDS were the most common cause of prolonged duration of hospital stays (>30 days).

A larger study in Europe by Karsdorp et al. assessed the outcome of antenatal Doppler velocimetry and indicated that the perinatal mortality was 40% for AEDV and even up to 70% for REDV. In our study, we report a perinatal mortality of 0.18% in the HRDF group and 38.8% in the AREDF group, with statistically significant differences.

Conclusion

In summary, perinatal death more commonly occurred in pregnancies with the AREDF group and in early onset IUGR as in the prospective observational trial to optimize pediatric health in intrauterine growth restriction (IUGR) (PORTO Study)[1] study. Preeclampsia with severe features was associated with >50% of the cases.

Screening and early detection of preeclampsia would prevent IUGR in these cases. Prompt diagnosis, counseling, and early referral will help reduce perinatal mortalities and morbidities.

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