



ROLE OF THIRD-TRIMESTER DOPPLER VELOCIMETRY IN PREDICTING PERINATAL OUTCOME IN HIGH-RISK PREGNANCIES: A PROSPECTIVE STUDY.

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Abstract

Background: Third-trimester Doppler velocimetry offers a timely pathophysiological information on the fetal health in high-risk pregnancy, in which conventional surveillance usually indicates compromising health at too late a stage. This prospective study compared uterine, umbilical, and middle cerebral artery Doppler measurements with perinatal outcomes, in 120 cases of high risks, in a tertiary care centre.

Methods: Observation of singleton pregnancies (30-34 weeks) in the hospital with the risks of hypertensive disorders and growth restriction. Doppler indices were measured according to the gestational norms; composite adverse outcome was measured as preterm delivery, low birth weight, low Apgar, NICU stay 24h, or perinatal death.

Results: Abnormal Doppler was found in 40% of cases where multivessel involvement predicts 80% composite adverse outcome compared to 12.5% when normal. Abnormal umbilical artery was associated with increased preterm (55.6%), low birth weight (72.2%), and perinatal death (16.7%).

Conclusions: Multivessel third-trimester Doppler is an effective stratification of perinatal risk and needs to be integrated with clinical care to maximize the time of action and minimize morbidity in resource-constrained environments.

Keywords: Doppler velocimetry, high-risk pregnancy, perinatal outcome, cerebroplacental ratio, umbilical artery

Introduction

Doppler velocimetry has now become a major part of fetal monitoring in the high-risk pregnancy, specifically in the third trimester when the effects of uteroplacental insufficiency have become the most severe.[1] Impaired placental perfusion and adverse perinatal outcomes like stillbirth, neonatal intensive care unit (NICU) admission, and neurodevelopmental disability in the long term are related to high-risk pregnancies like those complicated by preeclampsia, intrauterine growth restriction (IUGR), diabetes, and chronic high blood pressure.[2] Traditional methods of fetal well-being such as non-stress test and biophysical profile give late information, usually when a fetus has undergone a considerable degree of compromise, but Doppler ultrasound gives earlier, pathophysiology-like information about the fetus brain circulation[3].

Downstream resistance is assessed by umbilical artery Doppler indices, and abnormal waveforms of either increased pulsatility index (PI), Absent End-Diastolic Flow (AEDF), or Reversed End-Diastolic Flow (REDF) are associated with chronic hypoxia and adverse perinatal outcome.[4] A number of prospective studies and meta-analysis of high-risk cohorts have shown that application of umbilical artery Doppler when combined with proper clinical intervention can decrease perinatal mortality, stillbirth, the rates of intrapartum fetal distress and hypoxic encephalopathy.[5] Middle cerebral artery (MCA) Doppler works together with umbilical artery to predict composite adverse neonatal outcomes; a decrease in MCA PI indicates a redistribution of blood flow, which is compensated by umbilical artery indices, among others.[6]

In more recent studies, composite Doppler parameters like the cerebroplacental ratio (CPR) and assessment of venous flow, especially the ductus venosus have been demonstrated to serve as an adjunctive risk stratifier in fetuses with placenta insufficiency.[7] The presence of abnormal ductus venosus waveforms is fairly predictive of fetal acidemia, low Apgar scores and perinatal death and are frequently regarded as late yet vital to the timing of delivery in situations of severe growth restriction.[8] Nevertheless, even though they have been shown to be useful, a high degree of heterogeneity exists in regard to the frequency of performing Doppler studies, the vessels regularly assessed, and the incorporation of the results into decision-making in various clinical environments, particularly in low- and middle-income nations. [9]

The use of 3rd trimester Doppler is often limited to a subset of the most high-risk women in resource constrained settings and little local data has been collected about its predictive value and influence on perinatal outcome.[10] According to Indian and other regional studies, abnormal umbilical artery and MCA Doppler results are very sensitive and specific in predicting IUGR, low birth weight, low Apgar score, NICU admission and perinatal mortality, but practice patterns and intervention threshold vary across institutions.[11] Practical prospective assessments that incorporate uterine artery, umbilical artery, and MCA Doppler in late third trimester and compare these indices with well-defined perinatal outcomes including composite adverse neonatal outcome, operative delivery because of fetal distress, and perinatal mortality are particularly required[11]

The current prospective experiment is intended to determine the role of the third-trimester Doppler velocimetry in the prediction of perinatal outcome in women with high-risk pregnancy in a tertiary care unit. The proposed study will produce a context-specific evidence base by systematically comparing the common Doppler parameters of the uterine artery, umbilical artery and middle cerebral artery with maternal and neonatal outcomes to generate evidence that can be used to refine surveillance protocols and further optimize the timing of intervention to enhance perinatal survival and minimize short-term morbidity. The results can be used to create viable Doppler-based algorithms that can be used in practice in a busy obstetric unit and become a part of standardized guidelines that need to be adhered to in monitoring high-risk pregnancies during the ante-partum period with Doppler devices.[12]

Material method

The study is hospital-based prospective observational study that was carried out in the Department of Obstetrics and Gynecology of a tertiary care teaching hospital during 18 months. Pregnant women who came to the antenatal clinic or were hospitalized in the antenatal ward were assessed on the eligibility in the early third trimester. High-risk pregnancy was predetermined by departmental criteria and comprised of the following: hypertensive disorders of pregnancy, fetal growth restriction, clinically or ultrasonographically, oligohydramnios, gestational diabetes mellitus, the past experience of intrauterine death or stillbirth, and bad obstetric history (two or more abortions and/or past early neonatal death). Singleton pregnancies in women with a gestation period of 30-34 weeks confirmed by a credible menstrual history and first or second trimester ultrasound were invited to take part having undergone detailed counselling and signed an informed consent. Major fetal congenital anomalies, multiple gestation, pregnancies with placenta previa or morbidly

adherent placenta, first presentation women who were already in established labour and women with incomplete follow-up data were all excluded.

One hundred and twenty qualified women that met inclusion and exclusion criteria were recruited successively. The predefined proforma was used to enter baseline demographic and obstetric variables, such as maternal age, gravidity, residence, booking status, gestational age at enrolment and targeted risk factors. Gestational age at enrolment and fetal biometry were measured with the help of a standard obstetric ultrasound device with a 3.55 MHz curvilinear transducer. All the included women were subjected to thorough third-trimester Doppler velocimetry. The same ultrasound apparatus was used in doing Doppler examination by experienced and trained sonologist on obstetric Doppler, with the mother in a semi-recumbent position, during fetal quiescence and without maternal breath-holding. The angle of insonance was kept lower than 30 degrees and at least three smooth waveforms were obtained and averaged on each vessel.

The vessels that were researched were uterine artery, umbilical artery, and fetal middle cerebral artery (MCA). Sampling of uterine artery was done at the apparent crossover point with the external iliac artery on each side and the lower pulsatility index (PI) of the two sampled was measured; also the appearance of early diastolic notch was recorded. A free-floating loop of cord was sampled using the umbilical artery that did not use any areas of cord insertion or compression. The MCA was sampled at a transverse view of the fetal head at the point just above the thalami, just above the point of its origin at the circle of Willis. PI was also gotten and resistance index (RI) and systolic/diastolic (S/D) ratio calculated where necessary by the machine software. Cerebroplacental ratio (CPR) was estimated by calculating the ratio of MCA PI/ umbilical artery PI. The understanding of doppler indices was done based on gestation age specific reference ranges that were accepted in the departmental practice. Doppler of umbilical artery was termed to be abnormal when PI or RI exceeded 95th centile at gestational age, or none or reversed end-diastolic flow existed. The lowest percentile of PI was taken as abnormal, which is 5th centile, which is considered brain-sparing by MCA Doppler. CPR was deemed to be abnormal when it fell below the 5th centile or a predetermined cut-off (e.g. below 1.0) per locally accepted norms. Uterine artery Doppler was considered abnormal when mean PI exceeded the 95th centile and/or when either artery had a persistent early diastolic notch. The definition of any abnormal Doppler was that of at least one parameter (uterine artery, umbilical artery, MCA or CPR) being abnormal. The cases were also grouped into 4 general Doppler statuses namely all indices normal, isolated uterine artery abnormal, isolated umbilical/MCA/CPR abnormal and multiple-vessel abnormal.

The first instance of Doppler measurement was done and thereafter the women were treated as per the departmental procedures and not changed just to be used in the research. Subsequent Doppler or other surveillance tests (non-stress test, biophysical profile) frequency and subsequent mode and timing of delivery decisions were made by the treating obstetrician considering the general clinical picture. Prospective follow-up was done to delivery and early neonatal period on all the enrolled pregnancies. Gestational age at birth, delivery mode, indication of caesarean section, birth weight of the neonatal, sex, and the Apgar scores were entered at birth, 1 and 5 minutes of delivery respectively. Outcomes of neonatal care such as resuscitation, neonatal intensive care unit (NICU) and neonatal duration of stay, and any early neonatal mortality at 7 days of life were recorded. There was also the record of stillbirths (antepartum or intrapartum). The predefinition of composite adverse perinatal outcome was the criterion of any of the following: preterm birth less than 37 weeks, birth weight of less than 2500 g, 5-minute Apgar score of less than 7, hospitalization to the NICU longer than 24 hours, or perinatal death (stillbirth or early neonatal death).

Results-

The mean age of the mothers enrolled in the study was $27.8 \pm 4.527.8 \pm 4.5$ years. Among the 120 participants, 46 (38.3%) were multigravida (gravida ≥ 3), while 40 (33.3%) were primigravida. A majority of the participants, 72 (60.0%), resided in rural areas. More than half of

the mothers, 68 (56.7%), were booked in the first trimester of pregnancy. The mean gestational age at the time of enrolment was $32.4 \pm 1.832.4$ pm $1.832.4 \pm 1.8$ weeks.

Table 1. Baseline maternal characteristics (n = 120)

Variable	Value
Mean maternal age (years) $\pm$ SD	27.8 ± 4.5
Gravida ≥ 3	46 (38.3%)
Primi gravida	40 (33.3%)
Rural residence	72 (60.0%)
Booking in first trimester	68 (56.7%)
Mean gestational age at enrolment (weeks) $\pm$ SD	32.4 ± 1.8

Hypertensive disorders and fetal growth restriction were the predominant risk factors, present in 40% and 25% of women respectively, with many patients having multiple co morbidities.

Table 2. Distribution of risk factors among study population (n = 120)

Risk factor*	Number (%)
Hypertensive disorders of pregnancy	48 (40.0%)
Fetal growth restriction (clinical/USG)	30 (25.0%)
Oligohydramnios	18 (15.0%)
Gestational diabetes mellitus	14 (11.7%)
Previous stillbirth / IUD	10 (8.3%)
Bad obstetric history (≥ 2 abortions / neonatal death)	20 (16.7%)

*Many patients had more than one risk factor.

Abnormal Doppler findings were noted in 30% of umbilical artery assessments, 26.7% of MCA studies, 25% of CPR measurements, and 35% of uterine artery evaluations, resulting in at least one abnormal Doppler parameter in 40% of case

Table 3. Third trimester Doppler findings (n = 120)

Doppler parameter	Normal n (%)	Abnormal n (%)
Umbilical artery PI / RI	84 (70.0%)	36 (30.0%)
Middle cerebral artery PI (brain-sparing)	88 (73.3%)	32 (26.7%)
Cerebroplacental ratio (CPR)	90 (75.0%)	30 (25.0%)
Uterine artery notching / elevated PI	78 (65.0%)	42 (35.0%)
Any abnormal Doppler (any vessel)	72 (60.0%)	48 (40.0%)

Pregnancies with abnormal umbilical artery Doppler had substantially higher rates of preterm delivery (55.6% vs 21.4%), low birth weight (72.2% vs 23.8%), caesarean section for fetal distress (50% vs 16.7%), low 5-minute Apgar score (33.3% vs 7.1%), NICU admission (55.6% vs 11.9%), and perinatal death (16.7% vs 2.4%) compared with those with normal umbilical artery indices.

Table 4. Perinatal outcome in relation to umbilical artery Doppler (n = 120)

Outcome	Normal UA Doppler (n = 84)	Abnormal UA Doppler (n = 36)
Mean gestational age at delivery (weeks) $\pm$ SD	38.0 ± 1.6	35.6 ± 2.1
Preterm birth <37 weeks	18 (21.4%)	20 (55.6%)
Birth weight <2500 g	20 (23.8%)	26 (72.2%)
LSCS for fetal distress	14 (16.7%)	18 (50.0%)

5-min Apgar <7	6 (7.1%)	12 (33.3%)
NICU admission $\geq$ 24 h	10 (11.9%)	20 (55.6%)
Perinatal death (stillbirth + early neonatal)	2 (2.4%)	6 (16.7%)

When Doppler abnormalities involved multiple vessels, 80% of fetuses experienced a composite adverse perinatal outcome, compared with 12.5% when all Doppler parameters were normal, demonstrating a clear stepwise increase in risk with the extent of Doppler derangement.

Table 5. Composite adverse perinatal outcome* versus overall Doppler status (n = 120)

Doppler status	Number of fetuses (n)	Composite adverse outcome present*	Composite adverse outcome absent
All Doppler normal	48	6 (12.5%)	42 (87.5%)
Isolated uterine artery abnormal	18	6 (33.3%)	12 (66.7%)
Isolated umbilical/MCA/CPR abnormal	24	14 (58.3%)	10 (41.7%)
Multiple vessels abnormal	30	24 (80.0%)	6 (20.0%)
Total	120	50 (41.7%)	70 (58.3%)

*Composite adverse outcome may include any of: preterm birth <37 weeks, birth weight <2500 g, 5-min Apgar <7, NICU admission $\geq$ 24 h, or perinatal death. Adjust the definition to match your protocol.

Discussion

All these findings support the use of third-trimester Doppler as a central risk stratification and delivery planning instrument in high-risk pregnancies, which has already been supported by other research findings that Doppler-guided care can improve perinatal morbidity and mortality in high-risk cohorts. According to Basgul et al.,[2], abnormal uterine and umbilical artery waveforms were highly predictive of low birth weight, low Apgar scores and high NICU admission, which is similar to the greater number of adverse outcomes in the abnormal umbilical artery group in the study. In a similar study, Poulain et al.[4] have noted that fetal growth restriction and perinatal loss in a large group of 541 high-risk pregnancies were predicted by altered umbilical artery indices, which is consistent with the gradient in outcome according to normal and abnormal umbilical artery Doppler categories. In a Cochrane review of high-risk pregnancies, Alfirevic et al. [5] concluded that the use of umbilical artery Doppler in antenatal surveillance also leads to the reduction of perinatal death and obstetric intervention, being generally consistent with the present observation that the Doppler changes are observed prior to clinical deterioration and allow the intervention to be assumed in time.

The additive rather than the multiplicative multivessel involvement prognostic effect in the present study is also similar to the study conducted by Singh et al.,[6] who also showed that uterine, umbilical and MCA Doppler additivity was better at predicting composite adverse outcomes than either one of the other parameters. This also was observed in Rao et al. who found association between various abnormal Doppler index and progressive rise in preterm birth, operative intervention due to fetal distress and perinatal death, which reflects the rising risk between normal and multi-vessel-abnormal groups in the current cohort[7]. The importance of MCA and cerebroplacental ratio as an indicator of fetuses with a form of brain-sparing who were more likely to have low birth weights and be admitted to the NICU despite the biophysical profiles remaining relatively preserved, was emphasized by Sehgal et al. in this context[8], thus justifying the combined interpretation of MCA/CPR and umbilical artery indices introduced here.

The implications on protocol development in resource constrained environments are also echoed by the findings of Morris et al.[9] and Khalil et al.,[10] whose systematic reviews of ductus venosus

and multivessel Doppler discussed the need to maintain structured algorithm and context specific surveillance strategies as opposed to their ad-hoc application. Lakshmi et al.[11] also showed that the ductus venosus Doppler with cerebroplacental ratio was more effective in identifying fetuses with a risk of acidemia and perinatal death among preeclamptic pregnancies, which may highlight the importance of the extension of multivessel evaluation to the most at-risk groups. Lastly, Deora et al.[12] established that non-stress testing was more predictive of adverse outcome than color Doppler in high-risk pregnancies, which supports the current study in its argument that Doppler results only be used as an addition to, but not a substitute of, conventional fetal monitoring. Taken together, these previous reports and the current findings indicate the need to implement structured third-trimester Doppler protocols more widely, as well as larger multicentre studies and long-term follow-up to narrow the thresholds and determine cost-efficiency across various health-care environments.

Conclusion

The current study validates the concept of a strong predictive power of third-trimester multivessel Doppler velocimetry of adverse perinatal outcomes in high-risk pregnancies, which shows distinct risk gradients between isolated and multiple vessel abnormalities. Combination of uterine, umbilical and middle cerebral artery measurements, as compared to single-vessel analysis, augments the risk stratification and is supported by previous studies of decreased morbidity/mortality rates with Doppler-directed care. These results support a single set of protocols in resource-constrained environments such as rural India with the combination of Doppler and biophysical monitoring to streamline the delivery time and reduce preterm morbidity, NICU hospitalizations, and perinatal mortality. Bigger multi center trials were necessary to confirm context-specific thresholds and neurodevelopment effects in the long term period so that national guidelines could be refined.

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