ORIGINAL STUDY

Value of Third Trimester Uterine Artery Doppler in High-risk Pregnancies for Prediction of Adverse Perinatal Outcome

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Abstract

Objective: To determine the usefulness of uterine artery Doppler in evaluation of third trimester high-risk pregnancies in prediction of adverse perinatal outcome.

Methods: In this prospective study uterine artery Doppler parameters such as PI and early diastolic notch were recorded in a group of 60 high-risk pregnancies mainly consisting of pre-eclampsia and small for gestational age. Uterine artery score (UAS) was calculated from the Doppler parameters and a score $\geq$ 2 was considered abnormal. Perinatal outcome was then correlated to this score and compared with umbilical artery Doppler.

Results: Abnormal UAS was noted in 72% of the study group while umbilical artery Doppler was abnormal in only 35%. All the five perinatal deaths and high-rate of perinatal morbidity was observed when both uterine and umbilical artery Dopplers were abnormal. Perinatal morbidity parameters such as birth weight < 2 kg, gestational age < 34 weeks and NICU admission was significantly high in 23 women who had abnormal UAS with normal umbilical artery Doppler. In pregnancies beyond 34 weeks abnormal uterine artery Doppler was a better predictor of adverse outcome than umbilical artery Doppler.

Conclusion: Abnormal uterine artery Doppler is a reliable predictor of adverse perinatal outcome in high-risk pregnancies with pre-eclampsia and fetal growth restriction. Normal uterine artery Doppler in third trimester is reassuring. Thus inclusion of uterine artery Doppler along with umbilical artery Doppler in high-risk pregnancy in third trimester will improve fetal surveillance.

Keywords: Uterine artery Doppler, umbilical artery Doppler, uterine artery score**,** fetal growth restriction, pre-eclampsia, perinatal outcome.

INTRODUCTION

Doppler of uteroplacental circulation plays a significant role in management of high-risk pregnancies. It helps one to identify the fetus at risk and also helps to time the delivery. Umbilical artery Doppler has proved useful to monitor growth restricted fetuses and those with compromised vasculature as in hypertensive disorders complicating pregnancies. Uterine artery Doppler has only been used for screening around 24 weeks of gestation for later onset of fetal growth restriction and pre-eclampsia. However, there are studies indicating that uterine artery Doppler may be useful even in the third trimester to predict adverse perinatal outcome.[1,2] Hence our objective in this study was to find out the usefulness of third trimester uterine artery Doppler.

METHODOLOGY

This prospective study performed in a tertiary care center between 2005 to 2007 included sixty cases of high-risk pregnancy mainly pre-eclampsia and IUGR in the third trimester. Pre-eclampsia (mild and severe) and small for gestational age (SGA-fetal weight and abdominal circumference <10th percentile for gestational age) were defined according to the standard criteria.[2]

Both uterine artery and umbilical artery Doppler were performed and findings were correlated with perinatal outcome when the patients delivered. This study was performed with consent from patients, after hospital ethical committee approval.

Inclusion criteria for the study were patients admitted with hypertensive complications, fetal growth restriction and previous bad obstetric history (BOH) with recurrent fetal loss with no living children. Patients with above complications who were admitted in labor or those who refused to deliver in our center, and twins were excluded.

Doppler vascular study was performed using Doppler ultrasound of LOGIQ 700 (3.5 MHz) with a high pass filter. Doppler readings were taken from both uterine arteries and umbilical artery. The umbilical artery blood velocity signals were

obtained from free floating central part of the cord. Both uterine arteries were located by color.

Doppler. Blood flow velocity was recorded in the uterine artery just cranial to the anatomical crossing of the external iliac artery. The parameters studied were:

a. Pulsatility index—considered abnormal if > 1.2.[3]
b. Presence of early diastolic notch.

These parameters were then converted uterine artery scores (UAS) as described by Hernandez et al:[2]

0 = Normal blood velocity waveforms in both arteries
1 = One abnormal parameter present (high PI or notch)
2 = Two abnormal parameters present
3 = Three abnormal parameters present
4 = Four abnormal parameters present (high PI and notching in both arteries).

Umbilical artery Doppler was considered abnormal when the PI of UA >2 SD for gestational age and absence/ reversal of end diastolic flow.[4] Repeat Doppler was done after one week if the patient did not deliver. The last Doppler findings closer to delivery were correlated with perinatal outcome.

The perinatal outcome variables studied were cesarean delivery for fetal indication, birth weight, perinatal/neonatal mortality, neonatal intensive care unit (NICU) admission and neonatal morbidity. Descriptive statistics in terms of percentage, mean and range were calculated. The predictive capacity of the UAS and umbilical artery was evaluated in terms of sensitivity, specificity, positive and negative predictive values using statistical package SPSS.[13]

Table 1: Patient characteristics and pregnancy outcome

Parameters	*Number*
Number of patients	60
Median age	26.9 years range (20-31 years)
Gravidity	
• Primi	34 (56.7%)
• Multi	26 (43.3%)
Period of Gestation ≤ 34 weeks	24 (40%)
Delivery details	
• Vaginal	13 (23%)
• Cesarean	47 (77%)
– Maternal indication	15 (32%)
– Fetal indication	32 (68%)
Perinatal outcome	
Mortality:	5
• Fetal death	4
• Neonatal death	1
NICU admissions	30 (50%)
• ≤ 1 week	7 (23%)
• > 1 week	23 (77%)

Table 2: Uterine artery score and pregnancy complications

	Number	*Uterine artery scores*				
	60	0	1	2	3	4
Pre-eclampsia with SGA	24	1	2	3	6	12
Severe Pre-eclampsia	4	–	–	1	2	1
Chronic hypertension with SGA	5			1	3	1
SGA	15	8	4	2	1	
Oligohydramnios	5	4	0	1		
Bad obstetric history (BOH)	7	4	1	2		

SGA: Small for gestational age.

RESULTS

Maternal and labor characteristics of our study group consisting of sixty women are depicted in Table 1. The mean gestational age was 34 weeks with a range of 28 to 37 weeks. There were 24 (43%) women with both pre-eclampsia and small for gestational age (SGA).

The cesarean delivery rate was high at 77% as this was a high-risk group and threshold for cesarean was low. As 40% of women were ≤ 34 weeks, and needed delivery, cesarean was resorted to owing to the fact response to induction is poor in early preterm patients with unfavorable cervix. Prolonged induction and delivery would not be in the interest of compromised fetuses. Over all perinatal mortality was 83/1000 live births. Neonatal morbidity was significant with almost 50% requiring NICU admissions.

Table 2 shows that abnormal UAS was noted in all cases of severe pre-eclampsia and chronic hypertension with SGA. Majority of patients with SGA without pre-eclampsia, only oligoamnios, and patients with previous BOH in general, had normal UAS. When pre-eclampsia was associated with fetal growth restriction, UAS was abnormal in 87.5% of cases.

Table 3 shows the perinatal outcome in relation to abnormal and normal Doppler findings. Almost 33% had abnormal Doppler

Table 3: Perinatal outcome in relation to uterine and umbilical artery Doppler results

Doppler vessels	*Number 59*	*Birth weight ≤ 2 kg*	*Gestational age ≤ 34 weeks*	*NICU admission*	*Perinatal deaths*
Uter A and Umb A Normal	16 (27.1%)	None	None	1	None
Uter A and Umb A Abnormal	20 (33.8%)	20 (100%)	16 (80%)	17 (85%)	5 (25%)
Normal Umb A + Abnormal uter A	23 (38.9%)	15 (65%)	7 (30.4%)	11 (47.8%)	None

Uter A: Uterine artery; Umb A: Umbilical artery.

findings in both vessels while in 28% both vessels had normal velocimetry. In 72% of patients in the study group uterine artery abnormality was seen while umbilical artery Doppler was abnormal in only 35% of patients. There was only one case with abnormal umbilical artery Doppler and normal uterine artery Doppler. Hence it is not shown in the table.

Fifty-five percent of babies weighing ≤ 2 kg were in the group where both vessels were abnormal while 43% had abnormal uterine artery flow with normal umbilical artery flow. All the 5 perinatal deaths (4 fetal deaths +1 neonatal death) occurred in patients with severe pre-eclampsia and fetal growth restriction. Both uterine and umbilical artery Dopplers were abnormal in them.

The baby with neonatal death weighed 1025 gm at birth but died on day 5 due to necrotizing enterocolitis. It was delivered by cesarean at 33 weeks after steroid prophylaxis. All 4 fetal deaths weighed < 1000 gm with gestational age between 28 to 32 weeks. There were 2 cases of abruptio placenta where both cases had abnormal uterine artery Doppler. Only one of them also had abnormal umbilical artery Doppler. It was one of the 2 cases with birth asphyxia who needed prolonged ventilatory care.

We did a subgroup analysis to see the perinatal outcome with abnormal umbilical and uterine artery Doppler in pregnancies beyond 34 weeks as shown in Figure 1.

Thirty-six patients were beyond 34 weeks of gestation. Abnormal uterine artery Doppler was noted in 18 (50%) while only 6 (16.7%) had abnormal umbilical artery Doppler. Abnormal uterine artery Doppler showed higher adverse outcome than umbilical artery Doppler. The prevalence of abnormal uterine artery Doppler was 3 fold higher in pre-eclampsia and SGA fetuses.

When abnormal results were correlated with individual parameters such as SGA, Indicated preterm delivery, NICU stay >1 week, neonatal morbidity and cesarean delivery, umbilical artery was more sensitive and specific for neonatal morbidity while uterine artery Doppler was more specific and sensitive for indicated preterm delivery and NICU stay. Sensitivity of combined abnormal Doppler velocimetry was better. Sensitivity, specificity and positive predictive values (86%, 81% and 93% respectively) of uterine artery Doppler for all adverse outcomes was better than its negative predictive value of 68%. However, the combined Doppler results were more sensitive to abnormal outcome though specificity is not more than individual Doppler results.

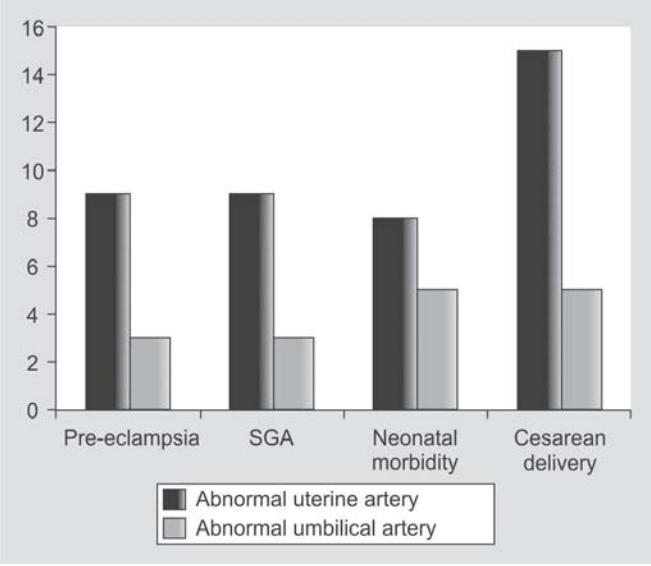

Fig. 1: Doppler in pregnancies beyond 34 weeks and outcome

DISCUSSION

We have assessed the usefulness of uterine artery Doppler in addition to umbilical artery Doppler in a selective group of high-risk pregnancy mainly comprising of pre-eclampsia, SGA and previous BOH. Uterine artery Doppler was interpreted as a score described by earlier workers.[1,2] UAS ≥ 2 was seen in majority of cases with pre-eclampsia and fetal growth restriction.

UAS was first proposed by Sekizuka et al who used resistance index (RI) with different cut off values for placental and nonplacental uterine arteries.[1] This was modified by Hernandez- Andarde et al to include uterine artery PI instead of RI.[2] They also concluded from their study that a uniform UAS ≥ 2 disregarding the location of the placenta, showed a substantial increase in risk of NICU admission, operative delivery for fetal distress, 5 minute Apgar score < 7, preterm delivery and SGA baby. High scores predict poor perinatal outcome. This scoring system makes interpretation simple for clinical practice.

In our study uterine artery Doppler abnormality was seen more frequently than umbilical artery Doppler. We observed abnormal uterine artery Doppler in 87% cases of pre-eclampsia with fetal growth restriction. In severe Pre-eclampsia all had abnormal UAS. But Li H and Gudnason et al reported that only 25% of pre-eclampsia in their study had abnormal uterine artery Doppler in the third trimester.[5] However, our findings show that morbidity is much less when uterine artery Doppler velocimetry is normal in pre-eclampsia. This important fact can be reassuring and pregnancy can be allowed to continue.

Perinatal outcome was poor when both vessels were abnormal. Nevertheless, even in the group with normal umbilical artery Doppler but abnormal UAS, indicated preterm deliveries, NICU admissions and babies weighing < 2 kg were high. This was all the more evident in fetuses beyond 34 weeks of gestation. The prevalence of abnormal uterine Doppler was four fold higher in pre-eclampsia and 2 to 3 folds higher in SGA. Third trimester fetus which is SGA with a normal umbilical artery Doppler poses a clinical dilemma. Earlier studies have shown that evidence of fetal hemodynamic redistribution may exist in the presence of normal umbilical artery Doppler in late pregnancy.[4,6] Hence fetal middle cerebral artery Doppler was included in the evaluation of SGA fetus in late gestation as perinatal morbidity was seen despite a normal umbilical artery Doppler.[6] Later Severi et al

included uterine artery Doppler in addition to middle cerebral artery Doppler.[7] They showed an increased risk for cesarean delivery for fetal distress in these fetuses, despite a normal umbilical artery velocimetry but abnormal uterine artery Doppler. Subsequent to this study Joern et al from Germany also reported that examining uterine arteries is essential in high-risk pregnancies to assess placental performance and fetal well-being.[8] They studied 142 pregnancies and compared the perinatal outcome in relation to Doppler of uterine and umbilical arteries. As expected, worst outcome was seen when all 3 vessels were abnormal. Results were marginally better compared to former group when uterine arteries were abnormal with normal umbilical arteries. This is in concordance with our findings.

Even mild placental insufficiency beyond 34 weeks causes increase in placental villous vascularization which decreases the impedance to flow. Hence, umbilical artery flow can be normal in compromized SGA babies near term but uterine artery Doppler may be abnormal. Adverse perinatal outcome occurred more frequently with abnormal uterine artery Doppler compared to normal uterine artery velocimetry as reported by Vergani et al in 294 fetuses with growth restriction beyond 34 weeks of gestation.[9] We also observed abnormalities in uterine artery more than umbilical arteries in gestation beyond 34 weeks though our study included pre-eclampsia, oligoamnios and previous BOH in addition to fetal growth restriction.

Many maternal problems like pre-eclampsia will affect uterine artery before showing umbilical artery Doppler changes. This was the premise that initiated screening for late onset pre-eclampsia and IUGR, with uterine artery Doppler in the second trimester.

Doppler of multiple vessels is said to be more useful than single vessel changes. Uterine artery Doppler can not replace umbilical artery Doppler and *vice versa*. Hence, combination of both vessels will give more information . Both are complementary to one another. Hence, Gudmundsson et al described a placental score combining umbilical and uterine artery indices and flow velocity waveforms.[10] They classified umbilical artery changes into blood flow classes and combined it with UAS to give a new placental score. This score needs to be evaluated on a larger scale and this may make interpretations of Doppler findings more meaningful and simple. The scoring system would probably help in clinical management and to compare between various studies. It obviates the need for checking the reference charts.

Hofstaetter et al reported unilateral uterine artery notch to be a better predictor of perinatal outcome than unilateral high PI.[3] This is in contrast to the findings of Ghosh et al where RI and PI were considered better indicators of vascular impedance in predicting adverse perinatal outcomes.[11] We did not find any difference between notch or PI and we think UAS as an integrated system is useful rather than individual abnormalities. Geerts et al noted that uterine artery PI was of no prognostic value in cases with early onset pre-eclampsia because 98.2% of the waveforms were abnormal in early gestation because of defective trophoblastic invasion.[12]

Limitations of our study is that the number of cases has been small. Patients who came in labor or with a complication like abruptio placenta were not included. We need to do a larger trial and preferably incorporate the placental score using both uterine and umbilical arteries. Inclusion of pregnancies with only SGA and pre-eclampsia would give a better homogenous population. We had a group of mixed high-risk pregnancies with previous BOH which would dilute the results.

Doppler changes occur sequentially in uterine, umbilical and fetal vessels. Placental perfusion is impaired when there is resistance in the uterine artery Doppler. Umbilical artery Doppler reflects placental resistance. Fetal vessel Doppler changes initially reflect the fetal adaptation to the impaired uteroplacental circulation when the fetus is still in the compensatory phase of growth restriction. With further deterioration, in the decompensatory phase the distress call is signaled by venous changes in Doppler prior to death. Thus the Doppler of multiple vessels helps in timing the delivery and also in prediction of neonatal outcome.

CONCLUSION

Umbilical artery Doppler is an integral part of monitoring pregnancies with pre-eclampsia and fetal growth restriction. Adverse perinatal outcome after 34 weeks of gestation is predicted better with uterine artery Doppler. Normal uterine artery Doppler in third trimester predicts good perinatal outcome and hence is reassuring. Thus inclusion of uterine artery Doppler in pre-eclampsia and fetal growth restriction will give additional information essential for management of pregnancies in third trimester.

REFERENCES

1. Sekizuka N, Hasegawa I, Takakuwa K, Tanaka K. Scoring of uterine artery flow velocity waveform in the assessment of fetal growth restriction and/or pregnancy induced hypertension. J Matern Fetal Invest 1997;7:197-200.
2. Hernandez-Andrade E, Brodszki J, Lingman G, Gudmundsson S, Molin J, Marsal K. Uterine artery score and perinatal outcome Ultrasound Obstet Gynecol 2002;19:438-42.
3. Hofstaetter C, Dubiel M, Gudmundsson S, Marsal K. Uterine artery color Doppler assisted Velocimetry and perinatal outcome. Acta Obstet Gynecol Scand 1996;75:612-19.
4. Harrington K, Carpenter RG, Nguyen M, Campbell S. Changes observed in fetal Doppler studies of the fetal circulation in pregnancies complicated by pre-eclampsia or the delivery of a small for gestational age baby-1 Cross-sectional analysis Ultrasound Obstet Gynecol 1995;6:19-28.
5. Li H, Gudnason H, Olofsson P, Dubiel M and Gudmundsson S. Increased uterine artery vascular impedance is related to adverse outcome of pregnancy but is present in only one third of late third trimester pre-eclamptic women Ultrasound Obstet Gynecol 2005;25:459-63.
6. Hershkovitz R, Kingdom JCP, Geary M, Rodek CH. Fetal cerebral blood flow redistribution in late gestation: Identification of compromise in small fetuses with normal umbilical artery Doppler. Ultrasound Obstet Gynecol 2000;15:209-12.

7. Severi FM, Bocchi C, Visentin A, Falco P, Cobellis L, Florio P, Zagonari S and Pilu G. Uterine and Fetal cerebral Doppler predict the outcome of third trimester small for gestational age fetuses with normal umbilical artery Doppler Ultrasound Obstet Gynecol 2002;19:225-28.
8. Joern Hendrik, Rath Werner. Comparison of Doppler Sonographic examinations of the umbilical and uterine arteries in high-risk pregnancies. Fetal Diagn Ther 1998;13:150-53.
9. Vergani P, Roncaglia N, Andreotti C, Alessandra A, Teruzzi M, Pezzullo JC, Ghidini A. Prognostic value of uterine artery Doppler velocimetry in growth restricted fetuses delivered near term Am J Obstet Gynecol 2002;187:932-36.
10. Gudmundsson S, Korszun P, Olofsson P and Dubiel M. New score indicating placental vascular resistance Acta Obstet Gynecol Scand 2003;82:807-12.
11. Ghosh G, Breborowicz A, Brazert M, Maczkiewicz M, Kobelski M, Dubiel M and Gudmundsson S. Evaluation of third trimester uterine artery flow velocity indices in relationship to perinatal Complications J of maternal-Fetal and Neonatal Medicine 2006;19:551-55.
12. Geerts L, Odendaal HJ. Severe early onset pre-eclampsia: prognostic value of ultrasound and Doppler assessment Journal of Perinatology 2007;27:335-42.