Contribution of Color Doppler in Assessment of Intrauterine Fetal Growth among High-Risk Pregnant Woman - A Observational Study

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ABSTRACT

Introduction: Globally, pregnancy-induced hypertension is a significant public health threat both in developed and developing countries contributing to high perinatal deaths. Reduced placental perfusion is thought to result from failure of trophoblast to invade maternal spiral arterioles in the first half of the pregnancy leading to the development of intrauterine foetal growth restriction.

Material and methods: A cross-sectional study was conducted on 50 high-risk pregnant women to determine the role of color Doppler in the assessment of intrauterine fetal growth. Color Doppler flowmetry for umbilical artery, uterine artery and middle cerebral artery pulsatility index (PI), resistive index (RI) and systolic/diastolic (S/D) ratio at 28-32 weeks of the pregnancy was determined. All the pregnancies were followed up until delivery. coGuide version V.1.0 was used for statistical analysis.

Results: The highest number of 31 (62%) cases were between 21-25 years, followed by below 20 years of age. Thirty-three (66%) cases show abnormal Doppler findings and the remaining 17 (34%) does not show any evidence of Intrauterine growth restriction on any single parameter. The Doppler study of the uterine artery is the most sensitive (72%) followed by umbilical artery (66%) and middle cerebral artery (28%) in predicting the intrauterine growth retardation.

Conclusion: We conclude that the Doppler study of the uterine artery is the most sensitive (72%) followed by umbilical artery (66%) and middle cerebral artery (28%) in predicting the intrauterine growth retardation.

Keywords: Ultrasonography, Hypertension, Pregnancy-Induced, Umbilical Artery.

INTRODUCTION

Pregnancy-induced hypertension (PIH) was defined as new hypertension that appears at 20 weeks or more gestational age of pregnancy with or without proteinuria, including gestational hypertension, preeclampsia, and eclampsia. Globally, PIH is a significant public health threat both in developed and developing countries contributing to high perinatal deaths. PIH complicates 2–8% of pregnancies in the western world. However, the magnitude of PIH in developing countries reaches up to 16.7%. The complication in PIH is reduced placental perfusion which is characteristic of abnormal implantation or underlying maternal vascular diseases. Reduced placental perfusion in PIH is thought to result from failure of trophoblast to invade maternal spiral arterioles in the first half of the pregnancy lead to the development of IUGR.[1]

Intrauterine growth restriction (IUGR) is defined as the non fulfilment of specific fetal biometric measures or estimated weight (less than 10th percentile) at a specified gestational age. IUGR is responsible for different types of pre-and post-natal morbidity and mortality. The prevalence of IUGR is about 3-10%. It is classified into 2 groups; early (before 32 weeks) and late (after 32 weeks) onset[2] based on time of onset. Some factors leading to IUGR include maternal causes (hypertension, diabetes, cardiopulmonary disease, anemia, malnutrition, smoking, drug use), fetal causes (genetic disease including aneuploidy, congenital malformations, fetal infection, multiple pregnancies), and placental causes (placental insufficiency, placental infarction, placental mosaicism).[3]

Women with hypertension or previous growth-restricted fetus, the incidence has increased to 15-20% or higher and it varies from region to region, and in the same region, there is variation in different subpopulations. According to recent UNICEF surveys, the incidence of IUGR is 25-30% in India[4]

Clinically, IUGR needs to be distinguished from constitutionally small for gestational age (SGA) fetuses, which represent "physiological smallness" and are not of the same clinical concern. The current standard of detection of

IUGR and differentiation from SGA is based on ultrasound examinations.[5]

Antenatal diagnosis has proven to reduce adverse perinatal outcomes and allows for proper and timely referral of the neonate to intensive care.[6] However, antenatal detection rates still are sparse and range at about 20–50%, even in high-income countries.[7] IUGR diagnosis is often made by observation of fetal growth velocity, which can only be confirmed with a significant delay in serial ultrasound measurements which are usually timed at least two weeks apart.

Doppler ultrasound studies reported that there is a significant reduction of middle cerebral arterial (MCA) pulsatility index in fetuses with IUGR when compared to normal foetuses.[8] Hypoxemia in fetuses with IUGR and an abnormal MCA pulsatility index showed a significant correlation in recently published meta-analysis which proved that systemic application of Doppler sonography has resulted in 50% reduction of perinatal mortality among high-risk pregnancies.[9]

With this background, in the present study, we examined the diagnostic potential of Doppler in measuring flow velocity waveforms in uteroplacental (uterine artery and umbilical artery) and fetoplacental (middle cerebral artery) circulations in situations of suspected placental insufficiency such as PIH and IUGR pregnancies which subsequently result in the birth of growth retarded infants,

Study aimed to evaluate the role of color Doppler in the assessment of intrauterine fetal growth. To evaluate the diagnostic accuracy of the uterine artery, umbilical artery and middle cerebral artery Doppler indices as predictors of perinatal outcome in clinically suspected IUGR pregnancies and comparing with other studies in the literature.

MATERIAL AND METHODS

Observational descriptive cross-sectional study was conducted in antenatal hospital on high-risk pregnant women with four weeks of gestation visiting antenatal hospital. The present study comprises of 50 high-risk singleton pregnancies antenatal cases selected through universal sampling. The period of study was 18 months from October 2018 to March 2020.

All the gathered data was considered confidential. Wwritten informed consent was taken from all participnats. Ethics approval was taken from the institutional review board of the concerned hospital. Confidentiality of the participants was maintained through out.

Inclusion Criteria

- Women with high-risk pregnancy between 26 and 30 weeks of gestation,.fetal growth < the 10th percentile for the weight of all fetuses at the same gestational age, gestational age 32+0 to 39+6 weeks, singleton pregnancy, and no major fetal anomalies.
- Women who are Nulliparous,
- Women withPreeclampsia or pregnancy-induced hypertension
- Women with less than 20 years and more than 35 years of age were not considered.

- Women with pregnancy confirmed by first-trimester ultrasound by Crown rump length OR Biparietal diameternulliparous or with known Last menstrual period.

Exclusion Criteria:

Post-term pregnancy, mother's decline, patient with congenital anomaly of the fetus, multiple gestations. All antenatal women less than 24 weeks.

Data Collection: Detailed history and thorough examination was done. All relevant investigations were carried out. The relevant data obtained were recorded in the standard prepared proforma, with color Doppler Philips EnVisor Machine using 3.5 MHz transducers we have assessed the flow velocity waveforms' of umbilical artery, both uterine arteries and fetal middle cerebral artery. The variables studied were systolic/diastolic ratio, pulsatility index and resistance index of the umbilical artery and the above parameters with a persistent notch taken for uterine arteries and pulsatility index for middle cerebral artery.

Doppler Ultrasonography examination was assessed by taking a detailed clinical history and Ultasonograph biometry. The subject will be considered cases if the fetus is diagnosed with intrauterine growth restriction based on greyscale ultrasound and subsequent Doppler ultrasound will be performed. Follow up Doppler at 28-30 weeks is performed only if indicated clinically to determine the favourable and worst trend of Doppler indices. However, only the results of patient's last Doppler ultrasound examination were used for the analysis of perinatal outcome.

STATISTICAL ANALYSIS

Descriptive analysis: quantitative variables were represented as mean and standard deviation and categorical variables were presented as frequency and proportion. Inferential statistics: The association between explanatory variables and categorical outcomes was assessed using Chi square test. The sensitivity, specificity, predictive values and diagnostic accuracy of the screening test along with their 95% CI were also presented calculated using coGuide version V.1.0 was used for statistical analysis.[10]

RESULTS

A total of 50 subjects were included in the final analysis.

Table1 -Among the study population, 13 (26%) participants were aged up to 20 years, 31 (62%) participants were aged between 21 to 25 years, and 6 (12%) participants were aged between 26 to 30 years. Thirty-three (66%) participants had normal Doppler, 17 (34%) participants had abnormal Doppler, 36 (72%) had abnormal uterine artery Doppler, and 14 (28%) had normal UA Doppler. Thirty-three 33 (66%) had anomalous umbilical artery, and 17 (34%) had normal umbilical artery Doppler; 14 (28%) had abnormal and 36 (72%) had normal middle cerebral artery Doppler; 32 (64%) had abnormal and 18 (36%) had normal cerebral/umbilical ratio.11 (22%) showed absent end-diastolic velocity and 4 (8%) showed reversal end-diastolic velocity for umbilical artery Doppler; 27 (54%) cases showed notch and 9 (18%) did not show notch; 21 (42%) showed unilateral notch, and

6 (12%) showed bilateral notch for uterine artery Doppler. Table 2- 33 (66%) for UA, 32 (64%) for umbilical A and 14 (28%) for MCA were abnormal for S/D ratio; 33 (66%) for UA, 29 (58%) for umbilical A and 18 (36%) for MCA were abnormal for PI and 32 (64%) for UA 30 (55%) for umbilical A 16 (32%) for MCA were abnormal for RI.

Table 3- Uterine artery Doppler showed 72% sensitivity compared to another study by Malick where the sensitivity was 37.7%. Umbilical artery showed 66%, and MCA showed 28% sensitivity compared to 64.4.% and 7.7% in Malick study.

Table 4-The uterine artery Doppler had sensitivity of 72% (95% CI 38.33% to 85.79%) in predicting Doppler. Specificity was 24.24% (95% CI 11.09%to 42.26%), false positive rate was 75.76% (95% CI 57.74%to 88.91%), false negative rate was 35.29% (95% CI 14.21% to 61.67%), positive predictive value was 30.56% (95% CI 16.35%to 48.11%), negative predictive value was 57.14% (95% CI 28.86% to 82.34%), and the total diagnostic accuracy was 38.00% (95% CI 24.65% to 52.83%). The umbilical artery Doppler had sensitivity of

Variables	Number of cases	Percentages
Age group		
Up to 20 years	13	26%
21-25 years	31	62%
26-30 years	6	12%
Abnormal Doppler	33	66%
Normal Doppler	17	34%
Abnormal uterine artery Doppler	36	72%
Normal uterine artery Doppler	14	28%
No. of cases with uterine artery notch	27	54%
No. of cases without uterine artery notch	9	18%
No. of cases with unilateral uterine artery notch	21	42%
No. of cases with bilateral uterine artery notch	6	12%
Abnormal umbilical artery Doppler	33	66%
Normal umbilical artery Doppler	17	34%
Absent end diastolic velocity of umbilical artery of (AEDV)	11	22%
Reversal end diastole velocity of umbilical artery (REDV)	4	8%
Abnormal middle cerebral artery Doppler	14	28%
Normal middle cerebral artery Doppler	36	72%
Abnormal cerebral/umbilical Doppler ratio	32	64%
Normal cerebral/umbilical Doppler ratio	18	36%

Table-1: Distribution of cases on the basis of normal and abnormal Doppler for different arteries (n=50)

Indices	Umbilical artery		Uterine artery		Middle cerebral artery	
	Present study N=50	Other study N=100 Singh SK et al.[16]	Present study N=50	Other study Tushar et al [17] N=36	Present study N=50	Other study N=100 Singh SK et al. [16]
Systolic/Diastolic ratio (S/D)						
>2.6	33(66%)	52%	32(64%)	21(58%)	14(28%)	58%
<2.6	17(34%)		18(36%)	15(47%)	36(72%)	
Pulsatile index						
Normal	17(34%)	63%	21(42%)	Not done	32(64%)	43%
Abnormal	33(66%)		29(58%)		18(36%)	
Resistance index						
>0.6	32(64%)	58%	Not done	20(55%)	16(32%)	47%
<0.6	18(36%)			16(44%)	34(66%)	
Cerebro to umblical ratio (C/U)	32(64%)	Not calculated	34(66%)	Not calculated	8(16%)	Not calculated

Table-2: Distribution according to Doppler indices and comparison with other studies

Variable	No. of Cases N=50	Present study	Other studies Malik et al.[18] (n=100)
Uterine artery	36/50	72%	37.7%
Umbilical artery	33/50	66%	64.4%
Fetal MCA	14/50	28%	7.7%

Table-3: Sensitivity of Various Vessels and comparing with other studies

66% (95% CI 50.10% to 93.19%) in predicting Doppler. Specificity was 30.30% (95% CI 15.59% to 48.71%), false positive rate was 69.70% (95% CI 51.29%to 84.41%), false negative rate was 23.53% (95% CI 6.81%to 649.90%), positive predictive value was 36.11% (95% CI 20.82% to 53.78%), negative predictive value was 71.43% (95% CI 41.90% to 91.61%), and the total diagnostic accuracy was 46.00% (95% CI 31.81% to 60.68%). The middle cerebral artery Doppler had sensitivity of 28% (95% CI 20.10% to 43.19%) in predicting Doppler. Specificity was 22.30% (95% CI 13.59% to 38.71%), false positive rate was 61.70% (95% CI 51.29% to 84.41%), false negative rate was 18.53% (95% CI 10.81% to 649.90%), positive predictive value was 25.11% (95% CI 21.82% to 58.78%), negative predictive value was 51.43% (95% CI 38.90% to 61.61%), and the total diagnostic accuracy was 46.00% (95% CI 31.81% to 60.68%).

DISCUSSION

In our study, we have taken fifty clinically suspected PIH/IUGR cases. The majority of cases in present study were between 21-25 years, followed by <20 years of age. In our study, 33 (66%) cases show abnormal Doppler findings consistent with IUGR and the remaining 17 (34%) does not show any evidence of IUGR on any single parameter. The Doppler study of the uterine artery is the most sensitive (72%) followed by umbilical artery (66%) and middle cerebral artery (28%) in predicting the intrauterine growth retardation.

In the present study, the discriminant role of different parameters was assessed primarily by IUGR group. This is in contrast to a study reported by Sachin et al[11] where they have differentiated between the IUGR and non-IUGR groups with the help of a comparison of the mean values of different parameters.

Umbilical Artery: There were 33 (66%) patients with abnormal umbilical Doppler. Among them, 33 (66%) had abnormal S/D ratio, 32 (64%) had abnormal RI, 33 (66%) had abnormal pulsatility index, and 11 (22%) had absent end-diastolic flow. These findings are in comparison to Teena et al[12] were 50 patients showed abnormal umbilical Doppler. out of 50,25 showed abnormal S/D ratio, 40 showed abnormal RI, and 5 did not show end-diastolic flow and sensitivity of S/D ratio, PI, RI is 62%, 66%, 64% respectively. In our study, we found abnormal PI is more sensitive among other parameters.

Absent or Reversal of End diastolic velocity: In our study, 11(22%) cases show absent or reversal of EDV, of which 4 cases showed reversal of EDV. All 4 cases of REDV died before30 weeks of gestation. Absent diastolic flow seen in 7 cases, 4 cases died, and 3 cases admitted in NICU with severe respiratory distress. Our study shows absent or reversal of EDV is more sensitive in predicting adverse fetal outcome.

Uterine Artery: The normal value S/D ratio is 2.6. Increased values are seen in cases of PIH/IUGR. In our study, about two-thirds of the cases show elevated S/D ratio. Out of 50 patients who had abnormal uterine artery, 32 had abnormal S/D ratio and 31 had abnormal RI. In all, 27 patients had persistent early diastolic notch; among them, six patients had

a bilateral notch, and 21 patients had a unilateral notch. This finding is similar to a study done by Teena et al[12] where,70 patients had abnormal uterine artery. Out of 70, 45 showed abnormal S/D ratio and 35 showed abnormal RI. 40 patients had persistent early diastolic notch of which 20 patients had a bilateral notch, and 20 patients had a unilateral notch.

Significance of Diastolic notch: It is defined as "a decrease in the maximal flow velocity below the maximum diastolic velocities occurring just after the systolic wave." In the non-pregnant state, the uterine artery is high resistance vessel. Decreased diastolic flow and early notching are peculiar features of non-pregnant uterine circulation. In second trimester, invasion of trophoblast into myocardium occur, converting the high resistance pattern into that of the low resistance pattern, characterized by an increase in diastolic flow and disappearance of the notch. Persistence of notch after 26 weeks of gestation is an indicator of PIH/IUGR and indicates unaltered vasospasm. The disappearance of the notch is seen firstly in uterine artery, which is present under the placenta.

In the present study, 27 (54%) cases had diastolic notch and 9(18%) were without notch.The number of cases with both unilateral and bilateral notch was 54%. Because of variations in placentation, it becomes important to study both the uterine arteries. In cases of the laterally located placenta, the placental side uterine artery is the main supplier and has decreased resistance, compared to the uterine artery present on opposite side. Examining both the arteries is an essential component of Doppler study to evaluate performance of placenta and its risk to the fetus. In our study, single uterine artery sensitivity is more (53%) in comparison with the bilateral study.

In our study of uterine artery Doppler velocimetry among 50 case group, 14 (28%) subjects had normal flow pattern in the uterine artery, and 36 (72%) had abnormal flow pattern with raised indices and diastolic notches. Out of 36 cases of PIH showing raised Doppler indices and diastolic notch, 9 (18%) cases showed a bilateral abnormality. The present study findings were inconsistent with Aharwal S et al[13] where among 41 case group, 15 (36.53%) subjects had normal flow pattern in the uterine artery, and 26 (63.46%) had abnormal flow pattern with raised indices and diastolic notches. Out of 26 cases of PIH showing raised Doppler indices and diastolic notch, 14 cases showed bilateral abnormality (B), either raised indices, diastolic notch or both leading to (34.1%) cases of the total.

Fetal Middle Cerebral Artery (MCA): Only one third (28%) of cases, show abnormal MCA Doppler finding in the present study. According to Katherine W. Fong, the PI value of MCA is more sensitive. In present study, the PI score of umbilical artery was more sensitive than the PI score of MCA. These are very common adverse adverse perinatal outcomes that demonstrate the significance of diagnosing IUGR and interventions at early stage. The finding was in contrast to a study done by Rahimi Sharbaf et al[2] where a significant correlation was observed between PI of CPR and MCA where CPR <1 was found to be a potential predictor of adverse outcome in small for gestational age[12] neonates.

The findings of the present study showed high sensitivity, specificity and predicting the value of middle cerebral PI (74%, 93% and 95%, respectively) in SGA prediction. Our finding was in contrast to other studies by Hemlata et al.[14] where the study reported the sensitivity, specificity, and positive predictive value of MCA to be 71%, 92% and 94% repectively for detecting SGA-related abnormal fetal outcomes. In another study reported by Monteith et al.[15] showed the importance of an abnormal serial CPR <1 as a potential predictor of adverse outcomes among 1116 SGA fetuses.

Prediction of critical perinatal outcomes is improved when venous and umbilical artery qualitative waveform analysis is combined. The incorporation of venous Doppler into fetal surveillance is therefore strongly suggested for all preterm IUGR foetuses.

Limitation: The main limitation is of the sample size, which is very small (50) in the present study and also we did not use controls in our study which could have reduced the confounders bias. Another limitation can be of single centre used, which can affect the external validity of the study. The data was limited to the third trimester of gestation, and we did not consider other maternal variables, such as other comorbidities and habits, which may influence the findings. Serial changes in Doppler indices with the progression of pregnancy from diagnosis to delivery were not recorded. Hence, large-scale prospective studies are required covering all these variables to prove the power of colour Doppler in integrated approaches of clinical practice.

CONCLUSION

We conclude that the Doppler study of the uterine artery is the most sensitive (72%) followed by umbilical artery (66%) and middle cerebral artery (28%) in predicting the intrauterine growth retardation. Identification of these findings creates the possibility of early intervention and therapy. Color Doppler may help us to identify the severity of PIH, in late pregnancy for predicting unfavourable outcome. Thus, it may contribute to improve maternal wellbeing and fetal health. However, there is an urgent need to standardize Doppler terminology and reference values of Doppler indices to allow direct comparison of studies carried out in an increasing number of cases.

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