

Study of triple vessel wave pattern by doppler study in high risk and normal pregnancies and perinatal outcome

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Abstract

Objectives: Role of Triple vessel umbilical, middle cerebral and uterine artery wave pattern by color Doppler study in high risk and normal pregnancies in relation to perinatal outcome. **Methods:** Fifty (50) patients with gestational age between 31-40 weeks who were re-diagnosed to have severe preeclampsia, preeclampsia with IUGR were studied and subjected to color Doppler ultrasonography. Findings of Doppler studies were correlated with the following adverse perinatal outcomes; Perinatal deaths, Emergency CS for foetal distress, Low Apgar score (5 min Apgar <7), and admission to NICU for complications of low birth weight. Pregnancy outcome was considered to be Uneventful or Favourable when the above complications were absent. The uterine artery, Umbilical artery and the Middle cerebral artery Doppler indices for the corresponding gestational age were compared with the reference values. The uterine artery and Umbilical artery Doppler indices were considered abnormal if the value was above the 95th percentile of previously published values for gestational age. The Middle cerebral artery Doppler index was considered abnormal if the value was below the 5th percentile of previously published values for gestational age. A single cutoff value (1.08) was used for Cerebroplacental Ratio (MCAPI/UAPI), above which the cerebroplacental ratio was considered normal and below which it was considered abnormal. **Results:** Acceptable wave forms were obtained from Uterine artery, MCA and UA in all these cases. All the cases were followed up for the perinatal outcome. Cerebroplacental ratio had higher sensitivity (95%) and NPV (85%) than UAPI (Sensitivity 66.66%, NPV 79.40%) and MCA PI (Sensitivity 83.33%, NPV 77.27%), UAPI had higher specificity (93.10%) and PPV (87.5%) compared to cerebroplacental ratio (Specificity 87%, PPV 88%) and MCAPI (Specificity 85%, PPV 89.28%). Diagnostic accuracy of Cerebroplacental ratio (Accuracy=90%) was better than UAPI (Accuracy=82%) and MCA PI (Accuracy=84%) in predicting adverse outcomes. **Conclusion:** In clinically diagnosed severe preeclampsia and suspected IUGR pregnancy, both Cerebroplacental ratio and Umbilical artery PI are strong predictors of adverse perinatal outcome. Cerebroplacental ratio is most sensitive and Umbilical artery PI is most specific index in predicting adverse outcome. Absent or reversed end diastolic flow in an umbilical artery is an ominous finding associated with major adverse perinatal outcome and mortality.

Key Words: High risk pregnancy; severe preeclampsia, IUGR and Triple vessel Doppler study; Perinatal outcome.

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INTRODUCTION

The main goal of antepartum fetal surveillance is to identify fetuses at increased risk for perinatal mortality and morbidity. Doppler ultrasound allows a non invasive assessment of fetal haemodynamics.^{1,2} Doppler investigation of the uterine and umbilical arteries provides information concerning perfusion of the fetoplacental circulation, while Doppler study of MCA detects the haemodynamic rearrangements that occur in response to fetal hypoxia. A meta analysis of

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randomized controlled trials of UA Doppler velocimetry in high risk pregnancies (mainly pregnancies with associated pregnancy induced hypertension and suspected IUGR) demonstrated that its use was associated with a trend towards reduction of perinatal mortality³. In response to prolonged fetal hypoxic stress, circulatory adaptation occurs, resulting in redistribution of the cardiac output to provide a constant oxygen supply to the brain and other essential organs (i.e., heart and adrenal gland) This compensatory adjustment, on which the brain sparing effect⁴ is based, causes cerebral vasodilatation, causing a decrease in Doppler indices such as the pulsatility index^{5,6}. At cordocentesis, a significant correlation has been observed between hypoxemia in fetuses with IUGR and abnormal middle cerebral artery (MCA) pulsatility index (PI). Recent studies indicate that the cerebroplacental ratio of pulsatility index of MCA and UA is the most sensitive Doppler index for predicting perinatal outcome in fetuses with IUGR^{7,8}. At least one third of IUGR fetuses show early signs of circulatory deregulation one week before biophysical profile deterioration and in most cases, Doppler deterioration preceded biophysical profile deterioration by one day⁹. This indicates the significance of Doppler study in these patients for early detection of fetal compromise. Our study was an effort at establishing the role of uterine artery; UA and MCA Doppler Ultrasound in predicting adverse perinatal outcome in the clinically suspected IUGR and preeclampsia associated pregnancies and to determine the role of Doppler velocimetry in clinical management of such pregnancies

AIMS AND OBJECTIVES

1. To analyze the blood flow in uterine artery, umbilical artery and middle cerebral artery using Doppler ultrasound in normal pregnancies and in a group of patients with severe preeclampsia and severe preeclampsia with IUGR
2. To evaluate the role of Doppler ultrasound in the management of patients with severe preeclampsia and severe preeclampsia with IUGR.
3. To assess the value of Doppler ultrasound in analyzing the perinatal outcome in patients with severe preeclampsia and severe preeclampsia with IUGR

METHODOLOGY

MATERIALS AND METHODS

The study was conducted on fifty women with high risk pregnancies with inclusion criteria and fifty women with normal pregnancies who were attending to department of obstetrics and gynecology of Santiram medical college and General hospital, Nandyal from November 2017 to Oct 2018

STUDY SUBJECTS

Patients with inclusion criteria admitted in department of obstetrics and gynaecology were assigned into two groups A and B. Each group included 50 cases. Group A included high risk pregnancies with inclusion criteria and group B included women with normal pregnancies as control groups.

INCLUSION CRITERIA

All antenatal cases more than 30 weeks of gestation with following inclusion criteria are included:

- Singleton pregnancies.
- Pregnant women with history and physical findings suggestive of
 - Severe preeclampsia,
 - IUGR (EFW < 10th percentile for gestational age)
 - Severe preeclampsia plus IUGR.
- Those who gave consent for the study

EXCLUSION CRITERIA

The pregnancies with following conditions were excluded;

- Cardio vascular disease
- Multiple gestations
- Fetuses with congenital anomalies
- Renal disease
- Essential hypertension prior to pregnancy and other high risk pregnancies
- Intrauterine death at the time of first Doppler examination.

The gestational age was based on last menstrual period (LMP), ultrasound biometry performed before the 20th gestational week, when the LMP is uncertain or not known and early ultrasound before 13 weeks has not been performed. Follow up Doppler studies were performed if clinically indicated to determine a favorable or a worsening trend in the Doppler indices. However, only the results of the first Doppler ultrasound were used for the analysis of perinatal outcome.

Statistical Analysis

Statistical analysis was done by using proportions. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were determined for all Doppler measurements.

RESULTS

In the present study out of fifty cases of study groups, 34 showed positive Doppler indices in any or combinations of the three vessels studied. There main 16 cases showed normal Doppler indices in all the three vessels studied. The following were the results of the study.

Table 1: Age Distribution of Cases

Age(Years)	Study Group	Control Group
<20	3	6
20-24	34	36
25-29	11	5
>30	2	3

68% (34 patients) and 72%(36 patients) were between 20-24 age group in study and control groups respectively

Table 2: Gestational Age Distribution in study group and control group

Gestational age(Wk)	Study Group	Control Group
31-32	9	0
33-34	5	1
35-36	10	3
37-38	19	37
39-40	7	9

Table 3: Gravida Distribution

Gravidity	Gravida1	Gravida2	Gravida3	Gravida4	TOTAL
Study Group	32	13	2	3	50
Control Group	34	8	7	1	50

Majority 64% in study group and 68% in control group were primi gravida.

Table 4: Amniotic Fluid distribution in the study group

AmnioticFluid	DopplerNormal	Doppler Abnormal	Total
Oligo	2	13	15
Normal	17	18	35
Total	19	31	50

30%(n=15) had oligo hydramnios and 70%(n=35) had normal amniotic fluid

Table 5: Mode of Delivery

Mode of delivery	Normal Doppler	Abnormal Doppler
ElectiveLSCS	1	0
EmLSCS	4	10
Normal vaginal delivery	13	22
Total	18	32

$$\chi^2 = 26.94 \text{ DF}=2 \text{ P}<0.001$$

There was significant association between normal Doppler and caesarean section delivery.

Table 6: Duration between Doppler and delivery

Duration	Normal Doppler	Abnormal Doppler
<24hours	0	6
1-2days	14	21
3-4days	5	2
5-6days	0	2

Table 7: Pregnancy Outcome in the study group

Pregnancy outcome	No. of cases		Percentage	
	Study group	Control group	Study group	Control group
Adverse	42	10	84	20
Uneventful	8	40	16	80
Total	50	50	100	100

84 % (n=42) fetuses had at least one abnormal outcome and remaining 8 fetuses had normal outcome.

Table 8: Adverse outcome Parameters in Study and Control Groups

Pregnancy outcome	No. of cases		Percentage	
	Study group	Control group	Study group	Control group
EmLSCS	15	9	30	18
Low Apgar Score	8	0	16	0
NICU Admission	19	0	38	0
Neonatal Death	8	0	16	0
Low Birth Weight	35	7	70	14
Preterm Delivery	24	3	48	6

70% of neonates (n=35) had birth weight of less than 2.5kg. Of the 50 neonates, 19 neonates were admitted to NICU, 8 neonates had 5 min Apgar score of less than 7 and 15 babies were born by emergency caesarian section for fetal distress

Table 9: Birth weight distribution in study group

	Abnormal		Normal		Total	
	No. of cases	percentage	No. of cases	percentage	No. of cases	percentage
1-1.50	11	78.50	3	21.50	14	100
1.51-2	11	68.75	5	31.25	16	100
2-2.50	7	46.60	8	53.30	15	100
2.50-3	1	25	3	75	4	100
>3	0	0	1	100	1	100
Total	30	60	20	40	50	100

$$\chi^2 = 25.96 \text{ DF} = 4 \text{ P} < 0.001$$

Doppler results considered for umbilical and middle cerebral arteries together are significantly associated with birth weight.

Table 10: Normal and Abnormal Doppler Wise Distribution of Cases

Doppler	Number	Percentage
Normal	16	32
Abnormal	34	68
Total	50	100

Table 11: Doppler velocimetry of umbilical artery and perinatal outcome

	Complications or death		Live or healthy		Total	
Abnormal	14	93.3%	1	6.7%	15	100
Normal	8	22.85%	27	77.14%	35	100
Total	22	44%	28	56%	50	100

$$\chi^2 = 31.04 \text{ DF} = 1 \text{ P} < 0.001$$

There is significant association between Doppler study result of umbilical artery and perinatal outcome.

Table 12: Doppler velocimetry of middle cerebral artery and perinatal outcome

	Complications or death		Live or healthy		Total	
Abnormal	21	72.41%	8	27.5%	29	100
Normal	7	33.3%	14	66.7%	21	100
Total	28	56%	22	44%	50	100

$$\chi^2 = 17.39 \text{ DF} = 1 \text{ P} < 0.001$$

There is significant association between Doppler study result of middle cerebral artery and perinatal outcome

Table 13: Diastolic notch of uterine artery and perinatal outcome

No. of cases	Adverse outcome		Live and Healthy	
20	11	55%	9	45%

Table 14: Cerebro-placental ratio (MCA PI/UA PI) in prediction of IUGR

Parameters	No. of IUGR Cases	Percentage
CPR < 1	16	72.73
CPR > 1	6	27.27
Total	22	100

Table 15: Spectral characteristics of umbilical artery and perinatal outcome

	No. of cases	Mortality	Percentage
AEDF	05	05	100
REDF	01	01	100

All 5 cases with AEDF and 1 case with REDF had neonatal death

Table 16: Performance Characteristics of Doppler Indices

Parameters	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
UAPI	66.66	93.10	87.50	79.40	82
MCAPI	83.33	85	89.28	77.27	84
CPR	95	87	88	85	90

Cerebroplacental ratio (MCA/UA PI Ratio was most sensitive (sensitivity=95%) than MCA PI sensitivity (sensitivity=83.33%) and UA PI sensitivity (sensitivity= 66.66%) Umbilical artery PI was the most specific (specificity=93.1%), than Cerebroplacental Ratio (specificity = 87%) and MCA PI (Specificity= 85%) Middle cerebral artery PI had highest Positive Predictive Value (PPV=89.28%) followed by Cerebroplacental ratio (PPV=88%) and umbilical artery PI (PPV=87.5%). Negative Predictive Value of Cerebroplacental Ratio was 85% when compared to 79.4 % for umbilical artery PI and 77.27% for MCA PI .Diagnostic accuracy of Cerebroplacental ratio (Accuracy=90%) was better than MCA PI (Accuracy=84%) and UA PI (y=82%) predicting adverse outcomes.

DISCUSSION

Doppler velocimetry is a noninvasive technique that evaluates abnormal fetal haemodynamics that take place in response to changes in placental resistance. A doppler index that reflects both of these are as can be useful for identifying fetuses with increased placental and decreased cerebral resistance. Preeclampsia and Intrauterine growth restriction is associated with increased placental and decreased cerebral resistance and hence there is increased risk of perinatal morbidity ,mortality and impaired neurological development. It is a challenge to differentiate the fetus with pathologic growth restriction and hence at risk for perinatal complications from constitutionally small but healthy fetus. Umbilical artery and middle cerebral artery Doppler ultrasound clearly depicts the information about placental resistance and the changes in the fetal haemodynamics in response to it. Umbilical arteries Doppler reflects the maldevelopment of the placental tertiary stem villi which increases the placental resistance leading to growth retarded fetus. Middle cerebral artery Doppler enables the confirmation of brain sparing in IUGR. Hence we chose the UA PI, MCA PI and MCA PI/UA PI i.e.cerebroplacental ratio as the tool for predicting the perinatal out come in IUGR. We studied the Doppler index of umbilical artery only after 30th week, because in Agreement with Gramellini, we believe that it is difficult to define normal or abnormal umbilical flow velocity before 30th week, with the exception of absent end diastolic flow velocity after 20thweek. We studied the Doppler index of middle cerebral artery because it is the most accessible artery to see the cerebral redistribution as it is the main branch of the circle of Willis and carries 80% of the blood flow to the ipsilateral cerebral hemisphere, a constant 3%–7% of

cardiac output through out gestation. The MCA PI and UA PI values for the corresponding gestational age were compared with reference values given by Harrington *et al*¹¹ normograms. MCA PI was considered abnormal when it is less than 5th percentile for that gestational age and UA PI was considered abnormal when it is more than 95th percentile for the corresponding gestational age. It is possible to use a single cut off value for cerebroplacental ratio after 30th week because cerebral-umbilical Doppler ratio does not vary significantly between 30th and 40th weeks as reported by Waldimiroff *et al*.⁵ After 26 weeks, the statistical comparison showed no significant differences between the intervals considered.Arbeile⁴ *et al* also found the cerebral-placental ratio constant during the pregnancy and suggested 1 as the cut off value and all values below 1 were considered abnormal. We considered the study of Gramellini *et al*⁶ that cerebroplacental ratio less than 1.08 as abnormal. We have studied about 50 pregnancies with preeclampsia and clinical suspicion of IUGR.70% of neonates (n=35) had birth weight of less than 2.5kg.Of the 50neonates,19 neonates were admitted to NICU, 8 neonates had 5 min Apgar score of less than 7and 15 babies were born by emergency caesarian section for fetal distress. There were 8 neonatal deaths. Of the 8 neonatal deaths, 1 case had reversal of diastolic flow and 5 had absent diastolic flow.

As compared with other studies present study also had majority of cases with abnormal Doppler indices Umbilical artery- It was found to have low sensitivity of 66.6% when compared to MAC PI and cerebroplacental ratio. The sensitivity was comparable with that of Fong KW *et al*⁴

The specificity of the UA PI 93.1% was found to be better than other variables. The specificity was

comparable with the above mentioned studies. The UA PI is effective to rule in the possibility of adverse perinatal outcome when it is abnormal. The Positive Predictive Value of UA PI 87.5% was more than that of MCA PI and Cerebroplacental ratio. It indicated the likelihood of adverse perinatal outcome in growth retarded fetus with abnormal UA PI. The positive predictive value was higher when compared to all other studies. The negative predictive value 79.4% obtained in our study was comparable with the above mentioned studies. This was less than that of MCA PI and cerebroplacental ratio. Our findings confirm the result of Fong KW *et al*¹⁴, Chan *et al*¹⁵ and Gramellini *et al* that abnormal UAPI is associated with adverse outcome like NICU admission for low birth weight and low Apgar scores than the one with normal UA PI. It provides the most useful information for differentiating fetuses already compromised or likely to become compromised from those that are non-compromised. Our findings agree with Harrington *et al*¹¹ that umbilical artery can be normal in term and near term with abnormal middle cerebral artery. Middle cerebral artery was found to have a sensitivity of 83.3% less than that of cerebroplacental ratio and more than that of UA PI. The values were not comparable with the below mentioned studies.

It showed specificity 85%. It agrees with Fong *et al*¹⁴ that MCA PI is less specific than cerebroplacental ratio and UA PI. The study had more number of false positive values. There are several possible explanations for the low specificity of the MCA pulsatility index for adverse perinatal outcome. Among several published normograms for MCA PI the cut off values for an abnormal MCA pulsatility index are similar up to about 30 weeks gestational age but differ after 32 weeks. The normograms we choose to use for analysis are from the largest published cross-sectional study by Harrington K *et al*¹¹. Positive predictive value of MCA PI 89.28% in predicting adverse perinatal outcome is more than that for other variables, which can be attributed to the less false positive values. The negative predictive value of 77.27% is comparable with that of Gramellini *et al* study. It is more useful in ruling out the possibility of adverse perinatal outcome. Cerebroplacental ratio- It had the highest sensitivity value of 95.6% more than any other variable. The values were not comparable with any other study because of variation in the prevalence of IUGR. The highest sensitivity of cerebroplacental ratio indicates its usefulness of cerebroplacental ratio in ruling out the possibility of adverse perinatal outcome in IUGR when the ratio is normal for the gestational age. It showed the specificity of 87% which is less compared to UA PI and better than the MCA PI. The values were comparable with Fong *et al*¹⁴ study.

The positive predictive values 88%. The value was comparable with Gramellini *et al*⁶ study. The negative predictive value 85% is better than that of UA PI and MCA PI. The values were comparable with that of Fong *et al*¹⁴ and Gramellini *et al*⁶ studies. It indicates that the likelihood of prediction of favorable outcome is better when the cerebroplacental ratio is normal. Our study agrees with that of Chan *et al*¹⁵ that the cerebroplacental ratio is more sensitive than UA PI, but at the expense of decreased specificity. In our study when we compare the overall diagnostic accuracy in prediction of adverse outcome in IUGR. Cerebroplacental ratio has the diagnostic accuracy of 90% which is more than UA PI (82%), MCA PI (84%). The values obtained in our study are comparable with that of Gramellini *et al*⁶. Present study has shown majority of cases (85.71%) with abnormal umbilical artery S/D ratio, which is comparable to the study conducted by Khalid *et al*¹⁸. In other studies majority showed abnormal uterine artery S/D ratio. In the present study, majority of the cases (63%) with abnormal Doppler indices had NICU stay where as Cutis Lowery Jr¹⁹ study showed 86% of NICU admissions with abnormal Doppler indices.

Perinatal morbidity in abnormal uterine artery S/D and abnormal umbilical artery S/D are respectively 70% and 63.33%. Fleischer *et al*¹⁰ and Bhatt CJ *et al* showed 67% and 60% of IUGR in abnormal Doppler indices where as in the present study it was 37.14% and in the study done by Khalid *et al*¹⁸ it was 30.56%.

100% mortality was seen in cases with reversed diastolic flow and absent diastolic flow. This confirms the findings of Karsdropet *et al*²³, which showed that absent and reversed diastolic flow is better indicator of the adverse perinatal outcome. The current study has shown that absent or reversed end – diastolic flow in the umbilical artery is strongly associated with major perinatal morbidity with mortality. This has been well recognized in the literature that there is strict correlation between the abnormal UA PI and poor perinatal outcome in IUGR. Studies have shown that absent and reversed diastolic flow in the umbilical artery is associated with increased perinatal mortality and morbidity 24 25 26 27.

The primary aim of antepartum fetal surveillance is timely recognition of fetal compromise to enable appropriate intervention and to prevent further serious complications. Timely intervention might save the baby. If the intrauterine environment is hostile, baby may be delivered and handed over to neonatologist. Hence Doppler of fetoplacental circulation plays a significant role in predicting the adverse perinatal outcome in IUGR fetus which helps in the management of such fetuses. Our results in evaluating the usefulness of umbilical artery and middle cerebral artery Doppler in predicting the

adverse perinatal outcome in preeclampsia and IUGR indicate that both abnormal umbilical Doppler indices and cerebroplacental ratio are strong predictors of adverse outcome in IUGR. The MCA PI alone is not a reliable indicator when used alone. The combination of umbilical and fetal cerebral Doppler indices may increase the utility of Doppler ultrasound in clinically suspected IUGR.

CONCLUSION

- Abnormal uterine, umbilical artery and middle cerebral artery Doppler flow velocimetry studies associated with severe form of hypertension and higher incidence of IUGR
- There is progressive fall of vascular resistance in uterine, placental and umbilical arteries as gestational age increases. This will result in high end diastolic blood flow in all these blood vessels.
- Absent end diastolic flow and Reverse diastolic flow in umbilical artery indicates severe fetal distress and is associated with 100% perinatal mortality.
- Abnormal PI of MCA/ umbilical artery ratio(CPR) is also associated with IUGR.
- CPR is more sensitive than MCA and umbilical artery.
- Because the changes in the uterine and umbilical circulation strongly correlate with the perinatal outcome, Doppler velocimetry is a primary tool for fetomaternal surveillance in cases with preeclampsia and IUGR.
- It is safe, non-invasive technique, easy to perform, easy to interpret, and hence most valuable tool in the management of high risk pregnancy.
- There was high incidence of LSCS due to fetal distress, low birth weight, increased incidence of NICU admission and low Apgar score at 1 and 5 minutes with abnormal Doppler indices in the study group.
- Thus triple vessel Doppler study is very useful in predicting high risk pregnancies with adverse perinatal outcome when the Doppler velocimetry is abnormal

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