Original Research Article

Prediction of adverse perinatal outcome by Doppler velocimetry of middle cerebral and umbilical artery

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Abstract

Background: The umbilical-placental and cerebral vascular beds are directly involved in the hemodynamic redistributions of fetal growth retardation. Some studies proved the cerebral doppler indices to be better predictor of adverse perinatal outcome. **Aim:** To predict adverse perinatal outcome by Doppler velocimetry of middle cerebral and umbilical artery. **Material and Methods:** The study population comprised of 100 pregnancies between 31-40 weeks of gestation. These 100 patients, were divided into 2 groups: Control Group: 50 patients with normal fetal parameters and without intrauterine growth retardation. Study Group: 50 patients with intrauterine growth retardation and without any obvious risk factor. All the 100 patients were then subjected to doppler examination. Flow velocity wave forms were recorded from the umbilical artery and fetal middle cerebral artery. **Results:** Among all the doppler indices evaluated, umbilical artery S/D ratio with a cut off value of 3 showed highest sensitivity (86.96%) and negative predictive value (94%) in prediction of overall perinatal outcome. AEDF/REDF had the lowest sensitivity (34.37%) and MCA PI <2 S.D. had the lowest negative predictive value (75%). **Conclusion:** All the indices and their ratios have high negative predictive value in prediction of adverse perinatal outcome (especially major adverse outcome); which means that absence of abnormal indices and their ratios have high likelihood of favorable perinatal outcome.

Keywords: Doppler velocimetry, middle cerebral artery, umbilical artery, perinatal outcome

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INTRODUCTION

Doppler ultrasound velocimetry was first reported to study human pregnancy in 1977 by Fitzgerald and Drumm who used continuous wave Doppler to obtain flow velocity wave form from the umbilical vessels.[1] Recently developed methods using real time ultrasound images superimposed with blood flow coded in color have made it possible to delineate vessels like the fetal middle cerebral artery with great ease and accuracy resulting in more accurate and quicker examination.[2] The umbilical-placental and cerebral vascular beds are directly involved in the hemodynamic redistributions of fetal growth retardation. Some studies proved the cerebral doppler indices to be better predictor of adverse perinatal outcome. While few other studies proved the cerebral-umbilical ratio as a better predictor for the same or for prediction of small for gestational age infants than either vessel's doppler alone. We have used various doppler indices of two fetal arteries i.e. umbilical and middle cerebral artery and evaluated their role in prediction of adverse perinatal outcome.

MATERIAL AND METHODS

This prospective study was carried out with the main aim to evaluate the usefulness of fetal umbilical and middle cerebral artery indices and their ratios in prediction of adverse perinatal outcome. The study population

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comprised of 100 pregnancies between 31-40 weeks of gestation. These 100 patients, were divided into 2 groups:

Control Group: Control group comprised of 50 patients with normal fetal parameters and without intrauterine growth retardation.

Study Group: Study group comprised of 50 patients with intrauterine growth retardation and without any obvious risk factor.

Inclusion criteria

Clinically diagnosed intrauterine growth retarded pregnancies with patient giving history of regular cycles of 3 to 4 days per 28 days with definitive knowledge of last menstrual period.

Exclusion criteria

Patients with clinically diagnosed intrauterine growth retardation having following risk factors –

Patients with irregular menstrual cycle or not sure of last menstrual period. Patients conceived in lactational ammenorrhoea. Patients with systemic diseases, viz, heart disease, sickle cell hemoglobinopathy. Pregnant patients with congenital anomalies in the fetus. Patient who lost to follow up.

Methodology

Detailed present obstetrical and menstrual history was noted for all 100 patients. Patients were then subjected to ultrasound examination. These patients were subjected to follow up ultrasound examination and consistent findings were confirmed. All the 100 patients were then subjected to doppler examination. Doppler examinations were then performed with Aloka Prosound (Model: SSD 4000) Color Doppler machine using a 3.5 MHz transducer with 3 mm sample volume and medium filter with the patient in a semirecumbent position and fetus in a quiet resting state. Flow velocity wave forms were recorded from the umbilical artery and fetal middle cerebral artery. Recordings were obtained from the umbilical artery by placing the sample volume in the lumen of the artery away from the placental and fetal cord insertion.[90] After recording a technically satisfactory doppler waveform, the pulsatility index and S/D ratio was noted. Pulsatility index of the middle cerebral artery was noted using a transverse section of the fetal head .at the level of the thalami and the cavum septum pellucidum. By moving the probe caudally, on a plane parallel to the previous one, we identified the pulsation of the middle cerebral artery in the sylvian fissure The doppler sample was placed in the center of the pulsation to obtain the maximum frequency shift After recording a technically satisfactory doppler waveform, pulsatility index and S/D ratio was noted. The MCA/UA PI ratio and MCA/UA S/D ratio were calculated from the pulsatility indices and S/D ratios of the middle cerebral and umbilical arteries. The pregnancies were followed up and the final perinatal outcome of each case was noted. Various neonatal indicators were used to assess the outcome. The major outcome included the stillbirths, early neonatal death, prolonged NICU admission (>7days), hypoxic ischemic encephalopathy (HIE), intracranial hemorrhage (ICH), necrotizing enterocolitis (NEC), and congestive cardiac failure (CCF). The minor outcome included LSCS for fetal hypoxia, preterm delivery (<37 weeks) and Apgar score at 5 minutes <7.

Interpretation of Doppler findings:

Doppler study was considered abnormal when-

1. Umbilical artery pulsatility index more than 95 percentile of reference values by Acharya G *et al.*.[3]
2. Umbilical artery S/D ratio more than 3 or more than 95 percentile of reference values by Acharya G *et al.*.[3]
3. Middle cerebral artery pulsatility index less than 5 percentile of reference values by Mari G *et al.*.[4]
4. MCA/UA PI ratio less than 1.08 or less than 2S.D. of reference values by Gramellini D *et al.*.[5]
5. MCA/UA S/D ratio less than 1.

Statistical Analysis

All the indices and ratios in the intrauterine growth retardation group were compared with that in the normal study group using the Chi Square Test and Student 't' Test. P <0.05 was significant. We calculated the sensitivity, specificity, predictive values and diagnostic accuracy of UA PI, UA S/D, MCA PI, MCA/UA PI ratio, and MCA/UA S/D ratio for predicting intrauterine growth restriction and adverse perinatal outcome.

RESULTS

In the present study, maximum number of patients were in the age group of 21-25 years (31 in study group and 30 in control group) followed by the age group of 26-30 years (12 in study group and 10 in control group). Mean age for study group was 25±3.7 years while that for control group was 24±3.9 years. The age wise distribution between study group and control group was statistically not significant. Out of 100 subjects, 60 (60%) were primigravida, 29 (29%) were second gravida and 7 (7%), 2 (2%), 2 (2%) were third, fourth and fifth gravida respectively. In the study group, 32 (64%) were primigravida and 18 (36%) were multigravida. While in the control group, 28 (56%) were primigravida and 22 (44%) were multigravida. The gravida wise distribution between study group and control group was statistically not significant. Maximum number of patients were in the gestational age group of 33-35 weeks (19 in study group and 17 in control group) followed closely by the gestational age group of 36-38 weeks (19 in study group and 15 in control group). Mean gestational age in study group was 35.3±2.48 weeks and in control group was 36±2.71 weeks. The gestational age wise distribution between study group and control group was statistically not significant.

Table 1: Diagnostic criteria of IUGR: Performance characteristics

Criterion	Sensitivity	Specificity	Predictive value		Accuracy
			Positive	Negative	
UmA PI ≥ [mean+2SD]	82	88	87.23	83.01	85
UmA S/D ≥ 3	71.79	92	87.5	80.70	83.14
UmA S/D ≥ [mean+2SD]	64.1	98	96.15	77	86.51
MCA PI < [mean+2SD]	40	81	69	57.75	61
MCA PI/UmA PI <[mean+2SD]	68	94	91.89	74.60	81
MCA [S/D] / UmA [S/D] >1	53.84	86	75	70.49	86.51
AEDF/REDF	22	100	100	56.18	61
MCA PI/UmA PI < 1.08	66	100	100	74.63	83

Table 1 shows performance characteristics of various parameters to evaluate their efficacy in diagnosing intrauterine growth restriction. Umbilical artery PI ratio had highest sensitivity in prediction of IUGR (82%) followed by umbilical artery S/D ratio (71.79%) with cut off value of 3. AEDF/REDF had lowest sensitivity. The specificity and positive predictive value in prediction was highest with AEDF/REDF and MCA PI/UmA PI with cut off value of 1.08 (100% each) and lowest with MCA PI (81 and 69% respectively). 19 (38%) patients delivered by LSCS and 31 (62%) delivered vaginally. In contrast, in control group, the figures were 3 (6%) and 47 (94%) respectively. The difference between two groups was statistically significant. In study group, 16 (84.21%) out of 19 patients delivered by LSCS, the indication was fetal distress and in remaining 3 (15.79%) patients, LSCS was indicated for other reasons (eg. previous LSCS etc.). The respective figures in control group were 1 (33.33%) and 2 (66.67%) respectively. The difference between two groups was however statistically not significant. Mean gestational age at delivery in the study group was 36.58 weeks as compared with 38.68 weeks in the control group. The difference between two groups was however statistically highly significant. Mean examination to delivery interval in study group was 1.24 weeks as against 2.72 weeks in control group. The difference between two groups was statistically significant. In study group, mean birth weight was 1487 gms with a standard deviation of 321 gms. While in control group, mean birth weight was 2781 gms with a standard deviation of 197 gms. The difference in mean birth weight between two groups was statistically significant. Maximum number of neonates had birth weights between 1-1.5 kg followed by 1.5-2 kg and none of them had birth weight > 2.5kg. While in control group, maximum number of neonates had birth weights between 2.5-3 kg and none of them had birth weight < 2 kg. The birth weight distribution between two groups was statistically significant.

Table 2: Adverse Perinatal outcomes

	Adverse Perinatal outcome indicator	Study no.	Control no.	Total no.	χ^2 value	P value	S
	Major						
1	Stillbirth	6	0	6	6.383	0.012	S
2	Neonatal death	5	0	5	5.263	0.022	S
3	NICU admission > 7 days	9	1	10	3.840	0.05	S
4	Hypoxic-ischemic encephalopathy (HIE)	2	0	2	2.041	0.153	NS
5	Intracranial hemorrhage (ICH)	2	0	2	2.041	0.153	NS
6	Necrotizing enterocolitis (NEC)	1	0	1	1.010	0.315	NS
7	Congestive cardiac failure (CCF)	1	0	1	1.010	0.315	NS
	Minor						
8	Cesarean delivery for fetal distress	16	1	17	15.946	0.000	HS
9	Premature birth	23	2	25	23.520	0.000	HS
10	5-min Apgar score <7	10	1	11	8.274	0.004	HS

Table 2 shows the adverse perinatal outcomes in study population. The outcomes were divided into major and minor groups. In study group, 6 babies were stillborn, 5 died in early neonatal period, 9 had NICU admission > 7 days. Postnatal complications (like HIE, ICH etc.) were seen in 6 patients. 23 babies had premature delivery, 16 were delivered by LSCS for intrauterine fetal distress and 10 babies had Apgar scores < 7. In control group, only 1 baby had major outcome in the form of NICU admission for > 7 days. 2 babies had premature delivery, 1 was delivered by LSCS for intrauterine fetal distress and 1 baby had Apgar scores < 7.

Table 3: Adverse [Major + Minor] perinatal outcome of study population according to doppler indices: Performance characteristics

Criterion	Sensitivity	Specificity	Predictive value		Accuracy
			Positive	Negative	
UmA PI ≥ [mean+2SD]	80	70.77	59.57	86.79	74
UmA S/D ≥ 3	86.96	71.21	51.28	94	75.28
UmA S/D ≥ [mean+2SD]	69.57	78.78	53.33	88.14	76.40
MCA PI < [mean+2SD]	47.06	81.81	57.14	75	70
MCA PI/UmA PI < [mean+2SD]	77.14	83.08	71.05	87.10	81
MCA [S/D] / UmA [S/D] <1	47.83	84.84	52.38	82.35	75.28
AEDF/REDF	34.37	100	100	76.40	79
MCA PI/UmA PI < 1.08	73.53	89.40	78.12	86.76	84

Table 3 is showing performance characteristics of various doppler indices in prediction of overall [Major + Minor] adverse perinatal outcome. Among all the doppler indices evaluated, umbilical artery S/D ratio with a cut off value of 3 showed highest sensitivity (86.96%) and negative predictive value (94%) in prediction of overall perinatal outcome. AEDF/REDF had the lowest sensitivity (34.37%) and MCA PI < 2 S.D. had the lowest negative predictive value (75%). AEDF/REDF had the highest specificity (100%) and positive predictive value. Umbilical artery PI ≥ 2S.D. had lowest specificity (70.77%) and umbilical artery S/D ratio with cut off value of 3 had the lowest positive predictive value (51.28%). MCA PI/UmA PI ratio with cut off value of 1.08 had highest accuracy (84%) followed by that of MCA PI/UmA PI ratio < 2S.D. (81%) in prediction of overall perinatal outcome while MCA PI < 2 S.D. had the lowest accuracy (70%).

Table 4: Adverse [Only Major] perinatal outcome of study population according to doppler indices: Performance characteristics

Criterion	Sensitivity	Specificity	Predictive value		Accuracy
			Positive	Negative	
UmA PI ≥ [mean+2SD]	94.74	62.96	37.5	98.08	69
UmA S/D ≥ 3	100	61.73	20.51	100	65.17
UmA S/D ≥ [mean+2SD]	87.5	71.6	23.33	98.30	73.03
MCA PI < [mean+2SD]	63.16	81.48	41.38	90.14	76
MCA PI/UmA PI < [mean+2SD]	89.47	75.31	45.94	96.83	78
MCA [S/D] / UmA [S/D] <1	75	81.48	28.57	97.06	80.90
AEDF/REDF	57.89	100	100	90	92
MCA PI/UmA PI < 1.08	89.47	81.48	53.13	97.06	83

Table 4 is showing performance characteristics of various doppler indices in prediction of only major adverse perinatal outcome. Umbilical artery S/D ratio with cut off value of 3 had highest sensitivity (100%) and negative predictive value (100%) while AEDF/REDF had the lowest respective values (57.89% and 90%). Highest specificity and negative predictive value was found in AEDF/REDF (100% each); while the respective value were lowest in Umbilical artery S/D ratio with cut off value of 3 (61.73 and 20.51% respectively). AEDF/REDF had the highest accuracy (92%) in prediction of major adverse perinatal outcome followed by MCA PI/UmA PI with cut off value of 1.08 (83%). Umbilical artery S/D ratio with cut off value of 3 had the lowest accuracy (65.17%).

DISCUSSION

Doppler ultrasound of the uterine, umbilical and middle cerebral arteries offer the potential to study the function and hence physiological changes in the uteroplacental and fetoplacental circulation and may help identity small for gestational age fetus suffering from hypoxia. Moreover, the test can be performed simply is non-invasive and relatively inexpensive.

Table 5: Performance characteristics of umbilical artery velocimetry study in prediction of adverse perinatal outcome

Parameter assessed		Author	Se	Sp	PPV	NPV	Acc
PI	>2sd	Gramellini *et al.*[5]	64	90.7	72.7	86.7	83.3
	>2sd	Fong *et al.*[6]	44.7	86.6	54	81.7	-
	>2sd	Lakhkar *et al.*[7]	50	59	66.6	41.9	-
	>95percentile	**Present study**	**80**	**70.77**	**59.57**	**86.79**	**74**
S/D	>2sd	Strigini *et al.*[8]	53	94	40	96	-
	>2sd	Lakhkar *et al.*[7]	66.6	45.4	66.6	45.4	-
	>3	**Present study**	**86.96**	**71.21**	**51.28**	**94**	**75.28**
	>95percentile	**Present study**	**69.57**	**78.78**	**53.33**	**88.14**	**76.40**

In prediction of adverse perinatal outcome, with the use of umbilical artery PI >95 percentile in the present study had higher sensitivity (80%) but lower specificity and positive predictive value as compared to Gramellini *et al.*[5] with comparable negative predictive value. In the present study, umbilical artery S/D ratio with a single cut off value of 3 had slightly higher sensitivity as well as specificity as compared to PI value; but with cut off value of >2 S.D. the sensitivity in prediction of adverse outcome was less. Predictive values and diagnostic accuracies of umbilical artery PI and S/D ratio in our study are comparable with each other as well as with that reported by various authors as in table 5.

Table 6: Performance characteristics of MCA velocimetry study in prediction of adverse perinatal outcome

Parameter assessed		Author	Se	Sp	PPV	NPV	Acc
PI	<2sd	Gramellini *et al.*[5]	24	100	100	77.3	78.8
	<1.5sd	Strigini *et al.*[8]	40	95	36	95	-
	<2sd	Fong *et al.*[6]	72.4	58.1	37.7	85.7	-
	<2sd	Lakhkar *et al.*[7]	41.6	90.9	88.2	48.7	-
	<5percentile	**Present study**	**47.06**	**81.81**	**57.14**	**75**	**70**

In the present study, MCA PI had sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of 47.06%, 81.81%, 57.14%, 75%, and 70% respectively in prediction of adverse perinatal outcome. Various authors have reported diverse values in prediction of adverse perinatal outcome on the basis of MCA PI alone (Table 6).

Table 7: Performance characteristics of MCA/UA ratio in prediction of adverse perinatal outcome

Parameter assessed		Author	Se	Sp	PPV	NPV	Acc
PI	<1.08	Gramellini *et al.*[5]	68	98.4	94.4	88.8	90
	<2sd	Bahado *et al.*[9]	63	90	81	77	-
	<5percentile	Odibo *et al.*[10]	65	73	73	65	-
	<1.08	Odibo *et al.*[10]	72	62	68	67	-
	<2sd	Fong *et al.*[6]	51.3	80.6	48.1	82.5	-
	<1	Lakhkar *et al.*[7]	47.2	86.3	85	50	-
	<1.08	**Present study**	**73.53**	**89.4**	**78.12**	**86.76**	**84**
	<2sd	**Present study**	**77.14**	**83.08**	**71.05**	**87.1**	**81**
S/D	<1	Lakhkar *et al.*[7]	55.5	72.7	76.9	50	-
	<1	**Present study**	**47.83**	**84.84**	**52.38**	**82.35**	**75.28**

In the present study, MCA PI / UA PI ratio with a single (<1.08) as well as gestational age specific cut off value (<2S.D.) had similar performance in prediction of adverse perinatal outcome. These values are also in consonance with that reported by various other authors (Table 7). MCA (S/D) / UA (S/D) ratio in our study had similar sensitivity in prediction of adverse perinatal outcome to Lakhkar *et al.*[7]; however, there are some differences between two studies with higher specificity and lower positive predictive value in our study.

Table 8: Performance characteristics of umbilical artery velocimetry study in prediction of major adverse perinatal outcome

Parameter assessed		Author	Se	Sp	PPV	NPV	Acc
PI	>2sd	Fong *et al.*[6]	58.3	81.8	22.2	95.7	-
	>2sd	Lakhkar *et al.*[7]	58	56.5	35	86.8	56.8
	>95percentile	**Present study**	**94.74**	**62.96**	**37.5**	**98.08**	**69**
S/D	>2sd	Lakhkar *et al.*[7]	75	41.3	25	86.3	48
	>3	**Present study**	**100**	**61.73**	**20.51**	**100**	**65.17**
	>95percentile	**Present study**	**87.5**	**71.6**	**23.33**	**98.3**	**73.03**

In prediction of major adverse outcome on the basis of umbilical artery doppler velocimetry alone, we have found higher sensitivity and specificity as compared with Lakhkar *et al.*[7] (Table 8). However; the predictive values and diagnostic accuracy for prediction are comparable in both the studies.

Table 9: Performance characteristics of MCA velocimetry study in prediction of major adverse perinatal outcome

Parameter assessed		Author	Se	Sp	PPV	NPV	Acc
PI	<2sd	Fong *et al.*[6]	91.7	53.9	15.1	98.6	-
	<2sd	Lakhkar *et al.*[7]	66.6	71.7	47	90	77
	<5percentile	**Present study**	**63.16**	**81.48**	**41.38**	**90.14**	**76**

In the present study, MCA PI alone has sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of 63.16%, 81.48%, 41.38%, 90.14%, and 76% respectively in prediction of major adverse outcome. These values are in consonance with Lakhkar *et al.*[7] (Table 9).

Table 10: Performance characteristics of MCA/UA ratios in prediction of major adverse perinatal outcome

Parameter assessed		Author	Se	Sp	PPV	NPV	Acc
PI	<2sd	Fong *et al.*[6]	62.5	75.5	18.5	95.8	-
	<1	Lakhkar *et al.*[7]	66.6	73.9	40	89.4	72.4
	<1.08	**Present study**	**89.47**	**81.48**	**53.13**	**97.06**	**83**
	<2sd	**Present study**	**89.47**	**75.31**	**45.94**	**96.83**	**78**
S/D	<1	Lakhkar *et al.*[7]	83	75	38.4	93.7	68.4
	<1	**Present study**	**75**	**81.48**	**28.57**	**97.06**	**80.90**

In the present study, MCA/UA PI ratio with different cut off values have similar diagnostic efficacy in prediction of major adverse perinatal outcome; these values are slighthly higher than the previously reported studies by Lakhkar *et al.*[7] and Fong *et al.*[6] as shown in table 10. However; MCA/UA S/D ratio in the present study had sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy comparable with Lakhkar *et al.*[7] in prediction of adverse outcome.

CONCLUSION

The ratios of indices between middle cerebral artery and umbilical artery are more accurate than independent evaluations in identifying fetuses developing fetal distress. All the indices and their ratios have high negative predictive value in prediction of adverse perinatal outcome (especially major adverse outcome); which means that absence of abnormal indices and their ratios have high likelihood of favorable perinatal outcome.

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