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ROLE OF UMBILICAL ARTERY AND MIDDLE CEREBRAL ARTERY DOPPLER IN PREDICTING PERINATAL OUTCOME IN PATIENTS WITH SEVERE PRE-ECLAMPSIA AND IUGR

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ABSTRACT

Background: Increase in blood flow resistance in the uterine arteries accompany a hazard of successive development of pre-eclampsia (PE) and Intra uterine growth restriction (IUGR). This study aimed to correlate the association between the Umbilical artery (UA) and Middle cerebral artery (MCA) doppler index with the perinatal outcomes in the pregnant patients suffering from PE and IUGR condition in fetus. **Method:** A randomized prospective observational study was conducted in a tertiary care teaching hospital. The study included 50 patients from third trimester i.e., 28 weeks of gestation onwards with severe PE as well as asymmetrical IUGR in fetal growth. The patients were diagnosed with sonography and UA [systolic/diastolic (S/D) ratio, Resistance index (RI) and Pulsatility index (PI)] and MCA [S/D ratio, RI, PI, Cerebro-placental (CP) ratio] flow rate was examined by color doppler technique. The perinatal outcomes (low birth weight, appearance pulse grimace activity (APGAR) <7, fetal distress, need of NICU, NICU for >48 hrs and mortality) were cross-checked with the patient's data. R- software version 1.2.5001., was used for data analysis Sensitivity, Specificity was calculated to analyze the various variables. **Results:** The mean age of study cohort was 22 ± 2.84 years. The primigravida were 82% and multigravida were 18%. The patients with severe PE were 54% (n=27), followed by 38% (n=19) in severe PE+IUGR, and the remaining 8% (n=4) confirmed with IUGR condition. In all findings, birth weight was sensitive (≈ 100%) with high values and specificity was with low values, mortality was with low sensitivity and high specificity (≈ 100%). **Conclusion:** The UA doppler and MCA doppler indices can be strong predictors of fetal distress, need of NICU and admission in NICU up to >48 hours.

KEYWORDS

Birth Weight, Fetal Growth Retardation, Placental Circulation, Pre-Eclampsia, Ultrasonography

INTRODUCTION

In pregnancy, physiological changes in women, which may influence biochemical parameters that mimic symptoms of medical diseases. At this stage, there is need to differentiate the normal structural and functional changes and characteristics of disease.[1] The placental blood flow is necessary for fetal growth, and the flow rate is helpful in predicting the fetal growth and development.[2] Intrauterine growth restriction (IUGR) is a major complication in fetus development. This is diagnosed when fetal birth weight is <10th percentile.[3] According to the United Nations Children's Fund (UNICEF) the low birth weight (LBW) estimation 2000-2015, in 2015 one in seven children were born with LBW, about 15% (20 million) of new-born with LBW all around the world. The frequency of LBW in south Asia is 26.4% of total LBW new-born in the world. In India, estimations are not clear due to partial data. [4] An Indian study conducted by Khan et al., by obtaining the data from the National Family Health Survey of 2005-2006 (NFHS-3) and 2015-2016 (NFHS-4) which had included 11,300 and 99,894 children respectively, concluded that, the prevalence of LBW has significantly declined from 20.4% (95%CI 19.4-21.4) to 16.4% (95% CI 16.1-16.8) in the previous decade.[5]

IUGR and small for gestational age (SAG) are interchangeable words and associated with perinatal morbidity as well as mortality. Maternal risk factors i.e., comorbidities – hypertension (HTN), diabetes (D.M), cardiopulmonary disease (CPD), Notational disorders - anaemia, malnutrition, Social habits - smoking, Miscellaneous - drug use. fetal causes i.e., genetic disease including aneuploidy, congenital malformations, fetal infection, multiple pregnancies. placental causes i.e., placental insufficiency, placental infarction, placental mosaicism. The perinatal, postnatal, and adult life development were mainly determined by Intrauterine growth by fetus.[6] Pre-eclampsia (PE) is a serious condition in which maternal and prenatal and postnatal morbidity and mortality can occur. This condition is primarily associated with elevated blood pressure and proteinuria. There is no complete cure only prevention can be made.[7] The doppler flowmetry method can predict the IUGR condition in the fetus of the pregnant women.[8] This research is mainly conducted to find the interconnection between the doppler findings i.e., umbilical artery (UA), middle cerebral artery (MCA) flow rate with the perinatal outcomes in gestational period who were already diagnosed accompanied by PE and having IUGR condition in fetus development.

MATERIALS AND METHODS

A randomized prospective observational study conducted in a third level teaching hospital for 2 years after obtaining ethical clearance from Institutional Review Board [DYPMCK/196/2019/IEC- Date 21/march/2019]. The formula: $N = \frac{Z^2 * P * (1-P)}{d^2}$ was used for sample size calculation. The prevalence is taken as 74%, and Z is taken as 1.64 (critical value at normal distribution), d is 11% of P (absolute precision).[9,10] The minimum sample size obtained was 43, here 50 subjects were recruited in the research. The women with gestation age of third trimester (28 weeks) onwards with singleton pregnancy and with severe PE and with asymmetrical IUGR were included. Multiple gestation, molar pregnancies, patient with congenital anomaly of foetus, symmetrical IUGR, and with other comorbidities were excluded.

The subjects were explained about non-invasive procedure i.e., sonography technique and informed consent done. The patients were examined in a semi recumbent position with Ultrasound machine (6E Healthcare LOGIQ F8 Expert) and recordings were bring off by using 2-3 MHz probe for UA and MCA flow rate by the method of color doppler. The patients were investigated with doppler to obtain the values of umbilical artery flow [systolic/diastolic (S/D) ratio, Resistance Index (RI),and Pulsatility Index (PI)] and middle cerebral artery flow [S/D ratio, RI, PI, Cerebroplacental (CP) ratio]. The perinatal outcomes i.e., LBW, Appearance Pulse Grimace activity (APGAR) <7, Fetal Distress, Need of Neonatal intensive care unit (NICU), NICU for >48 hours, Mortality were cross-check with the patient's data.

Statistical analysis:

Statistics was analysis with R- software version 1.2.5001., Categorical data has been represented as frequencies and proportions and qualitative data significance has been analyzed with Chi square test, Fisher Exact tests. Continuous data was represented as mean and standard deviation. Independent T-test was employed for testing of significant difference between the means in two unrelated groups. Sensitivity, specificity were calculated. The $P < 0.05$ was considered for significance. Graphs were prepared with the help of MS Excel.

RESULTS:

Mean age of pregnant women was 22 ± 2.84 years. Out of 50 patients, 38%(n=19) patients were between the age of 21 - 25 years, followed by 32%(n=16) with < 20 years,28% (n=14) belonged to 26 to 30 years,

only 2%(n=1) belonged to 31 to 35 years of age. Majority of the pregnant women were belonging to primigravida with 82% (n=41) and rest were multigravida with 18% (n=9) patients. Pregnant women were classified based on gestational age i.e., 56% (n=28) belonged to 37 to 40 weeks, 36%(n=18) belonged to 33 to 36 weeks remaining 8% (n=4) belonged to 28 to 32 weeks.

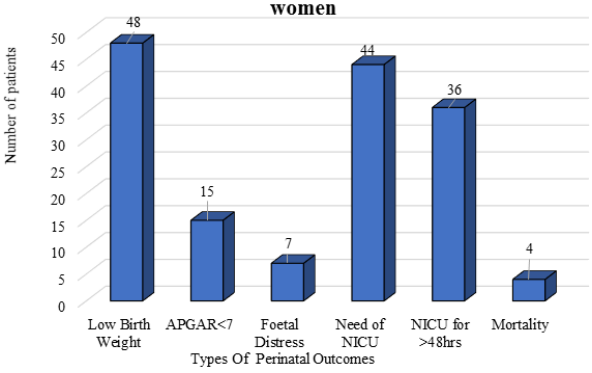
The subjects were categorised with respect to diagnosis mainly into three categories with 54% (n=27) in severe PE, followed by 38% (n=19) in severe PE+IUGR, remaining 8% (n=4) confirmed with IUGR condition.

Table 1: Umbilical artery and middle cerebral artery doppler indices

Doppler Indices:	Findings	Frequency N (%)
Umbilical Artery Doppler indices		
S/D Ratio	Elevated (>3.0)	33(66.0)
	Normal (≤ 3.0)	17(34.0)
Resistance index (RI)	Elevated (>0.7)	28(56.0)
	Normal (≤0.7)	22(44.0)
Pulsatility index (PI)	Elevated (>1.2)	30(60.0)
	Normal (≤1.2)	20(40.0)
Middle Cerebral Artery Doppler indices		
S/D Ratio	Low (≤4)	28(56.0)
	Normal (>4)	22(44.0)
Resistance index	Low (≤0.7)	35(70.0)
	Normal (>0.7)	15(30.0)
Pulsatility index	Low (≤1.2)	25(50.0)
	Normal (>1.2)	25(50.0)
Cerebroplacental ratio (CP Ratio)	Low (≤1.08)	33(66.0)
	Normal (>1.08)	17(34.0)

UA doppler index - the elevated values for S/D ratio, RI, PI were 66% (n=33), 56% (n=28), 60% (n=30) respectively. MCA doppler index the low values for S/D ratio, RI, PI, CP ratio were 56 % (n=28), 70% (n=35), 50% (n=25), 66% (n=33) respectively. (Table 1)

Figure 1: Perinatal Outcomes of the pregnant women



APGAR: Appearance Pulse Grimace activity, NICU- neonatal intensive care unit.

Figure 1 shows the types of perinatal outcomes, among which LBW was observed in 48 patients followed by need of NICU in 44 patients, whereas mortality was observed in 4 patients.

The correlation of UA doppler values with perinatal outcomes was analysed and expressed in Table 2. S/D ratio was observed to be a significant in predicting the case of need of NICU (p=0.000107) and NICU for <48 hrs (p<0.0001). RI, PI were significant predicting fetal distress (p= 0.0015 and p=0.0005) and the need of NICU outcomes (p= 0.01216 and p=0.0059), respectively. (Table 2)

Table 2: Association Of Umbilical Artery Doppler And Perinatal Outcomes:

Fetal Outcomes		S/D Ratio N (%)			Resistance index N (%)			Pulsatility index N (%)		
		Elevated	Normal	P-value	Elevated	Normal	P-value	Elevated	Normal	P-value
Birth weight (kg)	LBW	39(81)	9(19)	1.00	26(54)	22(46)	0.581	28(58)	20(42)	0.659
	Normal	2(100)	0(0)		2(100)	0(0)		2(100)	0(0)	
APGAR<7 (at 5 min)	Yes	14(93.33)	01(6.67)	0.335	11(73)	4(27)	0.192	12(80)	3(20)	0.116
	No	27(77)	8(23)		17(49)	18(51)		18(51)	17(49)	
Fetal Distress	Yes	15(100)	0(0)	0.077	14(93)	1(7)	0.002*	15(43)	20(57)	0.0005*
	No	26(74)	9(26)		14(40)	21(60)		15(100)	0(0)	
Need of NICU	Yes	40(91)	4(9)	0.0001*	28(64)	16(36)	0.012*	30(68)	14(32)	0.006*
	No	1(17)	5(83)		0(0)	6(100)		0(0)	6(100)	
NICU for >48hrs	Yes	35(97)	1(3)	<0.01*	23(64)	13(36)	0.138	25(69)	11(31)	0.062
	No	6(43)	8(57)		5(36)	9(64)		5(36)	9(64)	
Mortality	Yes	4(100)	0(0)	0.765	4(100)	0(0.0)	0.186	4(100)	0(0.0)	0.242
	No	37(80)	9(20)		24(52.17)	22(47.83)		26(56.52)	20(43.48)	
Total		41(82)	9(18)		28(56)	22(44)		30(60%)	20(40)	

APGAR: Appearance Pulse Grimace activity, LBW- low birth weight, S/D- systolic and diastolic, NICU- neonatal intensive care unit. N-Number, %-percentages. Kg- kilograms, *-statistically significant

The association of MCA doppler values with perinatal outcomes were analysed and expressed in table no 3. The RI, PI, CP Ratio values in sonography of MCA were significant with fetal distress (p<0.0001, p=0.00014 and p=0.0027) and need of NICU (p= 0.01673 p=0.01216 and p= 0.0015) respectively. The RI and CP Ratio values are significant for APGR<7(at 5 min) (p=0.0064 and p=0.01901) respectively. The PI,CP Ratio values are significant for APGR<7(at 5 min) (p= 0.0059 and p=0.0123) respectively. (Table 3)

The relationship between the doppler values and the perinatal outcomes were plotted with their sensitivity values, specificity values as graphs in figure 2. In all findings, birth weight was more sensitive and with less specificity, mortality is with low sensitivity and high specificity. (Figure 2)

Table no 3: Association Of Middle Cerebral Artery Doppler And Perinatal Outcomes

Fetal Outcomes		S/D Ratio [N (%)]			RI [N (%)]			PI N [(%)]			C/P Ratio [N (%)]		
		Low	Normal	P-value	Low	Normal	P-value	Low	Normal	P-value	Low	Normal	P-value
Birth weight (kg)	LBW	26(54)	22(46)	0.581	27(56)	21(44)	0.401	28(58)	20(42)	0.367	31(65)	17(35)	0.784
	Normal	2(100)	0(0)		0(0)	2(100)		0(0)	2(100)		2(100)	0(0)	
APGAR<7 (at 5min)	Yes	8(53)	7(47)	1.00	13(87)	2(13)	0.006*	12(80)	3(20)	0.054	14(93)	1(7)	0.019*
	No	20(57)	15(43)		14(40)	21(60)		16(46)	19(54)		19(54)	16(46)	
Fetal Distress	Yes	9(60)	6(40)	0.954	15(100)	0(0)	<0.01*	15(100)	0(0)	<0.01*	15(100)	0(0)	0.003*
	No	19(54)	16(46)		12(34)	23(66)		13(37)	22(63)		18(51)	17(49)	
Need of NICU	Yes	22(50)	22(50)	0.060	27(61)	17(39)	0.016*	28(64)	16(36)	0.012*	33(75)	11(25)	0.002*
	No	6(100)	0(0)		0(0)	6(100)		0(0)	6(100)		0(0)	6(100)	
NICU for >48hrs	Yes	17(47)	19(53)	0.091	23(64)	13(36)	0.053	25(69)	11(31)	0.006*	28(78)	8(22)	0.012*
	No	11(79)	3(21)		4(29)	10(71)		3(21)	11(79)		5(36)	9(64)	
Mortality	Yes	2(50)	2(50)	1.00	4(100)	0(0.0)	0.161	4(100)	0(0.0)	0.1858	4(100)	0(0.0)	0.3440
	No	26(56.5)	20(43.5)		23(50)	23(50)		24(52)	22(48)		29(63.1)	17(37.9)	
Total		28(56)	22(44)		35(70)	15(30)		28(58)	22(42)		33(66)	17(34)	

APGAR: Appearance Pulse Grimace activity, S/D- systolic and diastolic, NICU- neonatal intensive care unit. N- Number, %- percentages.

DISCUSSION

IUGR is a key complication that arises in fetus during pregnancy. The infants have a chance of getting many neonatal complications at birth which include perinatal asphyxia, hypothermia, hypoglycaemia, and polycythaemia and long-term complications like growth retardation, and major complications include subtle neurodevelopmental handicaps, and developmental origin of health and disease.[11] To intercept the complication advance observation and detection of the IUGR condition is needed and possible mainly with the help of sonography techniques. The main parameters are the UA and MCA flow metery. According to Novac et al., Doppler indices from fetal circulation can detect fetal compromises, birth weight, this can predict poor outcomes in Apgar score <7 (at 5 min), admission to NICU at the primary stages of pregnancy.[12]

Figure 2: Association of Doppler index with different perinatal outcomes

Figure 2: Association of Doppler index with different perinatal outcomes. (UA- umbilical artery, MCA- Middle cerebral artery, S/D – systolic and diastolic, CPR- Cerebral-placental ratio)

According to Bansal et al., diagnostic accuracy of doppler is high with 100% sensitivity and 77.78% specificity.[13] According to Khanduri et al., UA PI was more sensitive and specific for the prognosis of IUGR at all stages of gestation period, with the maximum sensitivity (82.1%) and specificity (87%), and Cerebral-umbilical PI at the pregnancy period of 32-36 weeks shows the sensitivity (82.1%) and specificity (96.7%) for the prognosis of IUGR.[8]

In studies conducted by Singh et al., and Lakhkar et al., the perinatal outcomes observed as LBW (45%, 60.2%), APGAR<7 (at 5min) (33%, 6.8%), foetal distress (17%, 38.8%), need of NICU (53%, 66%), NICU for >48 hrs (32%, --), mortality (10%, 12.06%) respectively. However these observations does not corelate with the present study.[14,15] In accordance with metanalysis by NIHR Journals Library, Southampton (UK), Diagnostic performance of CP ratio is more prognosis than umbilical artery doppler.[16] In this research UA RI was showing high sensitivity for APGAR <7 (at 5min) (86.67%) and foetal distress (100%) and mortality (100%) and highest specificity for need of NICU (83.33%) but Singh and Mishra found UARI was highly sensitive for APGAR<7 (5 min) (100%), Lakhkar et al., found UA RI had low sensitivity (44.4%) and high specificity (81.8%) in predicting fetal outcomes.[15]

According to Lakhkar et al. the result of sensitivity, specificity of UAPI, MCAPI, CP ratio were (58%, 56.5%), (66.6%, 71.7%), (66.6%, 73.9%) respectively. These values don't associate with the present study but have a similar pattern.[15]According to Gramellini et al., diagnostic accuracy for the cerebral-umbilical ratio was 90%, compared with 78.8% for the MCA and 83.3% for the UA.[17] these values are in the same pattern as in this study.

UA S/D ratio values are significant with need of NICU and NICU for > 48hours with sensitivity (97.56%,85.37%) and specificity (55.56%,88.89%) respectively. UA RI and UA PI are significant with fetal distress with sensitivity (50% and 50%) and specificity (0% and 95.45%) and need of NICU with sensitivity (100% and100%) and specificity (28.57% and 27.27%) respectively. For MCA PI, MCA RI, MCA CP ratio were significant with fetal distress of sensitivity (53.57%, 55.56%, 45.45%) and specificity (100%, 100%, 100%), need of NICU of sensitivity (100%, 100%, 100%), specificity (27.27%, 26.09%, 35.29%) respectively. The MCA PI, MCA CP ratio were significant with APGR<7 min with sensitivity (42.86%, 42.42%) and specificity (86.36%, 94.12) respectively. The MCA RI and MCA CP ratio were significant with sensitivity (85.19%, 84.85%) and specificity (43.48%, 52.94%) respectively.

The study has explained about different parameters of doppler flowmetry, but the statistical significance is seen as low for some parameters as P-value is >0.005, this was possibility overcome by including a large sample size in the research and further studies are required to state the necessity in ultrasound doppler effect analysing the IUGR condition in predicting perinatal outcomes.

CONCLUSION

Evidence to predict the fetal compromise can be provided with the help of doppler imaging. This makes in improving the fetus outcomes in higher risk pregnancies with IUGR condition. The perinatal outcomes are significant (P <0.05) with doppler imaging in certain conditions. In the UA doppler (S/D ratio, RI, PI) and middle cerebral artery doppler (RI, PI, CP ratio) are significant in finding need for ICU in the fetus. In the UA doppler (RI, PI) and middle cerebral artery doppler (RI, PI, CP ratio) are significant in finding the fetus distress, and middle cerebral artery doppler (PI, CP ratio) are significant in finding the NICU for <48hrs.

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