Original Article

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Colour Doppler and Adverse Perinatal Outcomes in Pregnancies with Foetal Growth Restriction: A Prospective Longitudinal Study

Obstetrics and Gynaecology Section

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ABSTRACT

Introduction: Foetal Growth Restriction (FGR) accounts for a significant proportion of perinatal morbidity and mortality. The study was done to diagnose the foetuses "at risk", so that timely intervention could prevent perinatal morbidity and mortality, as FGR foetuses with deranged velocimetry of Uterine Artery (UA), Umbilical Artery (UMA), Middle Cerebral Arteries (MCA) are associated with high perinatal morbidity and mortality.

Aim: To evaluate the usefulness of blood flow velocimetry of UA, UMA, and MCA as well as a Cerebroplacental Ratio (CPR) on colour doppler and their prediction of adverse perinatal outcome.

Materials and Methods: This was a prospective longitudinal study done in the Department of Obstetrics and Gynaecology, Government Medical College and Rajindra Hospital, Patiala, Punjab, India from October 2021 to March 2022. The study was conducted among 200 antenatal patients, who had a singleton pregnancy, irrespective of age and parity and had FGR foetuses. Blood flow velocities in the UA, UMA, MCA, and CPR were measured. Patients were divided into four groups with 50 patients in each group. Group I included FGR foetuses with normal blood velocities, group II included FGR foetuses with abnormal UA velocimetry, group III included FGR foetuses with abnormal UMA and MCA velocimetry and group IV included FGR foetuses with abnormal CPR. Adverse perinatal outcomes in the form of Respiratory Distress Syndrome (RDS), prematurity, Appearance, Pulse, Grimace, Activity and Respiration (APGAR) <7 at 5 minutes, admission to Neonatal Intensive Care Unit (NICU), and perinatal mortality were assessed in relation to these doppler blood flow patterns. Categorical variables were analysed with the help of Chi-square test and Fisher-exact test. Continuous variables were analysed with ANOVA when data were normally distributed otherwise Kruskal Wallis H test was used.

Results: The mean birth weight was 2432±423, 2209±329, 2100±223 and 1329±403 grams in groups I, II, III, and IV (p-value of <0.001.) The mean gestational age was 38.1±2.3, 37.3±3.2, 36±3.6 and 33.1±3.1 weeks in groups I, II, III, and IV (p-value of <0.001). Perinatal morbidity in the form of RDS and prematurity were compared among four groups with 0, 3 (6%), 17 (34%), and 39 (78%) in groups I, II, III, and IV (p-value of <0.001). APGAR score <7 at 5 minutes was 0, 2 (4%), 9 (18%), and 13 (26%) in groups 1, II, III, and IV (p-value of <0.001). A total of 6 (12%), 16 (32%), 37 (74%) and 46 (92%) C-sections were performed in group I, II, III and IV, respectively, p-value of <0.001. Maternal mortality of 1 (2%) in group III and 2 (4%) was observed in group IV. But no maternal death was there in group I and II.

Conclusion: The adverse perinatal outcomes were seen with changes in Pulsatility Index (PI) value of UA, UMA, MCA. But the patients with a deranged CPR ratio had got worse perinatal outcomes than either deranged MCA, PI or UMA PI alone. Hence, doppler ultrasound especially CPR ratio should be an integral component of routine evaluation of FGR pregnancies, as it helps in obstetrical surveillance and management, and thereby improving adverse perinatal outcomes.

Keywords: Cerebroplacental ratio, Middle cerebral artery, Umbilical artery

INTRODUCTION

Foetal Growth Restriction is defined as a foetus with an estimated foetal weight below the 10th percentile for gestational age (I). Despite recent advances in antenatal care, FGR remains the major cause of perinatal morbidity and mortality, so, the screening of FGR may allow vigilant antenatal surveillance and appropriate timing of foetal delivery in order to avoid serious sequelae [1].

Doppler techniques have been the focus of interest and research activity in obstetrics since, the initial report of signals from the UMA by Fitzgerald DE and Drumm JE [2]. The compromised blood flow through uterine, placental and foetal vessels results in FGR [3]. The abnormalities of blood flow in these vessels can be measured by colour doppler Ultrasonography (USG) [4]. There is a decrease in blood flow of uterine, placental and foetal vessels in growth restricted foetus. During early pregnancy extra villous cytotrophoblasts invade the uterus and spiral arteries transforming them into large vessels of low resistance. Failure of trophoblast invasion and spiral artery transformation occurs in FGR [5], which results in abnormal blood flow in various blood vessels of uterus, foetus and placenta. The doppler assessment of these vessels helped in screening of FGR foetuses. The colour doppler studies tells about presence or the absence of blood flow, direction of blood flow, velocity profile, flow volume and impedance. The UMA and MCA are easily accessible and reproducible. MCA of foetuses is helpful in evaluating the foetal hypoxia [6]. The blood flow in the umibilical artery depends on the vascular changes in foetal placental circulation. As the pregnancy, advances the number of tertiary stem villi increases so, resistance in the UMA decreases, resulting in increased blood flow. There is a progressive increase in the blood flow during diastole in UMA. This increased blood flow pattern starts appearing from 15 weeks of gestation [7]. This blood flow increases as, there is an increase in gestational age. The normal UMA blood flow shows low resistance and there is gradual increase in blood flow during diastole [8]. Three abnormal UMA waveform patterns were described: decrease in

diastolic flow, absence of diastolic flow, and reversal of diastolic flow. These parameters result in increased UMA-PI. The foetuses with absent diastolic flow and reverse end diastolic flow have very poor prognosis. These foetuses require very close monitoring as sudden foetal demise can occur in these patients [9]. There is a redistribution of foetal blood in chronic foetal hypoxia to heart, kidney and brain. The blood flow to MCA increases so, there is decrease in PI of MCA. This increase in circulation is known as brain sparing effect and these results in CPR ratio less than 1. But, if hypoxia continues the blood flow of MCA returns to normal level, MCAPI level returns to normal level [10]. This does not show foetal well-being but continuous acidosis or brain oedema hampers the brain sparing effect [11]. The abnormal velocimetry of UA and presence of diastolic notch is associated with reduced birth weight and increase incidence of abruption placenta [12]. Prediction of FGR is valuable for earlier prevention and chance for better outcomes and treatment [13].

The objective of the study was to show the usefulness of colour doppler flow of UA, UMA and MCA as well as CPR and their association with adverse perinatal outcome.

MATERIALS AND METHODS

This was a prospective longitudinal study done in the Obstetrics and Gynaecology department of Government Medical College and Rajindra Hospital, Patiala, Punjab, India from October 2021 to March 2022. The ethical committee clearance was obtained from the Ethical Committee of Government Medical College and Hospital (No. Trg.9 (310)2022/38219).

Inclusion criteria: A total of 200 patients with singleton FGR foetuses were included in the study. FGR foetus was defined as foetus with an estimated foetal weight less than the 10th percentile for gestational age by prenatal ultrasound [1].

Exclusion criteria: The patients with multiple pregnancies, foetus with congenital malformations, rhesus immunisation were excluded from the study.

Sample size calculation: Calculation was done by using the formula.

$$n=\frac{z^2\times\hat{p}(1-\hat{p})}{\varepsilon^2}$$

where, Z was the critical value of the Normal distribution (e.g., for a confidence level of 95%, 'α' was 0.05 and the critical value was 1.96), 'ε' was the margin of error, 'p' was the sample proportion. Confidence Interval=95%, p=9.5% [14], MOE=5%, So 'n' came out to be=195.92 so n=196 $\frac{(1.96)^2\times0.15\times(1-0.15)}{(0.05)^2}$. To reduce the margin of error total sample size was taken as 200. The 200 patients were divided into four groups with 50 patients in each group:

Group I: (50 patients) FGR, foetus with normal blood velocimetry.

Group II: (50 Patients) FGR foetus with abnormal UA velocimetry.

Group III: (50 Patients) FGR foetus with abnormal UMA and MCA velocimetry.

Group IV: (50 Patients) FGR foetus with abnormal CPR ratio.

Study Procedure

After selection, all patients had undergone colour doppler USG. Gestational age was estimated on the basis of the last menstrual period and by the earliest scan that patients had. The different foetal parameters and Amniotic Fluid Index (AFI) were recorded. Foetal weight was estimated by the Hadlock FB et al., [15] three parameter formula based on the combination of head circumference, abdominal circumference, and femur length.

Pulsed wave doppler was used to obtain flow velocity wave forms from ascending branch of UA at the point closest to its origin from internal iliac artery. The mean PI of left and right UA was calculated. PI value was considered abnormal if it was above 95th percentile for gestational age or presence of diastolic notch [7]. Doppler measurements of UMA were taken from a free floating loop of the umbilical cord near the abdominal insertion site. Care was taken to ensure the loop of cord was not compressed between uterine wall and the foetus. UMA PI of 0.87±0.16 was considered normal and values above that were considered abnormal [13]. Doppler measurements of MCA were taken overlying the anterior wing of the sphenoid bone near the base of the skull close to origin of MCA from internal carotid artery. MCA PI of 1.61±0.15 was considered normal and values below that were considered abnormal [11].

All Doppler wave forms were recorded when there was no breathing movement of foetus and uterus was relaxed. The UMA and MCA PI were recorded. CPR was calculated by dividing the doppler indices of the MCA by those of UMA. CPR equal to or less than one was considered abnormal while CPR more than one was considered normal [6]. The decision on the mode of delivery was based on foetal compromise, foetal maturity, conditions of cervix. Birth weight, gestational age, mode of delivery (C-section, normal vaginal delivery), length of hospital stay were assessed. Five minutes APGAR score below 7, neonatal health including perinatal morbidity in the form of RDS, prematurity, admission to NICU, and neonatal deaths were assessed.

STATISTICAL ANALYSIS

The analysis of categorical variables was done by Chi-square test and Fisher-exact test. The analysis of continuous variables was done by ANOVA when data were normally distributed otherwise Kruskal Wallis H test was used. The data was analysed using SPSS version 22 and Microsoft excel. A p-value of ≤0.05 was taken as statistically significant.

RESULTS

The patients in all four groups were mostly primigravida patients [Table/Fig-1]. The mean gestational age at delivery was highest in group I (38.1±2.3 weeks) and lowest in group IV (33.1±3.1 weeks), showing patients in group IV needed delivery at early gestational age due to the severity of colour doppler changes. In group I no foetus had perinatal morbidity as compared to the 78% in group IV [Table/Fig-2].

Patients with FGR foetuses were affected with PIH in all four groups, with the highest (54%) in group IV. Two (4%) maternal mortality was observed in group IV due to severe preeclampsia, and in group III one (2%) maternal death was due to disseminated intracoagulopathy due to abruption placenta [Table/Fig-3].

Parameters	Group I	Group II	Group III	Group IV	p-value	Name of test
Mean age (in years)	23.86±2.79	22.44±2.64	21.61±5.01	22.32±2.62	0.1	Kruskal Wallis Test
Parity						
Primi	36 (72%)	40 (80%)	41 (82%)	42 (84%)	0.658	Fisher-exact Test
Second	9 (18%)	8 (16%)	8 (16%)	6 (12%)	0.538	Fisher-exact Test
Multi	5 (10%)	2 (4%)	1 (2%)	2 (4%)	0.626	Fisher-exact Test

[Table/Fig-1]: Demographic profile of patients.

Parameters	Group I	Group II	Group III	Group IV	p-value	Name of test
Mean gestational age (in weeks)	38.1±2.3	37.3±3.2	36±3.6	33.1±3.1	0.001	Kruskal Wallis Test
Mean birth weight (in gms)	2432±423	2209±329	2100±223	1329±403	0.001	Kruskal Wallis Test
Perinatal morbidity (due to RDS and prematurity) n (%)	0	3 (6%)	17 (34%)	39 (78%)	0.001	Fisher-exact Test
APGAR <7 at 5 minutes n (%)	0	2 (4%)	9 (18%)	13 (26%)	0.001	Fisher-exact Test
Mean Hospital stay (in days)	4.48±1.68	5.52±2.02	10.98±4.09,	17.66±2.90	0.001	Kruskal Wallis Test
Admission to NICU	0	2 (4%)	15 (30%)	34 (68%)	0.001	Fisher-exact Test
Perinatal mortality n (%)	0	1 (2%)	3 (6%)	5 (10%)	0.01	Fisher-exact Test

[Table/Fig-2]: Perinatal outcomes (50 patients in each group).

Variables	Group I	Group II	Group III	Group IV	p-value	Name of Test
PIH	2 (4%)	4 (8%)	16 (32%)	27 (54%)	0.01	Fisher-exact Test
Oligo hydramnios	2 (4%)	7 (14%)	13 (26%)	17 (34%)	0.01	Fisher-exact Test
Abruption placenta	0	3 (6%)	4 (8%)	5 (10%)	0.1	Fisher-exact Test
C-section 24 (c)	6 (12%)	16 (32%)	37 (74%)	46 (92%)	0.001	Chi-square Test
Maternal mortality	0	0	1 (2%)	2 (4%)	0.619	Fisher-exact Test

[Table/Fig-3]: Maternal complications (Each group contains 50 patients).
PIH: Pregnancy induced Hypertension; C-section: Caesarean-section

DISCUSSION

The FGR is a pathological condition strongly related to the development and function of uteroplacental and foetoplacental circulations. Adequate foetal circulation is necessary for normal foetal growth. To facilitate this, remarkable changes occur in the maternal, placental, and foetal vasculatures.

In the present study, it was found that group IV patients with deranged CPR value were delivered at an earliest mean gestational age of 33.1±3.1 weeks among four groups. This was in accordance with the study done by Efraim Z et al., in which the mean gestational age was 32.1±2.1 weeks in patients with deranged CPR suggesting that these FGR foetuses required delivery at an early gestational age [11]. The mean birth weight of foetuses in group IV was lowest, 1329±403 gm among the four groups. This was in accordance with a study done by Benitez-Marin M et al., which showed that the foetuses with deranged CPR were having low mean birth weight [10]. In group IV patients the babies with APGAR <7 at 5 minutes were highest, 13 (26%). The NICU admission of group IV babies were highest, 34 (68%) among the four groups. This was in accordance to a study done by Benitez Marin M et al., who showed more babies had APGAR <7 at 5 minutes and admissions to NICU with deranged CPR values [10]. Perinatal mortality was highest in group IV, 5 (10%) in the study. This was in accordance with a study done by Ute F et al., who found that the foetuses with deranged CPR values had 8% mortality [16]. Group IV patients with deranged CPR value had the highest 27 (54%) incidence of PIH. It was in accordance with a study done by Zhu YC et al., which suggested that the association of PIH with deranged CPR was very high [12]. group IV patients were associated with 17 (34%) cases of oligohydramnios. This was in accordance to a study done by Efraim Z et al., which showed oligohydramnios was associated with 31% of cases of deranged CPR [11]. Abruption placenta was highest in group IV, 5 (10%) in this study. All the patients with abruption placenta were associated with PIH. This was in accordance with a study done by Zhu YC et al., which showed 8% of patients with FGR foetuses with deranged CPR developed abruption placenta [12]. Group IV patients required maximum number of C-sections in 46 (92%) cases. The high incidence of C-section was in accordance with the study done by Khalil AA et al., who also showed a C-section rate of 84% in patients with CPR less than one [17].

Maternal mortality was highest in group IV, 2 (4%). The two deaths in group IV were due to severe preeclampsia. This was in accordance with a study done by Zhu YC et al., which showed 3% maternal mortality in patients with FGR with deranged CPR [12]. The patients had severe preeclampsia leading to Disseminated Intravascular Coagulation (DIC), and abruption placenta.

Colour doppler study of foetal vessels is a simple, quick, non invasive procedure and multiple vessel study has high accuracy for antepartum foetal surveillance. If there is abnormal PI of UMA and MCA, CPR ratio should be performed to know the extent of brain sparing.

Limitation(s)

The study was limited to short-term intrapartum events and perinatal outcomes.

CONCLUSION(S)

The adverse perinatal outcomes were seen with changes in the PI value of UA, UMA, MCA. But the CPR ratio which takes into consideration of both MCAPI and UMAPI when deranged is associated with more perinatal adverse effects than either MCAPI or UMAPI alone. There is no change in CPR value in advance gestational age and abnormal CPR is more commonly associated with adversed foetal outcome. Hence, doppler ultrasound especially CPR ratio should be an integral component of routine evaluation of FGR pregnancies as it helps in foetal monitoring and management and thereby improving adverse perinatal outcome.

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