

ALTERED ARTERIAL DOPPLER FLOW PATTERN AND PERINATAL OUTCOME IN INTRAUTERINE GROWTH RESTRICTION

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ABSTRACT

Objectives: Intrauterine growth restriction (IUGR) is one of the common conditions that interfere with the growth of the fetus accounting for 10-15% of pregnant woman. Literature explores a wide range of incidence of perinatal complication including mortality among IUGR pregnancies. Limited data available on these complications confined to coastal Karnataka and its association with abnormal arterial Doppler flow pattern. To study the perinatal complications associated with IUGR pregnancies and its prevalence in comparison to healthy controls of comparable gestational age.

Methods: This cohort study screened 53 IUGR fetuses by an antenatal scan at gestational age of 27 weeks or more. The diagnosis of IUGR was made according to established criteria from SOGC clinical practice guidelines August 2013. The data also included 48 appropriate for gestational age fetuses with healthy mothers with the comparable gestational week. Experienced cardiac sonographer and gynecologist performed fetal echocardiography (ECHO) using Vivid 7, GE health-care system ECHO machine with the convex transducer of frequency 1.7-2.4 MHz. The study was conducted at south Indian tertiary care center.

Results: This study included 53 IUGR cases and 48 non-IUGR controls. The mean age was 27±4.37 and 26.88±3.14 years in IUGR and non-IUGR groups, respectively. Fetal Doppler study variables showed a significant decrease in peak aortic velocity and velocity time integral which was not evident on other valves, though mitral antegrade flow during atrial contraction was found to be lower among IUGR group. In two-dimensional chamber quantification of IUGR group revealed significant increase in pulmonary artery dimension, right ventricular (RV) dimension and RV thickness than the control group (p<0.05). The anthropometric parameters such as weight and length; abdomen circumference was significantly lower in IUGR group, whereas head circumference found to be more in IUGR group (p<0.001). The gestational weeks at delivery was significantly different among two groups with IUGR group depicting the early delivery group. p<0.001(35.58±2.92 and 38.5±0.96 in IUGR and non-IUGR groups, respectively). IUGR group also had prolonged neonatal intensive care unit stay when compared to controls (p<0.001).

Conclusions: IUGR carries profound course in altered Doppler indices and cardiac function which explore its prediction on mortality and adverse perinatal outcome. This study showed significant perinatal mortality accounting for 5.6% among IUGR cases when compared to normal. Although tissue Doppler indices show normal variants, IUGR possesses significant adverse perinatal outcome, however with lesser incidence compared to severe form of IUGR subsets who show altered tissue annular velocities.

Keywords: Intrauterine growth restriction, Echocardiography, Doppler, Perinatal.

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INTRODUCTION

Intrauterine growth restriction (IUGR) is one of the common conditions that interfere with the growth of the fetus accounting for 10-15% of pregnant women [1]. In India, this prevalence could be as high as 28% with associated low birth weight for approximately 21% of cases [2]. The literature showed a wide range of discrepancy in estimated fetal weight in defining IUGR which spreads through <1 percentile to <25th percentile for gestational age [1,3,4]. IUGR is usually characterized as a small-for-gestational-age (SGA) fetus whose estimated fetal weight (EFW) is below the 10th percentile for that gestational age according to a reference population. However, some SGA fetuses are constitutionally small and not jeopardized by unfavorable placental health [3].

IUGR could be the result of uteroplacental insufficiency. Although restricted fetal growth per se may not be the concern, the IUGR diagnosis holds important finding since it is associated with significant risks of perinatal morbidity and mortality. Data in the literature limits prevalence of IUGR associated complication among the population in

coastal Karnataka region. Hence, this study was conducted to find the prevalence of adverse perinatal outcome in IUGR cases among coastal Karnataka population.

IUGR and the cardiovascular system: IUGR has its impact on fetal blood flow dynamics which is regulated by certain factors including fetal oxygenation, vascular reactivity, and organ autoregulation. In the fetus, placental dysfunction interferes with the relative filling in the right and left heart chambers. Decrease in left ventricular (LV) afterload and increase in right ventricular (RV) afterload enhances shift of cardiac output toward LV. IUGR possess brain sparing effect which results in redistribution of flow toward important vital organs including brain, heart, and kidney, which leads to preferential streaming of blood in descending aorta with the demand of re-oxygenation from the placenta. Although IUGR interferes with the normal course of pregnancy, it also shows an adverse effect after birth over the years. Disturbances of normal fetal growth can result in abnormal weight, body mass, or body proportion at birth. The two principal fetal growth disorders, IUGR, and

macrosomia are related with increased perinatal mortality rates and short- or long-term morbidity rates [1].

IUGR related perinatal complication had been studied extensively in foreign countries. Indian data related to complications associated with IUGR limits derivation of the coastal area population. Hence, this cohort study carried out to find the perinatal complication associated with IUGR pregnancies and its prevalence in comparison to healthy controls of comparable gestational age.

METHODS

This cohort study screened 53 IUGR fetuses for an antenatal fetal scan in a pregnant woman with age gestational age of 27 weeks or more. The diagnosis of IUGR was made according to established criteria from SOGC clinical practice guideline August 2013 [5]. The data also included 48 appropriate for gestational age fetuses with healthy mothers with the comparable gestational week. The study was conducted in the Department of Cardiology and Department of OBG, Kasturba Medical College, Manipal University Manipal.

Fetuses with the complex fetal anomaly, complex congenital heart disease, detected or suspected chromosomal abnormality, fetal arrhythmias like complete heart block, pericardial effusion, pleural effusion, multiple gestations, are excluded from the study. From all participant, informed consent obtained before the study comments. Institutional ethical committee approved the study.

Experienced gynecologist performed an antenatal scan for study subjects for determining gestational age, placental assessment and amniotic fluid volume by ultrasonography and the cases screened here were enrolled for this study.

Fetal echocardiography (ECHO) was performed using Vivid 7, GE health-care system ECHO machine with the convex transducer of frequency 1.7-2.4 MHz. Conventional mitral and tricuspid Doppler velocities were recorded in four chamber view (Figs. 1 and 2). Peak E wave velocity, A wave velocity and E/A ratio and fetal heart rate (HR) were recorded in this view. Aortic velocity recorded in three-chamber view and pulmonary velocity is recorded in short axis view or great arterial crisscrossing view of apical three-chamber view. Peak aortic and pulmonary velocity, velocity time integral (VTI) are recorded in this view along with the dimensions of both great arteries in the two-dimensional (2D) view. Myocardial tissue annular velocity was recorded in apical four chamber view (Fig. 3) with low filter, low gain and Niquist limit of 0-30 cm/s were used. The sample volume was placed at three points of the basal lateral wall, basal septum, and the basal wall of the RV. Caution was taken for the alignment of ultrasound beam was parallel to or at an angle of incidence $<20^\circ$ to the orientation of the interventricular septum (IVS) or ventricular wall. No angle correction applied in the recording of myocardial tissue Doppler. The velocities of

early ventricular filling E', Atrial contraction A', and systolic wave S wave were recorded at each position. The reproducibility of conventional Doppler and tissue Doppler measurements was tested. Intraobserver variability was assessed in five both group fetuses by repeating the measurements in two different occasions, and intraobserver variability was assessed in six fetuses by measuring same day by a second observer blinded to the first operator examination. Subjects were followed till the delivery and the looked for the perinatal outcome. Adverse perinatal outcome measures included neonatal death, prolonged neonatal intensive care unit (NICU) stay, distress syndrome, and preterm birth.

Statistical analysis performed with the help of SPSS package. The analysis is performed using the χ^2 test for categorical variables and t test for continuous variables. A $p < 0.05$ is considered to be statistically significant. Additional analysis carried by Pearson correlation test.

RESULTS

The present study included 53 cases with IUGR and 48 controls. The mean age between two groups was comparable with IUGR and controls about 27.43 ± 4.37 years and 26.88 ± 3.14 years, respectively. Adverse perinatal outcomes including neonatal death, prolonged NICU stay, and premature delivery were more prevalent in IUGR cases. This study evidenced three neonatal deaths among IUGR cases. Gestational weeks at delivery was significantly lower in IUGR group in comparison to controls (35.58 ± 2.92 weeks vs. 38.5 ± 0.96 weeks; $p < 0.001$). IUGR group also possessed prolonged NICU stay when compared to controls. The mean values of neonatal parameters such as birth weight, length, head circumference, abdomen circumference showed significance difference between two groups, i.e., 2844.51 ± 646.9 versus 1821 ± 536.6 g

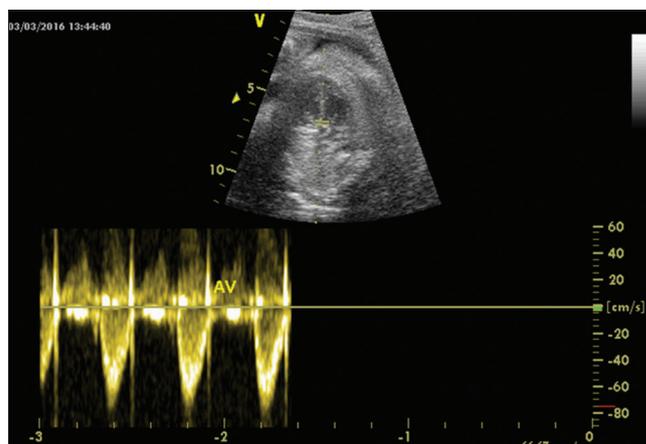


Fig. 2: Fetal heart showing aortic valve: Conventional Doppler

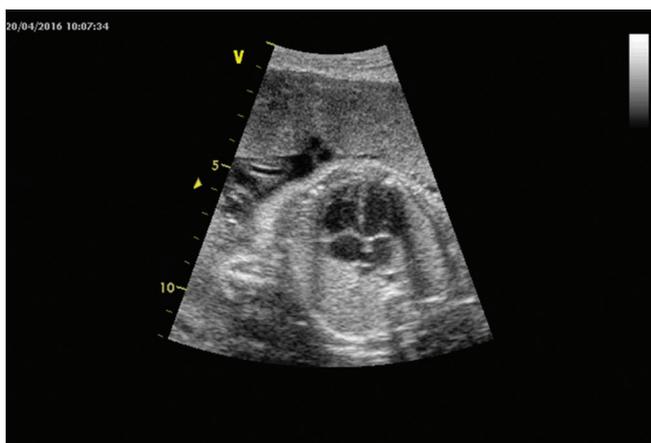


Fig. 1: Fetal heart showing four chamber view

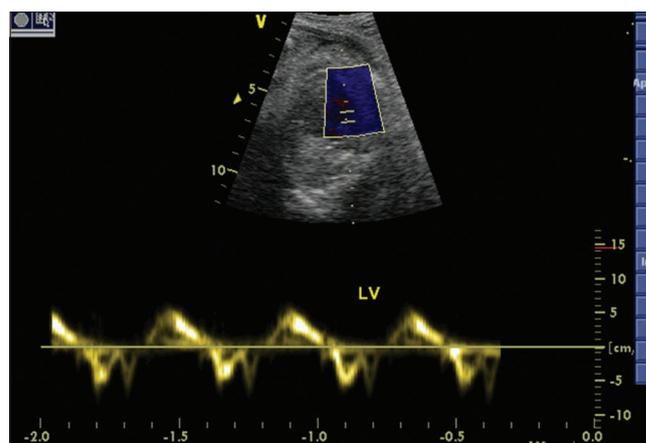


Fig. 3: Tissue Doppler tracing of left ventricle lateral wall

($p < 0.001$), 46.59 ± 3.5 versus 40.73 ± 4.19 mm ($p < 0.001$), 30.28 ± 2.25 versus 33.39 ± 1.9 mm ($p < 0.001$) and 29.806 ± 2.49 versus 25.56 ± 3 mm ($p < 0.001$), respectively. Table 1 depicts the anthropometric parameters among IUGR cases and controls.

2D chamber quantification revealed (Table 2) a significant increase in the pulmonary artery dimension (6.53 ± 1.17 vs. 7.54 ± 2.18 mm, $p < 0.05$), RV dimension (11.16 ± 2.08 vs. 11.36 ± 2.87 mm, $p < 0.05$) and RV thickness (4.03 ± 0.45 vs. 4.9 ± 0.66 mm, $p < 0.05$). Whereas LV lateral wall, interventricular septal thickness and aortic root did not show significant difference among two groups. Doppler study variables did not show a significant difference in pulmonary and aortic valvular velocities, but there seem to be significant decrease in peak abdominal aortic velocity and VTI (65.26 ± 14.23 vs. 57.53 ± 15.75 cm/second $p < 0.05$ and 1.29 ± 0.65 versus 1 ± 0.305 cm $p < 0.05$) among IUGR subjects. Mitral valve Doppler showed a significant decrease in the forward velocity during atrial contraction (58.32 ± 7.91 vs. 52.85 ± 12.32 cm/second $p < 0.05$), whereas LV passive filling phase during early diastole, E wave velocity did not differ between two groups. Tricuspid valvular velocities did not deviate among IUGR subjects. Table 3 shows the distribution of Doppler parameters across mitral, tricuspid, aortic, and pulmonary valves. The tissue annular velocities measured at RV, IVS and lateral wall sites during early diastole, late diastole and systole did not show any significant difference between these two groups (Table 4).

DISCUSSION

The present study revealed 5.6% (3/53) of perinatal death among IUGR pregnancies. IUGR also possessed significant increase in the course of NICU stays due to respiratory/fetal distress. Doppler flow across aortic valve with VTI was found to be significantly altered among IUGR subjects when compared to controls; however, tissue annular velocity of the basal ventricular wall and IVS did not show statistically significant

Table 1: Perinatal outcome measures among IUGR and non IUGR subjects

Parameters	Group		p value
	Mean±SD		
	Non IUGR	IUGR	
Gestational weeks at delivery	38.50 ± 0.968	35.58 ± 2.926	<0.001
NICU stay (days)	0 (0)	2 (0-33)	<0.001
Weight (g)	2844.51 ± 646.9	1821 ± 536.6	<0.001
Length (cm)	46.59 ± 3.50	40.735 ± 4.19	<0.001
Head circumference in (cm)	30.284 ± 2.25	33.39 ± 1.90	<0.001
Abdomen circumference (cm)	29.806 ± 2.49	25.56 ± 3.00	<0.001

IUGR: Intrauterine growth restriction, SD: Standard deviation, NICU: Neonatal intensive care unit

Table 2: Cardiac chamber quantification using 2D and m-mode technique

Parameters	Group		p-value
	Mean±SD		
	Non-IUGR	IUGR	
Aortic root	5.57 ± 1.26	8.75 ± 13.62	NS
Pulmonary artery	6.53 ± 1.17	7.54 ± 2.18	<0.05
RV	11.16 ± 2.08	11.36 ± 2.87	<0.05
LV	10.14 ± 1.98	9.93 ± 2.34	NS
IVS thickness	3.16 ± 0.51	3.28 ± 0.62	NS
Lateral wall thickness	3.26 ± 0.52	3.53 ± 0.83	NS
RV thickness	4.03 ± 0.45	4.90 ± 0.66	<0.05

IVS: Interventricular septum, RV: Right ventricle, NS: Not Significant, IUGR: Intrauterine growth restriction, SD: Standard deviation, 2D: Two-dimensional

difference among two groups. The literature shows a wide range of incidence of perinatal death among IUGR cases accounting for 13-26.6%. The studies also showed that altered arterial flow pattern and Doppler indices have a significant role in predicting adverse perinatal outcome. Few observational studies showed that myocardial performance index could predict perinatal death in preterm IUGR, with better prediction when used in combination with ductus venosus flow pattern. In the study of Hecher *et al.*, Doppler-derived ductus venosus pulsatility index variation and short-term fetal HR variability also could indicate timing of delivery in IUGR subjects with <32 weeks of gestation. In addition, Figueras *et al.* observed that abnormal alteration in aortic isthmus blood flow occurs 1 week prior than does that in ductus venosus among preterm growth restricted fetuses. Doppler evidence of retrograde flow in the aortic isthmus also found to be strongly correlated with adverse perinatal outcome in IUGR complicated pregnancies as explored in the study observed by Figueras *et al.* [6-10]. The study conducted by Hernandez-Andrade *et al.* at Spain reported 22% of perinatal death among IUGR subjects which showed significant prediction with predetermined myocardial performance index as well as prolonged NICU stay [6]. Studies have proven that altered cardiac function have poorer perinatal outcome [10,11] which in turn reflect the significant

Table 3: Doppler flows across atrio-ventricular/semilunar valves and abdominal aortic flow between IUGR and non IUGR cases

Parameters	Variables	Groups		p
		Mean±SD		
		Non-IUGR	IUGR	
Mitral velocity	E velocity	42.47 ± 9.21	42.25 ± 11.14	NS
	A velocity	58.32 ± 7.91	52.85 ± 12.32	<0.05
	IVRT	45.79 ± 8.35	44.53 ± 11.01	NS
Tricuspid velocity	E velocity	45.36 ± 10.59	44.42 ± 11.81	NS
	A velocity	62.85 ± 10.36	58.11 ± 12.88	NS
Aortic velocity	Peak velocity	80.70 ± 12.79	1.14 ± 2.14	NS
	VTI	76.70 ± 15.83	1.06 ± 2.68	NS
Pulmonary velocity	Peak velocity	67.64 ± 12.06	63.51 ± 15.18	NS
	VTI	10.3 ± 1.86	10.9 ± 3.27	NS
Abdominal aortic velocity	Peak velocity	65.26 ± 14.23	57.53 ± 15.75	<0.05
	VTI	12.9 ± 0.65	10.0 ± 0.30	<0.05

NS: Not Significant, IUGR: Intrauterine growth restriction, SD: Standard deviation, VTI: Velocity time integral

Table 4: Tissue Doppler imaging parameters among cases and control

Parameters	Groups		p
	Mean±SD		
	Non-IUGR	IUGR	
HR	145.16 ± 7.50	147.06 ± 8.85	NS
L_E'	0.04 ± 0.008	0.05 ± 0.06	NS
L_A'	0.06 ± 0.01	0.05 ± 0.01	NS
L_S	0.04 ± 0.009	0.05 ± 0.06	NS
IVS_E'	0.03 ± 0.008	0.03 ± 0.013	NS
IVS_A'	0.04 ± 0.015	0.04 ± 0.01	NS
IVS_S	0.04 ± 0.009	0.04 ± 0.008	NS
RV_E'	0.07 ± 0.08	0.06 ± 0.01	NS
RV_A'	0.09 ± 0.03	0.09 ± 0.02	NS
RV_S	0.06 ± 0.01	0.07 ± 0.06	NS

NS: Not Significant, IUGR: Intrauterine growth restriction, SD: Standard deviation, HR: Heart rate, RV: Right ventricle, IVS: Interventricular septum

difference in mortality rate among the IUGR group on its severity, as the present study depicted normal myocardial annular velocity.

CONCLUSION

IUGR carries profound course in altered Doppler indices and cardiac function which explore its prediction on mortality and adverse perinatal outcome. This study showed significant perinatal mortality accounting for 5.6% among IUGR cases. Although tissue Doppler indices show normal variants, IUGR possesses significant adverse perinatal outcome.

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