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ASSESSMENT OF CARDIAC FUNCTION IN FETUSES WITH INTRAUTERINE GROWTH RESTRICTION (IUGR)

By

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ABSTRACT

Background: Fetal growth restriction (FGR), also known as intrauterine growth restriction, includes different conditions in which a fetus fails to reach its own growth potential. In recent years, more attention has been paid to changes in cardiac function in children with features of intrauterine growth retardation. Many articles describe the disorders appearing as early as in the fetus, revealing subclinical changes in the myocardium detected on echocardiographic examination.

Objective: To evaluate the cardiac functions in intrauterine growth restricted fetuses using fetal echocardiography.

Patients and methods: This were a prospective study carried out on 100 pregnant women who had singleton fetuses 28 weeks of gestation or older. It was conducted at Obstetrics and Gynecology Department at Bab Al-Sh'aaria, Al-Azhar University Hospital during the period from June 2020 to May 2021. The subjects were divided into 2 equal groups: Group I (Patients group): women with IUGR fetuses, and Group II (Control group): disease free women.

Results: The mean of inter-ventricular septal diameter (IVST) was significantly higher in fetuses with IUGR compared to normal fetuses. It was 54.09 ± 4.05 cm in IUGR patient's groups compared to 44.38±1.87 cm in the control group. In addition, the isovolumic relaxation time (IVRT) significantly prolonged in fetuses with IUGR compared to normal fetuses. It was 37.53 ± 1.66 ms in IUGR patient's groups compared to 35.18±1.08 ms in the control group. The ejection time (ET) reduced significantly in IUGR fetuses as compared to normal control fetuses. The diastolic function across the right and left side of the heart was performed by calculating the E/A ratio across the tricuspid and the mitral valve. The average mitral E/A ratio and tricuspid E/A ratio were significantly higher in IUGR fetuses as compared to normal control fetuses. They were 0.74±0.05 and 0.77±0.06 in patients group vs 0.72±0.05 and 0.73±0.05 in control group (P=0.014 & P=0.004). Also, lower mitral annular plane systolic excursion (MAPSE), and tricuspid annular plane systolic excursion (TAPSE) were recorded in IUGR fetuses (5.14±0.38 & 6.68±0.52) compared to that detected in normal fetuses (6.1±0.6 & 7.88±0.6). The LV-MPI and RV-MPI were calculated in all fetuses in the study population. The mean LV- MPI measured 0.55±0.04 in IUGR fetuses vs. 0.45±0.02 in normal fetuses, while the mean RV-MPI measured 0.56±0.04 in IUGR fetuses vs. 0.46±0.03 in normal fetuses.

Conclusion: Cardiac function impaired in IUGR etuses, thus fetal Echo may be a useful tool in the assessment of fetus with IUGR beside to Doppler. These data supported prenatal cardiovascular remodeling as a mechanistic pathway of increased risk later in life in cases of IUGR.

Keywords: Cardiac function, Fetuses, Intrauterine growth restriction, Echocardiography.

INTRODUCTION

Intrauterine growth restriction (IUGR) is defined as the failure of a fetus to reach its growth potential and is often caused by placental insufficiency, leading to inadequate nutrients and oxygen supply to the fetus. IUGR occurs in 3–10% of pregnancies, and is one of the major causes of prenatal and perinatal mortality and morbidity *(Dai et al., 2021)*.

Fetal programing is a process whereby permanent alterations in physiology and metabolism result from insult or stimuli during critical early periods of development. IUGR may be described as maladaptation with deleterious effects on the developing cardiovascular system *(Sehgal et al., 2016)*.

The fetal cardiovascular system is also not spared and several studies have proved the effect of the pathological process of placental dysfunction in IUGR on the fetal heart. Fetal cardiac function is complex and depends on myocardial contractility as well as on extra-cardiac factors such as developmental maturation, loading conditions and fetal disease. As the foetus is increasingly jeopardized, signs of cardiovascular dysfunction appear *(Basu et al., 2017)*.

Fetal cardiac involvement has been found in the late stages with developmental retardation, as supported by various studies. Accordingly, the fetal heart is the main organ involved in adaptation mechanisms to placental insufficiency, and fetal development retardation plays a central role in physiopathology *(Palalioglu et al., 2021)*.

Fetal hypoxia leads to fetal blood flow being redirected to the brain and heart. Intrauterine growth restriction predisposes to lower cardiac compliance, increased arterial stiffness, increased cardiac afterload, and end-diastolic ventricular filling. This decrease in longitudinal motion and impaired relaxation may be a fetal adaptive mechanism to the chronic hypoxia and volume/pressure overload of placental insufficiency. These mechanisms, which are the heart's attempt to adapt to an insult, constitute a process known as cardiac remodeling *(Sharma et al., 2019)*.

Subclinical myocardial changes in term FGR fetuses and neonates might still have a detrimental impact on the burden of disease and increase the risk of cardiovascular morbidity and mortality later in life *(Patey et al., 2019)*.

Cardiac function can be adequately evaluated in most fetuses when appropriate expertise, equipment and time are available. Fetal cardiac function assessment is a promising tool that may soon be incorporated into clinical practice to diagnose, monitor or predict outcome in some fetal conditions *(Crispi et al., 2013)*.

Fetal echocardiography has great advances in recent years, and is characterized by an easily accessible non-invasive method, and can be applied during gestation to explore the cardiac anatomy and function of the fetus accurately. Moreover, evaluation of the myocardial performances depends in majority of investigations on conventional Doppler US, which demonstrates global cardiac function *(Bayoumy et al., 2020)*.

The aim of the study was to evaluate the cardiac functions in intrauterine growth restricted fetuses using fetal echocardiography.

PATIENT AND METHODS

This was a prospective study carried out on 100 pregnant women who had singleton fetuses, 28 weeks of gestation or older. It was conducted at Obstetrics and Gynecology Department at Bab Al-Sh'aaria, Al-Azhar University Hospital during the period from June 2020 to May 2021. The subjects were divided into 2 equal groups: **Group I (Patients group):** Women with IUGR fetuses, and **Group II (Control group):** Disease free women.

Inclusion criteria: Gestational age ≥28 weeks according to a reliable date for the last menstrual period and ultrasound evaluation, singleton living fetus, and patient with a diagnosed IUGR fetus.

Exclusion criteria: Gestational age less than 28 weeks, patients with multiple gestation, women with congenital malformation, and pregnancy. with chronic medical disorder, and those with psychosocial disorders in their background.

Approval of ethical committee was obtained from quality education assurance unit, Al-Azhar University Faculty of Medicine, Egypt. Verbal consent was taken from every patient a before participation in this study.

All patients were subjected to the following:

1. **Delineated history was taken with special emphasis on:**

- Personal history, menstrual history by last menstrual period data and confirmed by first-trimester sonography, past history, previous operations, past obstetric history, history of drug intake, patient complaint, and history of the current pregnancy.

2. **Clinical examinations:**

- General examination especially measurement of weight, height and body mass index (BMI) using the formula: BMI= weight (kg) / [height (m)]2, and assessment of vital signs (body temperature, pulse and blood pressure) to assess the hemodynamic status.
- Cardiac and chest examination.
- Abdominal examination fundal level, lie and presentation of the fetus, auscultation of fetal heart rate (FHR), and presence of scar of previous laparotomy.
- Local examination: for assessment of vaginal bleeding.

All cases were subjected to routine laboratory investigation including complete blood picture (CBC), blood group, Rh typing and urine analysis, liver and kidney functions, coagulation profile.

3. **Abdominal ultrasonography:**

The ultrasound equipment used was (MINDRAY DC-30, China) using a 3.5- 5-MHz transabdominal probe at the ultrasound unit of the Obstetrics and Gynecology, AlAzhar University, Egypt.

All cases underwent transabdominal ultrasound examination at admission for assessment of fetal viability, number, fetal biometry [biparietal diameter (BPD), fetal length (FL), abdominal & circumference (AC)], placental (site & maturity), liquor (amount described as amniotic luid index (AFI) & turbidity).

Patients were first scanned in the routine fashion using B-mode. Then, the vessels of interest were confirmed by color Doppler. The Doppler signal was then obtained by placing the Doppler gate directly over the vessel of interest. The flow velocity waveforms were obtained in periods of fetal inactivity and apnea. The angle of insonation was kept < 30 degrees in all measurements. The mechanical and thermal indices were maintained at < 1, and the wall filter was set to 70 Hz. Fetoplacental Doppler parameters were obtained from 3 or more successive waveforms in each vessel. Doppler examination included uterine arteries, the umbilical artery (UA), fetal middle cerebral artery (MCA), according to the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) published in 2013. UA-PI was measured from a free loop of the umbilical cord. MCA-PI was measured distal to the junction of the internal carotid artery in a transverse view of the fetal skull at the level of the circle of Willis *(Bhide et al., 2016)*. The cerebroplacental ratio was calculated as MCA-PI/UA-PI *(Zohav et al., 2019)*.

Fetal echocardiography Fetal echocardiography included a comprehensive examination to assess structural heart integrity and rule out cardiac defects following standard protocols *(Bhide et al., 2016)*. Then, fetal cardiac morphometry and function were evaluated *(Crispi et al., 2013)*. Left myocardial performance index was obtained in a cross-sectional image of the fetal thorax, placing the Doppler sample volume on the medial wall of the ascending aorta and including the leaflets of the aortic and mitral valves. The final value of the MPI was calculated as follows: MPI = (ICT + IRT)/ET. Only one set of measurements for each patient was included in the analysis *(Cruz-Martinez et al., 2011)*.

Statistical analysis:

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) or Fisher's exact test was used to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation), median, and range. Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

There was no difference between number of studied females with increased maternal age between two studied group (P=0.079). Moreover, the mean age of patients with IUGR fetuses was 24.61±3.14 years, while the mean age of control subjects was 26.06±4.2 years. There were no statistically significant differences between the two groups regarding age (P=0.064). There were no statistically significant differences between both studied groups regarding BMI (P=0.647).

There was a statistically significant increase in number of cases who had previous history of IUGR, pregnancy-induced hypertension, and those presented with anemia in patients group compared to control group (P=0.025, P<0.001, P=0.01; respectively). However, no significant difference was detected between both studied groups regarding number of cases who had previous history of miscarriage (P=0.272) **(Table 2)**.

The current study showed that umbilical artery pulsatility index was significantly higher in IUGR fetuses compared to normal fetuses [(1.42 ±0.09 vs. 1.14 ± 0.09); (P<0.001)]. However, both middle cerebral artery pulsatility index and cerebro-placental ratio were significantly lower in IUGR fetuses compared to normal fetuses [(1.49 ±0.13 vs. 1.85 ± 0.25 for middle cerebral artery PI), and (1.06± 0.12 vs. 1.64 ±0.27 for cerebro-placental ratio) (P<0.001)] *(Table 1)*.

Table (1): Comparison between both studied groups regarding age, BMI, parity, risk factors and doppler indices

Parameters \ Groups		Patients group N=50	Control group N=50	P-value
Age (years):				
18-25	N (%)	34 (68%)	23 (46%)	0.079
26-30	N (%)	13 (26%)	23 (46%)	
31-35	N (%)	3 (6%)	4 (8%)	
Range Mean ± SD		21–33 24.61±3.14	18–35 26.06±4.2	0.064
BMI (Kg/m^2)	Mean ± SD	26.96±4.06	26.64±4.2	0.647
Parity:				
zero	N (%)	12 (24%)	13 (26%)	0.983
1	N (%)	18 (36%)	18 (36%)	
2	N (%)	13 (26%)	11 (22%)	
3	N (%)	6 (12%)	7 (14%)	
4	N (%)	1 (2%)	1 (2%)	
Risk factors:				
History of previous miscarriage	**No**	32(64%)	24(48%)	0.272
	1	12(24%)	17(34%)	
	2	6(12%)	9(18%)	
History of previous IUGR	**No**	24(48%)	35(70%)	0.025
	Yes	26 (52%)	15 (30%)	
Pregnancy induced hypertension	**No**	37(74%)	50(100%)	<0.001
	Yes	13(26%)	0(0%)	
Presence of anemia	**No**	28(56%)	40(80%)	0.01
	YES	22(44%)	10 (20%)	

Doppler indices:				
Umbilical artery pulsatility index	Mean ± S. D	1.42±0.09	1.14±0.09	<0.001
MCA PI	Mean ± S. D	1.49±0.13	1.85±0.25	<0.001
Cerebro-placental ratio	Mean ± S. D	1.06±0.12	1.64±0.27	<0.001

The mean of inter-ventricular septal diameter (IVST) was significantly higher in fetuses with IUGR compared to normal fetuses. It was 54.09 ± 4.05 cm in IUGR patients' groups compared to 44.38±1.87 cm in the control group (P<0.001). In addition, the isovolumic relaxation time (IVRT) was significantly prolonged in fetuses with IUGR compared to normal fetuses. It was 37.53 ± 1.66 ms in IUGR patients' groups compared to 35.18±1.08 ms in the control group (P<0.001).

The ejection time (ET) reduced significantly in IUGR fetuses as compared to normal control fetuses (P<0.001). The diastolic function across the right and left side of the heart was performed by calculating the E/A ratio across the tricuspid and the mitral valve. The average mitral E/A ratio and tricuspid E/A ratio were significantly higher in IUGR fetuses as compared to normal control fetuses. They were 0.74±0.05 and 0.77±0.06 in patients' group vs. 0.72±0.05 and 0.73±0.05 in control group (P=0.014 and P=0.004). Also, lower mitral annular plane systolic excursion (MAPSE), and tricuspid annular plane systolic excursion (TAPSE) were recorded in IUGR fetuses 5.14±0.38 and 6.68±0.52 compared to that detected in normal fetuses 6.1±0.6 and 7.88±0.6 (P<0.001).

The LV-MPI and RV-MPI were calculated in all fetuses in the study population. The mean LV- MPI measured 0.55±0.04 in IUGR fetuses vs. 0.45±0.02 in normal fetuses (P<0.001), while the mean RV- MPI measured 0.56±0.04 in IUGR fetuses vs. 0.46±0.03 in normal fetuses (P<0.001) **(Table 2)**.

Table (2): Cardiovascular function assessed by ultrasound using 2-D and Doppler ultrasound modes

Parameters \ **Groups**		**Patients group (N= 47)**	**Control group (N= 50)**	**P-value**
IVCT(ms)	**Mean ± SD**	**37.53 ± 1.66**	**35.18±1.08**	<0.001
	Median (Range)	**37(35–41)**	**35(33-38)**	
IVST(cm)	**Mean ± SD**	**54.09 ± 4.05**	**44.38±1.87**	<0.001
	Median (Range)	**55(45–60)**	**44(41-50)**	
Left Ejection time (ms)	**Mean ± SD**	**156.36 ± 4.02**	**169.34 ± 3.49**	<0.001
	Median (Range)	**155(148–166)**	**170(160–178)**	
Right ET (ms)	**Mean ± SD**	**156 ± 3.79**	**168.94 ± 3.39**	<0.001
	Median (Range)	**155(148–166)**	**169(160–175)**	
Mitral E/A ratio	**Mean ± SD**	**0.74±0.05**	**0.72±0.05**	0.052
	Median (Range)	**0.75(0.67-0.85)**	**0.7(0.67-0.8)**	
Tricuspid E/A ratio	**Mean ± SD**	**0.77±0.06**	**0.73±0.05**	<0.001
	Median (Range)	**0.77(0.67-0.85)**	**0.71(0.67-0.85)**	
MAPSE (mm)	**Mean ± SD**	**5.14±0.38**	**6.1±0.6**	<0.001
	Median (Range)	**5.2(4.6-5.8)**	**6.15(5.1-7.1)**	
TAPSE (mm)	**Mean ± SD**	**6.68±0.52**	**7.88±0.6**	<0.001
	Median (Range)	**6.8(5.8-7.4)**	**7.9(6.9-9)**	

Left MPI	**Mean ± SD**	**0.55±0.04**	**0.45±0.02**	<0.001
	Median (Range)	**0.55(0.49–0.63)**	**0.45(0.42–0.51)**	
Right MPI	**Mean ± SD**	**0.56±0.04**	**0.46±0.03**	<0.001
	Median (Range)	**0.57(0.49-0.63)**	**0.46(0.42-0.52)**	

In the present study, there were 3 intrauterine death, and 97 live births. All of intrauterine deaths were detected in IUGR cases; but without significant difference (P=0.242). In the present study, 60.8 % of women delivered by cesarean section and 39.2% of women had vaginal delivery. Approximately, three-quarters of cases included in patients' group (76.6%) and 46% of cases in control group gave birth by cesarean section. There was a statistically significant difference between two studied groups regarding mode of delivery (P=0.002).

Considering neonatal birth weight, it was detected that the neonatal birth weight of women who had IUGR fetuses was lower than that of control women [1877±206.01 vs. 2659±311.6; respectively]. There was statistically significant difference between two studied groups regarding neonatal birth weight (P<0.001).

Three newborns (6.4%) of women with IUGR had weight less than 1500 g and 70.2% of them had neonatal birth weight ranged between 1500 and 2000 g, while only 23.4% had neonatal birth weight >2000 g. In control group, one (2%) baby had neonatal birth weight ranged from 1500 to 2000 g and the other 49 had fetal birth weight more than 2000 g.

Considering neonatal birth weight, it was detected that the neonatal birth weight of women who had IUGR fetuses was lower than that of control women [1877±206.01 vs. 2659±311.6; respectively]. There was statistically significant difference between two studied groups regarding neonatal birth weight (P<0.001) **(Table 3)**.

Table (3): Comparison between both studied group according to incidence of intrauterine growth restriction (IUGR), mode of delivery and fetal birth weight

Parameters \ **Groups**		**Patients group (N= 47)**	**Control group (N= 50)**	**P-value**
IUFD:				
No	**N (%)**	47 (94%)	50 (100%)	0.242
Yes	**N (%)**	3 (6%)	0 (0%)	
Mode of delivery:				
Vaginal delivery	**N (%)**	11 (23.4%)	27 (54%)	0.002
Cesarean section (CS)	**N (%)**	36 (76.6%)	23 (46%)	
Fetal birth weight (g)	Range Mean ± SD	1475–2475 1877±206.01	1750–3150 2659±311.6	<0.001

There was a statistically significant difference between the two studied groups in the number of neonates admitted to NICU and stayed there for more than 15 days (P=0.001). There was no statistically significant different between numbers of babies with neonatal sepsis in both groups (P=0.485). The overall mortality was shown in ten IUGR babies (21.3%) and one baby in control group. Very low birth weight had been the cause of mortality for babies born to three women. In addition, neonatal sepsis had resulted into mortality for one baby.

The current study displayed that, among 50 women in patients' group, there were 28 women had 1 min APGAR score < 7 and 20 women had 5 min APGAR score <7 while in control group there were only 7 women had 1 min APGAR score < 7 and 2 women had 5 min APGAR score <7. There were statistically significant differences between the two groups regarding number of cases that had 1 min APGAR score and 5 min APGAR score <7 (P=0.001 & P<0.001) **(Table 4)**.

Table (4): Frequencies of NICU, neonatal sepsis, neonatal death, 1 min APGAR score and 5 min APGAR score in both stdied groups

Parameters \ Groups		Patients group (N= 47)	Control group (N= 50)	P-value
NICU:				
No	**N (%)**	24 (51.1%)	42 (84%)	0.001
Yes	**N (%)**	23 (48.9%)	8 (16%)	
Neonatal sepsis:				
No	**N (%)**	46 (97.9%)	50 (100%)	0.485
Yes	**N (%)**	1 (2.1%)	0 (0%)	
Neonatal death:				
No	**N (%)**	37 (78.7%)	49 (98%)	0.003
Yes	**N (%)**	10 (21.3%)	1 (2%)	
1 min APGAR score:				
No	**N (%)**	19 (40.4%)	43 (86%)	0.001
Yes	**N (%)**	28 (59.6%)	7 (14%)	
5 min APGAR score:				
No	**N (%)**	27 (57.4%)	48 (96%)	<0.001
Yes	**N (%)**	20 (42.6%)	2 (4%)	

DISCUSSION

Results of the current study revealed the cases and controls were matched by mean age, mean BMI, and parity.

Our results revealed that the majority of the participants in both studied groups (57%) were in 18-25 years age group followed by 26-30 years, whereas least number of participants were seen in the age group of more than 30 years. Moreover, the mean age of patients with IUGR fetuses was 24.61±3.14 years while the mean age of control subjects was 26.06±4.2 years

Malik and Saxena (2012) and *Ganju et al. (2019)* also found that young mothers in the age group of 21-25 years, comprised the largest number of total, i.e. 15% belonged to the age of over 30 years in the former study and that maximum number (42%) of subjects were in the range of 21–25 years reported by the latter one. This observation has led to believe that most of the high-risk mothers were in the active reproductive age group.

In agreement to our findings, *Veerabathini et al. (2020)* reported that the majority of the patients (58%) were in 26-30 years age group with slight difference from ours. The average age of the patients was 28.16 years. Least number of patients were seen in the age group of more than 30 years.

In line to our findings also, *Ernst et al. (2017)* and *Rotshenker-Olshinka et al. (2019)* and *El-Kady et al. (2020)* found

non-significant difference between IUGR cases and controls regarding age, BMI, and parity.

In addition, the mean gestational age at the time of first scan was 32±2.15 weeks in patients with IUGR and 32.04±2.63 in control cases. None of the antenatal mothers was examined before 28 weeks of gestational age.

Regarding risk fators, the current study showed that there was a statistically significant increase in number of cases who had previous history of IUGR (52% vs 30%), pregnancy-induced hypertension (26% vs 0%), and those presented with anemia (44% vs 20%) in patients group compared to control group. However, no significant difference was detected between both studied groups regarding number of cases who had previous history of miscarriage.

Veerabathini et al. (2020) compared IUGR cases versus controls and declared that about 20% of cases had anemia complicating the pregnancy and hypertensive disorders were present in maximum of 50% of pregnancies complicated with IUGR. Similar findings were seen in Sharma et al. (2016) with 50% cases having pre-eclampsia, 35% had anemia.

Among the maternal factors, hypertension is one of the main leading factors related with IUGR. Both chronic hypertension and preeclampsia are associated with low birth weight *(Hung et al., 2018* and *Turbeville & Sasser, 2020).*

The current study showed that umbilical artery pulsatility index was significantly higher in IUGR fetuses compared to normal fetuses. However, both middle cerebral artery pulsatility index and Cerebro-placental ratio were significantly lower in IUGR fetuses compared to normal fetuses.

Sharma et al. (2019), in concordance to our reults reported that IUGR fetuses showed raised umbilical artery pulsatility index (UMPI), decreased middle cerebral artery pulsatility index (MCAPI), and mean cerebroplacental ratio (C/P) compared with control group.

Veerabathini et al. (2020) in line to our results reported that in umbilical artery, PI of IUGR fetuses were significantly higher han that of normal fetuses and middle cerebral artery, PI of IUGR fetuses was significantly lower than that of normal fetuses and Cerebro-placental ratio of IUGR fetuses was significantly lower than that of normal fetuses.

Added to that, results of the present work revealed that the mean of inter-ventricular septal diameter (IVST) was significantly thicker in fetuses with IUGR compared to normal fetuses. In addition, the isovolumic relaxation time (IVRT) was significantly prolonged in fetuses with IUGR compared to normal fetuses. The ejection time (ET) reduced significantly in IUGR fetuses as compared to normal control fetuses. The diastolic function across the right and left side of the heart was performed by calculating the E/A ratio across the tricuspid and the mitral valve. The average mitral E/A ratio and tricuspid E/A ratio were significantly higher in IUGR fetuses as compared to normal control fetuses. Also, lower mitral annular plane systolic excursion (MAPSE), and tricuspid annular plane systolic excursion (TAPSE) were recorded in IUGR fetuses compared to that detected

in normal fetuses. The mean LV- MPI measured 0.55±0.04 in IUGR fetuses vs. 0.45±0.02 in normal fetuses, while the mean RV- MPI measured 0.56±0.04 in IUGR fetuses vs. 0.46±0.03 in normal fetuses.

Sharma et al. (2019), in agreement to our results, reported that the mean myocardial performance index was 0.62±0.02 in IUGR group, while in control group, it was 0.45±0.01 and that was statistically significant. The IVRT and IVCT were longer and ejection time was shorter in IUGR fetuses compared with control group respectively.

Youssef et al. (2020) declared that cases complicated by PE and/or FGR showed signs of fetal cardiac remodeling in the form of larger, hypertrophic, and more globular hearts as well as cardiac dysfunction manifested by increased myocardial performance index. They found that ost cardiac parameters remained significantly different in complicated pregnancies even after statistical adjustment for potential confounders such as chronic hypertension, pregestational diabetes, assisted reproductive technologies, and smoking.

In our study, IUGR fetuses showed signs of both systolic and diastolic dysfunctions and prolonged isovolumic times. Similar results were obtained by *Levine et al. (2015)* who studied myocardial performance index in 50 FGR fetuses and 50 appropriate for gestational age (AGA) fetuses. MPI in FGR fetuses was higher as compared to control group. *Woods et al. (2018)* found in their study for gestational age fetuses matched for gestational age that myocardial performance index was higher in IUGR fetuses as compared to the AGA fetuses. They suggested that this was due to systolic and diastolic dysfunctions of fetal heart in IUGR fetuses. Our results were also comparable to the study done by *Singh et al. (2013)* who studied cardiac function in intrauterine growth-restricted fetuses. They observed that myocardial performance index in IUGR fetuses was higher as compared to AGA fetuses (0.64 vs. 0.45). *Peter et al. (2015)* studied reported that the mean MPI in IUGR fetuses was 0.58 ± 0.093 and that of AGA fetuses was 0.45 ± 0.070. *Beyer et al. (2019)* also found that the FGR group showed a significantly increased MPI in comparison to the control group.

Fouzas et al. (2014) also reported that the IUGR neonates presented distinct changes in cardiac morphology as reflected by the relative IVS hypertrophy and LV dilatation. Similar echocardiographic findings have previously been reported in neonates and children exposed to IUGR *(Crispi et al., 2012)*, whereas chronic intrauterine substrate deprivation has been associated with alterations in cardiac geometry in human fetuses and animal models *(Akazawa et al., 2016)*.

However, contradictory to our resuts, observations from author who studied adults who were born with IUGR (22–25 years old) did not confirm this theory *(Bjarnegård et al., 2013)*. These differences may have been due to the degree of restriction abnormalities, which was different in the various groups studied.

The large multicenter prospective study in fetuses with IUGR have found only a modest increase in the left mod-

MPI and that was not of clinical utility in comparison to the assessment of umbilical artery and ductus venous [DV] Doppler *(Unterscheider et al., 2013).*

Other authors have found no significant difference between the left MPI measurements of normal-growth fetuses, when compared to those fetuses with IUGR. There were no significant difference between-groups [cases and controls] in the left MPI. This result contradicts to the current study. The difference may come from the fact that most study population are less than 34 weeks at time of enrollment, which denotes an early onset IUGR which is the most severe form, and also all populations in the current work have an abnormal UA Doppler and/or evidence of brain sparing. In other words, we have included only fetus with evidence of pathological probability and the abnormal perinatal outcomes *(Öcal et al., 2019).*

Furthermore, in the present study, the mean gestational age at delivery was significantly lower in patients with IUGR than that detected in controls an approximately three-quarters of cases included in patients' group (76.6%) and 46% of cases in control group gave birth by cesarean section.

This finding was comparable to the statistically significant relation noted by *Singh et al. (2013)* with 61.5% cesarean deliveries in their study. *Ganju et al. (2019)* noted that 59% cesarean deliveries and 41% vaginal deliveries among IUGR fetuses with abnormal Doppler indices.

One reason for increased cesarean delivery rates in the IUGR group would be the fetus' inability to tolerate labor. Another might be obstetricians' anxiety about IUGR fetal status, leading to a greater tendency to perform a caesarean delivery *(Wilk et al., 2019).* Perhaps a combination of these factors, as well as others like increasing CS rate worldwide and nationwide, could explain our findings.

In addition, regarding outcomes in our study, the present study indicated that 74% of newborns diagnosed with IUGR had birth weight below the fifth percentile, and 26% of them had birth weight ranged between 5th -10th percentile for gestational age and sex at the time of birth, In the present study, there were 3 IUFD cases detected in IUGR cases. Considering neonatal birth weight, the mean birth weight of women who had IUGR fetuses was significantly lower than that of control women. There was also significant increase in numer of neonates admittd to NICU more than 15 days in IUGR group. Neonatal sepsis has been detected in only one IUGR baby (2.1%) and the overall mortality was shown in ten IUGR babies (21.3%) and one baby in control group. Very low birth weight had been the cause of mortality for babies born to three women. In addition, neonatal sepsis had resulted into mortality for one baby. There were statistically significant differences between the two groups regarding number of cases that have 1 min APGAR score and 5 min APGAR score <7 as higher number of cases were in the IUGR group.

In the study by *Mallikarjunappa et al. (2013),* cases of PIH with IUGR had an average birth weight of 1708 g. which correlates with this study. *Nimmagadda et al. (2017)* in line to or results reported that in control group 90% cases had BW> 2.5

kg and the mean birth weight is 2749 gm while the mean birth weight is 1806 gm and 96% shows birth weight < 2500 gm.

Niewiadomska-Jarosik et al. (2017) in their analysis of the medical records confirmed statistically significant differences in birth weight, while they reported no significant difference for gestational age between the groups.

A very nearly similar mean birth weight was declared by *Muhammad et al. (2010).*

In addition, it was reported that perinatal morbidity and mortality are inversely proportional to percentile of birth weight, with progressive increase in these rates when the fetal weight drops below the tenth percentile towards the first, and more dramatically below the fifth percentile. The worst outcomes are observed in severe IUGR cases, with extreme prematurity and very low weight, who present important deterioration in umbilical flow *(Nardozza et al., 2017).*

Seal et al. (2019) reported that elective cesarean section rate was found to be 52% and a further 16% emergency caesarean section were done in IUGR group, in comparison to control group had only 12% cesarean section. They also found that the obstetrical outcome in the present series was 8% perinatal mortality in IUGR group and no catastrophy in the control group. In 16% of fetal growth retarded cases babies had birth weight of more than 2.5 Kgs and further 68% babies were between 2-2.5 Kgs weight.

CONCLUSION

Cardiac function impaired in IUGR etuses, Thus, fetal Echo may be a useful tool in the assessment of fetus with IUGR beside to Doppler. These data supported prenatal cardiovascular remodeling as a mechanistic pathway of increased risk later in life in cases of IUGR. Fetal life seemed to constitute a unique window of opportunity for the early diagnosis and prevention of cardiovascular disease. Thus, assessing fetal cardiac remodeling might be useful to monitor the fetus but also to identify those cases with increased risk of cardiovascular disease later in life.

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تقييم وظيفة القلب في الأجنة مقيدى النمو داخل الرحم

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خلفيـــة البحـــث: يتضـــمن تقييـــد نمـــو الجنـــين، المعـــروف أيضًـــا باســـم تقييـــد النمـــو داخـــل الـــرحم، ظروفًـــا مختلفـــة يفشـــل فيهـــا الجنـــين فـــي الوصـــول إلـــى إمكانـــات نمـــوه الخاصـــة. فـــي الســـنوات الأخيـــرة، تـــم إيـــلاء المزيـــد مـــن الاهتمـــام للتغيـــرات فـــي وظـــائف القلـــب لـــدى الأطفـــال الـــذين يعـــانون مـــن تـــأخر النمـــو داخـــل الـــرحم. تصـــف العديـــد مـــن المقـــالات الاضـــطرابات التـــي تظهـــر فـــي وقـــت مبكـــر كمـــا فـــي الجنـــين، وتكشـــف عـــن التغيـــرات تحت الإكلينيكية في عضلة القلب التي تم اكتشافها في فحص تخطيط صدى القلب.

الهـــدف مـــن البحـــث: تقيـــيم وظـــائف القلـــب فـــي الأجنـــة المقيـــدة النمـــو داخـــل الـــرحم باستخدام تخطيط صدى القلب الجنيني.

المريضـــات وطـــرق البحـــث: أجريـــت هـــذه الدراســـة علـــى 100 مـــن الســـيدات الحوامـــل ممـــن حضـــرن الـــي قســـم التوليـــد وأمـــراض النســـاء بكليـــة الطـــب جامعـــة الأزهـــر خـــلال الفتـــرة مـــن يونيـــو 2020 إلـــى مـــايو 2021. وقـــد تـــم تقســـيمهن إلـــى مجمـــوعتين متســـاويتين: المجموعـــة الأولـــى (مجموعـــة المرضـــى) ضـــمت النســـاء ذوات أجنـــة متـــأخرة النمـــو داخـــل الـــرحم, والمجموعـــة الثانيـــة (المجموعـــة الضـــابطة) تضـــمنت النســـاء الأصـــحاء واللائـــي كـــن يحملـــن فـــي أرحـــامهن أجنـــة بـــأوزان مناســـبة لعمـــر الحمل.

نتـــائج البحـــث: كـــان متوســـط قطـــر الحـــاجز بـــين البطينـــين أعلـــى بشـــكل ملحـــوظ فـــي الأجنـــة مـــع تقييـــد النمـــو داخـــل الـــرحم مقارنـــة بالأجنـــة الطبيعيـــة. الـــذي 54.09 ± 4.05 ســـم فـــي مجموعـــة مرضـــى تقييـــد النمـــو داخـــل الـــرحم مقارنـــة بـــ 44.38 ± 1.87 ســـم فـــي المجموعـــة الضـــابطة. بالإضـــافة إلـــى ذلـــك، وتـــم إطالـــة وقـــت الاســـترخاء الانزلاقـــي بشـــكل كبيـــر فـــي الأجنـــة مـــع تقييـــد النمـــو داخـــل الـــرحم مقارنـــة بالأجنـــة الطبيعيـــة. التـــي كانـــت 37.53 ± 1.66 ملـــي ثانيـــة فـــي مجموعـــات مرضـــى تقييـــد النمـــو داخـــل الـــرحم مقارنـــة بـــ 35.18 ± 1.08 ملـــي ثانيـــة فـــي مجموعـــة الـــتحكم. وقـــد إنخفـــض وقـــت

الإخـراج بشـكل ملحـوظ فـي أجنـة تـأخر النمـو داخـل الـرحم مقارنـة بالأجنـة العاديـة. وتـم إختبـار الوظيفـة الانبسـاطية عبـر الجانـب الأيمـن والأيسـر مـن القلـب عـن طريـق حسـاب نسـبة A / E عبـر الصـمام ثلاثـي الشـرف والصـمام التـاجي. كـان متوسـط نسـبة Mitral E / A ونسـبة E / A ثلاثيـة الشـرف أعلـى بشـكل ملحـوظ فـي الأجنـة التـي تقيـد نمـو الجنـين داخـل الـرحم مقارنـة بالأجنـة الضـابطة العاديـة. كانـت 0.74 ± 0.05 و 0.77 ± 0.06 فـي مجموعـة المرضـى مقابـل 0.72 ± 0.05 و 0.73 ± 0.05 فـي المجموعـة الضـابطة. وتـم تسـجيل النـزوح الانقباضـي المسـتوي الحلقـي التـاجي السـفلي ، والانحـراف الانقباضـي للطـائرة الحلقـي ثلاثـي الشـرف فـي أجنـة تقييـد النمـو داخـل الـرحم 5.14 ± 0.38 و 6.68 ± 0.52 مقارنـة بتلـك المكتشـفة فـي الأجنـة الطبيعيـة 6.1 ± 0.6 و 7.88 ± 0.6, وتـم حسـاب LV-MPI و-RV MPI فـي جميـع الأجنـة فـي مجتمـع الدراسـة. يقـيس متوسـط LV-MPI 0.55 ± 0.04فـي الأجنـة المقيـدة للنمـو داخـل الـرحم مقابـل 0.45 ± 0.02 فـي الأجنـة العاديـة ، بينمـا يقـيس متوسـط RV-MPI 0.56 ± 0.04 فـي الأجنـة التـي تقيـد النمـو داخـل الرحم مقابل 0.46 ± 0.03 في الأجنة الطبيعية.

الاسـتنتاج: وظيفـة القلـب كانـت ضـعيفة فـي مجموعـة تـأخر النمـو داخـل الـرحم، وبالتـالي قـد يكـون صـدى الجنـين أداة مفيـدة فـي تقيـيم الجنـين مـع تـأخر النمـو داخـل الـرحم بجانـب دوبلـر. وتـدعم هـذه البيانـات تقيـيم القلـب والأوعيـة الدمويـة قبـل الـولادة لتحديد زيادة المخاطر لاحقًا في الحياة في حالات تأخر النمو داخل الرحم.

الكلمـات الدالـة: وظيفـة القلـب، الأجنـة، تقييـد النمـو داخـل الـرحم، تخطـيط صـدى القلب.