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Cardiac Remodelling and Fetal Adaptive Changes Related to Intrauterine Growth Restriction: A Comparative Study

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Abstract **Original Research Article**

In the modern world, cardiovascular disorders are the leading cause of morbidity and mortality, which in most cases undergo a long subclinical phase that can last decades before the first clinical symptoms appear. The aim of the present study was to evaluate whether reduced fetal growth is associated with fetal cardiac dysfunction. Methods and results: This study was prospective cohort study starting in early fetal life. A prospective study was conducted in S.M.S Medical College Jaipur, involving 72 singleton foetuses ≥28 weeks of gestation divided into two groups 36 intrauterine growth restricted foetuses and 36 appropriate for gestational age foetuses. Isovolumetric relaxation time was obtained by fetal echocardiography. The mean Isovolumetric relaxation time in the IUGR foetuses and AGA foetuses was statistically significant and that was 57 ± 3.20msec and 42.11 ± 1.45msec respectively, respectively; (p value: <0.0001). These findings suggest that IUGR induces primary cardiac changes, which could explain the increased predisposition to cardiovascular disease in adult life [13]. Fetal echocardiographic parameters (IVRT) identify a high risk group within the IUGR fetuses, which could be targeted for early screening of blood pressure and other cardiovascular risk factors, as well as for promoting a healthy diet and exercise.

Keywords: Isovolumetric relaxation time, Fetal echocardiography, Intrauterine growth restricted fetus.

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INTRODUCTION

Aside from the well –known risk factors related to lifestyle and genetics, there is growing evidence that in a proportion of cases, the predisposition to cardiovascular disease lies in prenatal life [1]. In the initial stages of an insult, the heart usually manages to adapt and there is along subclinical period of cardiac dysfunction before end-stage heart failure [2, 3]. During this period of cardiac adaptation, changes in cardiac function, as well as in the heart's shape and size, can be measured. IUGR illustrates how cardiac dysfunction in the fetus is largely subclinical and requires sensitive methods for its identification [2]. 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 remodelling [3]. Fetal growth restriction is most commonly due to placental insufficiency and the resulting hypoxia leads to fetal blood flow being redirected to the brain and heart. Intrauterine growth restriction predispose to lower cardiac compliance, increased arterial stiffness, increased cardiac afterload and end- diastolic ventricular filling [4, 5]. Fetal echocardiography has developed as the primary non- invasive modality to evaluate fetal cardiac function. In this study we evaluate the Isovolumetric relaxation time of IUGR foetuses for identification of foetuses at increased cardiovascular risk that would benefit from lifestyle preventive strategies and potentially improve their future cardiovascular health.

MATERIAL AND METHODS

This study was a prospective observational study conducted between April 2016 and November 2017 in the department of obstetrics and gynaecology, S.M.S medical college and attached hospitals, Jaipur. This study included two groups consisting of 36 women in each group. Group-A included ≥28 weeks with IUGR, Group-B included ≥28 weeks with AGA foetuses. Women with multiple pregnancy, congenital malformation and pregnancy with chronic medical disorder were excluded. Approval from Institutional Research, Review Board and Ethical Committee was taken. Ultrasound and Doppler Measurements were performed by Aloka Prosound Alfa-6 4D Machine

using 4-6 MHz curved transducer. Umblical artery pulsatility index, middle cerebral artery pulsatility index and cerebroplacental ratio were calculated. The Isovolumetric relaxation time was measured by obtaining a cross-sectional view of the fetal thorax at the level of the four-chamber view of the heart. Isovolumetric relaxation time was calculated as the time from closure of the aortic valve to the opening of mitral valve.

STATISTICAL ANALYSIS

Continuous variables were summarized as mean and standard deviation while nominal / categorical variables as proportion. Parametric test will be used for continuous variable whereas $\chi 2$ test and fisser-exact test will be used for nominal / categorical variability. P-value < 0.05 will be taken as significant.

RESULTS

The mean age of pregnant women was 25.05±2.96 years in the study group, 25.89±3.86 years in the control group. No significant difference in maternal age (p value-0.308) and gestational age (p value-0.893) was observed between the groups. The umbilical and middle cerebral artery Doppler was done in both groups. In study group IUGR foetuses showed raised umbilical artery pulsatility index, decreased MCAPI and mean cerebroplacental ratio compared to control group. CP ratio <1 shows poor perinatal outcome.

The mean Isovolumetric relaxation time was 57±3.20msec in IUGR group, while in control group it was 42.11±1.45msec and that was statistically significant (p value: <0.001).

Table-1

Group	UMPI	MCAPI	C/P
Study group	1.69±0.37	1.65±0.42	0.98± 0.27
Control group	1.005±0.21	1.86±0.86	1.88±0.61
P-value	<.0001	0.046	<0.0001

Table-2

Cardiac parameter	IUGR Group	Control Group	p-value
IVRT(msec)	57±3.20	42.11±1.45	<0.001

In our study IUGR fetuses showed signs of diastolic dysfunction and prolonged isovolumetric relaxation time. A chronic increase in the mechanical load on the fetal heart substantially changes the heart architecture. In turn, this may cause nonuniformity of LV contraction and relaxation. The adaptive changes in the structure and function of the fetal heart exposed to a chronic increase in the afterload seem to be more intricate than a similar remodeling of the adult human heart because proliferation and functional and structural maturation of cardiomyocytes are still in progress in the developing heart. Our results were also comparable to the study done by WA Hassan *et al*. [6] who studied isovolumetric relaxation time in 48 AGA fetuses and 12 IUGR fetuses. IVRT in AGA fetuses was 42 msec as compared to IUGR group it was 57 msec. Similar study done by Fatima Crispi *et al*. [7] who studied 37 FGR and 37 AGA fetuses, tissue doppler imaging was performed to get isovolumetric relaxation time. In FGR fetuses IVRT was 52 msec as compared to 44 msec in AGA fetuses group. M Perez-Cruz *et al*. [8] assessed IVRT in 150 IUGR fetuses and 150 AGA fetuses. IVRT in IUGR fetuses was significantly higher as compared to control group (53 ± 9 v/s 45 ± 6 msec). The shape, non-uniformity of contractions, and diastolic function of the heart in IUGR fetuses are considered to be an adaptation to increased afterload as a result of an elevated resistance of placental vessels.

CONCLUSION

Isovolumetric relaxation time characterizes cardiac function and morphometry prenatally, demonstrating subclinical cardiac dysfunction and cardiac remodeling in IUGR. Isovolumetric relaxation time also helps in prediction of postnatal hypertension and arterial remodeling better than perinatal severity parameters currently used. This study suggests that fetal echocardiography could be incorporated into clinical practice for identification of foetuses at increased cardiovascular risk that would benefit from lifestyle preventive strategies and potentially improve their future cardiovascular health.

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