Senses Sci (Educ Sci Tech) 2022: 9 (4) 1680-1691
doi: 10.14616/sands-2022-4-16801691

Article

Fetal cardiac morphological assessment as part of fetal cardiac remodelling in cases with preeclampsia. An observational case control study

Hagar Gamal Okda*, Amal Zaki Azzam, Hossam Ibrahim Azab, Hisham Hosny El Gammal

Department of Obstetrics and Gynaecology, Faculty of Medicine, Alexandria University, Egypt.

***Correspondence**: Hagar Gamal Okda, Department of Obstetrics and Gynaecology, Faculty Of Medicine Alexandria University, 29 Nasr Ahmed Zaki street, Moharem Bek, Alexandria, Egypt. Tel. +201017263870, E-mail: hgokda@hotmail.com

Abstract. *Background:* Preeclampsia, which affects about 2%-8% of pregnancies, is a major cause of perinatal and maternal morbidity and mortality. The morphological assessment of the fetal heart conveys important information regarding the cardiovascular adaptation of a fetus in the face of vascular resistance in the uteroplacental circulation. The aim of this work was to assess fetal cardiac morphological changes as part of fetal cardiac remodelling of non growth retarded fetuses in pregnancies complicated with mild and severe preeclampsia. *Methods:* A case control study was performed at the ultrasound unit of El-Shatby Maternity University Hospital on 150 pregnant women who were divided into three groups. Group 1 included 40 mild preeclamptic pregnant women. Group 2 included 35 severe preeclamptic pregnant women and group 3 included 75 non preeclamptic pregnant women. Fetal ECHO included measurement of cardiothoracic ratio, aortic, pulmonary, mitral and tricuspid valve annuli, sphericity index, interventricular septum and left ventricle posterior wall diameter at systole and diastole and atrial and ventricular diameter lengths. Data were analysed using SPSS software. *Results*: Atrial and ventricular diameter lengths, cardiothoracic ratio and left ventricular posterior wall diameter were lower in cases with preeclampsia while the sphericity index was higher in cases with preeclampsia. No difference between study groups regarding valves annuli and interventricular septum measurement. *Conclusions*: Our study showed that fetuses of mothers with preeclampsia showed larger and hypertrophied hearts as shown in higher sphericity index but lower atrial and ventricular diameter length which indicate increased cardiac contractility as response to pressure overload which resulted from placental resistance.

Keywords: Preeclampsia, fetal morphological changes, sphericity index, cardiothoracic ratio, atrial and ventricular diameters.

Introduction

Preeclampsia, which affects about 2%-8% of pregnancies, is a major cause of perinatal and maternal morbidity and mortality.(1)

Although the exact cause of preeclampsia remains unclear, many theories center on the problems of placental implantation and partial or complete failure of trophoblastic invasion.(2)

Inadequate trophoblastic invasion of the maternal spiral arteries is thought to give rise to vascular resistance in the uteroplacental circulation.(3)

As a result of impaired uteroplacental blood flow, manifestations of preeclampsia may be seen in the fetal–placental unit. Clinical manifestations that follow from this uteroplacental ischemia include fetal growth restriction, oligohydramnios, placental abruption, and non-reassuring fetal status demonstrated on antepartum surveillance.(4)

Consequently, fetuses of women with preeclampsia are at increased risk of spontaneous or indicated preterm delivery.(5)

The term cardiac remodelling is used to define changes that produce geometrical rearrangement of the normal structures of the heart, together with complex biological and molecular alterations.(6)

The morphological assessment of the fetal heart conveys important information regarding the hemodynamic status and cardiovascular adaptation of a fetus in the face of several perinatal complications.(7)

Preeclampsia reduces the amount of oxygen a fetus receives through the placenta.(8) This results in cardiac enlargement and thickening of the cardiac and aortic walls.(9)

Also, The increased vascular placental resistance may affect the fetal cardiac function by causing an increase in the fetal cardiac afterload.(10)

Since the contractility of the heart is markedly affected by preload and afterload, we hypothesized that fetal cardiac morphology might be impaired in preeclamptic mothers.

Thus, we are conducting this study to evaluate the effect of preeclampsia on fetal cardiac function.

Objective

The aim of this work was to assess fetal cardiac morphological changes as part of fetal cardiac remodelling of non growth retarded fetuses in pregnancies complicated with mild and severe preeclampsia,

Methods

Study design, setting and participants

This study was an observational case control study performed at the ultrasound unit of El-Shatby Maternity University Hospital

150 pregnant women were included in the study. The cases were divided into 3 groups:

Group I: 40 mild preeclamptic pregnant women.
Group II: 35 severe preeclamptic pregnant women.
Group III: 75 non preeclamptic pregnant women with matching gestational age to group I and group II in a ratio of 1:1 as control group.
Group III was divided into group III a that included 40 patients with matching gestational age to cases in group I and group III b that included 35 patients with matching gestational age to cases in group II.

Inclusion criteria

Preeclamptic patients with singleton pregnancy of gestational age 28 weeks till full term were diagnosed and classified into mild and severe PET according to the criteria recommended by The American College of Obstetricians and Gynecologists (ACOG).(11)

-Measurement of cardiac; ventricular, and atrial diameters in an apical or basal four-chamber view. Ventricular parameters, in the form of longitudinal ventricular diameters, were standardized to be measured at end-diastole (at maximal ventricular distension at the frame when the atrioventricular valves close) as shown in **figure 1.**

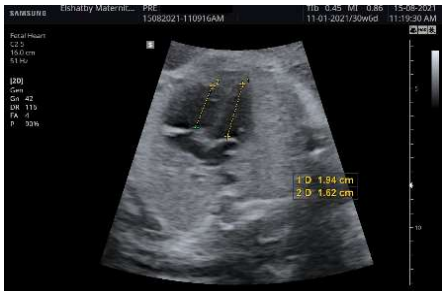


Figure 1: Measurement of right and left ventricular longitudinal diameters.

Atrial dimensions, in the form of longitudinal atrial diameters, were assessed at end-systole (maximal atrial distension just before the opening of atrioventricular valves) as shown in **figure 2**

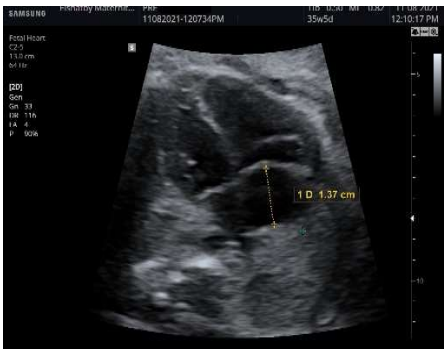


Figure 2: Measurement of right atrial diameter longitudinal length.

Cardiac shape (sphericity index) was measured by dividing longitudinal per transverse diameters. A longitudinal line was drawn from the apex to the base of the cardiac outer edge and a transverse line is drawn from the sidewall of the left ventricle to the sidewall of the right ventricle in the longest dimension according to the prompts as shown in **figure 3**.

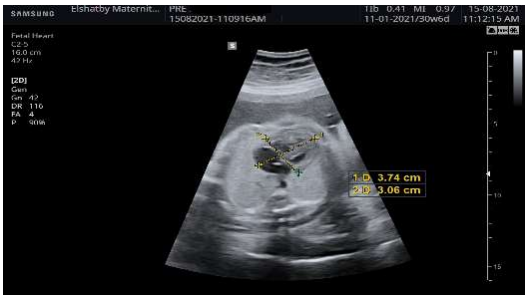


Figure 3: Measurement of the sphericity index.

- The cardiothoracic ratio was calculated as heart area divided by thoracic area.

Both the heart and thorax were measured by electronic ellipse method. First, an ellipse was positioned surrounding the cardiac apex, the outer epicardial borders, and the upper edge of the atrial septum. The cardiac area was automatically calculated using a software program installed in the ultrasound machine. Another ellipse was positioned to encircle the area covering the posterior edge of the vertebra, the outer borders of the ribs, and the anterior chest wall without including subdermal tissues. The thoracic area was then automatically demonstrated. Lastly, fetal cardiothoracic area ratio was derived by dividing the cardiac area by the thoracic area.

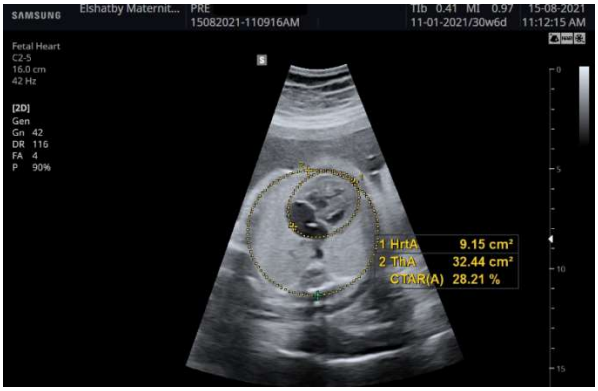


Figure 4: Measurement of cardiothoracic ratio.

The diameter of the aortic valve (figure 5) and pulmonary valve (figure 6) was measured in two dimensional imaging during systole by the leading edge-to-leading edge method.

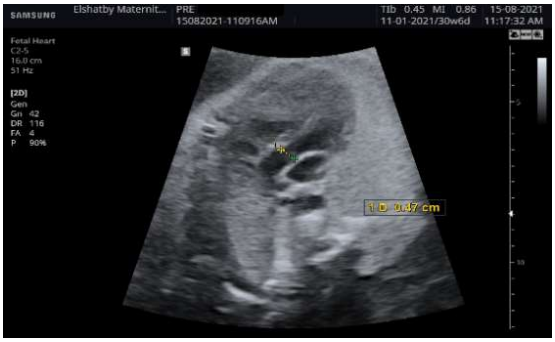


Figure 5: Measurement of aortic valve annulus.

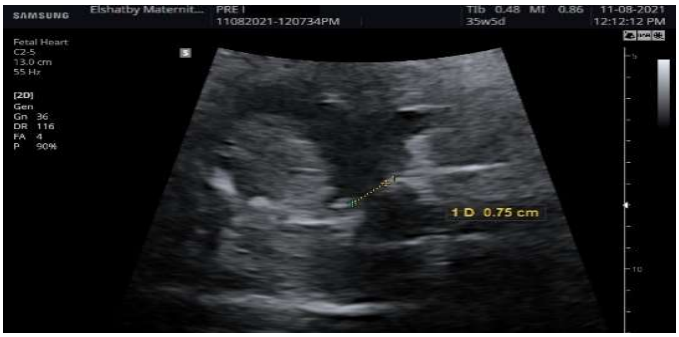


Figure 6: Measurement of pulmonary valve annulus

Mitral (**figure 7**) and tricuspid (**figure 8**) annular diameters were measured at end-diastole in the basal or apical four-chamber view.

-

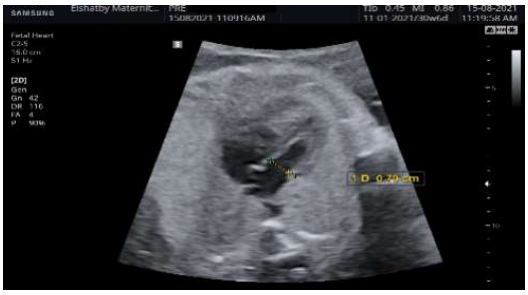


Figure 7: Measurement of mitral valve annulus

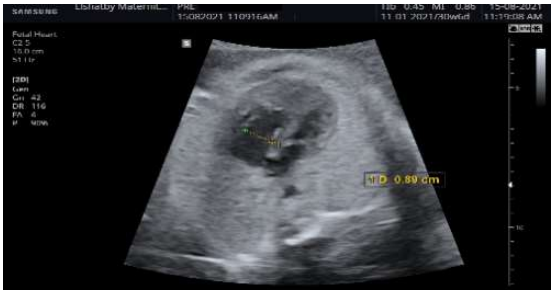
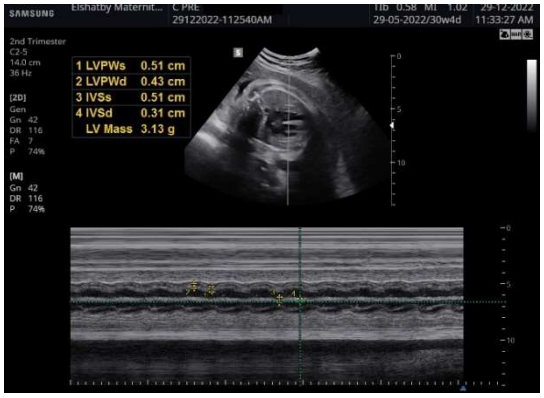


Figure 8: Measurement of tricuspid valve annulus

Interventricular septum diameter and left ventricle posterior wall diameter at systole and diastole in mm were measured using M mode in lateral cardiac view.

Figure 9: Measurement of left ventricle posterior wall diameter and interventricular septum in systole and diastole using M mode.



Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). For continuous data, they were tested for normality by the Shapiro-Wilk test. Quantitative data were expressed as range (minimum and maximum), mean, standard deviation and median. Student t-test was used to compare two groups for normally distributed quantitative variables. On the other hand, Mann Whitney test was used to compare two groups for not normally distributed quantitative variables. Significance of the obtained results was judged at the 5% level.

Results

Table (1): Comparison between the studied groups according to sphericity index, left ventricle posterior wall diameter and interventricular septum in systole and diastole.

	Mild preeclampsia		**Severe preeclampsia**	
	Cases (Grp I) (n = 40)	**Control (Grp IIIa) (n = 40)**	**Cases (Grp II) (n = 35)**	**Control (Grp IIIb) (n = 35)**
Sphericity index%				
Mean ± SD.	1.27 ± 0.17	1.18 ± 0.11	1.22 ± 0.14	1.19 ± 0.12
Median (Min. – Max.)	1.23 (1.0 – 1.67)	1.17 (1.01 – 1.40)	1.21 (0.90 – 1.57)	1.19 (1.02 – 1.52)
t(p)	t=3.041*,p=0.003*		t=1.006,p=0.318	
Left ventricle post wall diameter				
Systole (mm)				
Mean ± SD.	4.65 ± 1.97	5.37 ± 1.48	4.65 ± 1.77	5.61 ± 1.23
Median (Min. – Max.)	4.15 (2.10 – 11.30)	5.15 (3.0 – 9.50)	4.0 (1.04 – 7.80)	5.80 (3.70 – 8.50)
t(p)	t=1.848,p=0.068		t=2.651*,p=0.010*	
Diastole (mm)				

Mean ± SD.	5.41 ± 2.26	4.04 ± 1.08	4.94 ± 1.88	4.52 ± 1.32
Median (Min. – Max.)	4.75 (1.30 – 10.70)	3.90 (2.0 – 6.70)	4.70 (1.14 – 9.70)	4.30 (1.60 – 7.60)
t(p)	t=1.078,p=0.285		t=3.444*,p=0.001*	
IVS systole (mm)				
Mean ± SD.	7.14 ± 2.08	7.14 ± 1.62	6.60 ± 2.20	6.85 ± 1.73
Median (Min. – Max.)	6.70 (3.30 – 13.40)	7.0 (3.90 – 11.40)	6.20 (2.90 – 13.0)	6.60 (4.30 – 11.0)
t(p)	t=0.018,p=0.986		t=0.526,p=0.601	
IVS diastole (mm)				
Mean ± SD.	5.48 ± 2.08	4.77 ± 1.17	4.82 ± 2.15	4.37 ± 1.35
Median (Min. – Max.)	5.35 (2.70 – 12.70)	4.70 (2.0 – 7.90)	4.30 (1.30 – 12.0)	4.0 (2.30 – 8.0)
t(p)	t=1.047,p=0.299		t=1.868,p=0.067	

SD: Standard deviation t: Student t-test

p: p value for comparing between cases and control in mild preeclampsia and severe preeclampsia

*: Statistically significant at $p \leq 0.05$

Regarding the sphericity index, it was higher in cases with preeclampsia than control group but this difference was only statistically significant in cases with mild preeclampsia.

The left ventricular posterior wall diameter in systole and diastole were found to be lower in cases with preeclampsia than control group but this only reached significant difference in cases with severe preeclampsia.

As for the interventricular septum measurement in systole and diastole, there was no significant difference between the groups of study although IVS in systole was lower in cases with preeclampsia and IVS in diastole was higher in cases with preeclampsia.

Table (2): Comparison between the studied groups according to atrial and ventricular diameter length

	Mild preeclampsia		**Severe preeclampsia**	
	Cases (Grp I) (n = 40)	**Control (Grp IIIa) (n = 40)**	**Cases (Grp II) (n = 35)**	**Control (Grp IIIb) (n = 35)**
Atrial diameter length(cm)				
Right				
Mean ± SD.	1.26 ± 0.23	1.43 ± 0.26	1.24 ± 0.29	1.40 ± 0.25
Median (Min. – Max.)	1.20 (0.90 – 1.89)	1.43 (0.82 – 1.92)	1.20 (0.85 – 2.08)	1.32 (1.06 – 1.93)
t(p)	t=3.061*,p=0.003*		t=2.447*,p=0.017*	
Left				
Mean ± SD.	1.26 ± 0.23	1.43 ± 0.25	1.23 ± 0.33	1.38 ± 0.27
Median (Min. – Max.)	1.20 (0.86 – 1.78)	1.42 (0.94 – 2.18)	1.20 (0.75 – 2.07)	1.43 (0.83 – 1.93)
t(p)	t=3.038*,p=0.003*		t=2.129*,p=0.037*	
Ventricular diameter length(cm)				
Right				

Mean ± SD.	1.97 ± 0.40	2.23 ± 0.30	2.04 ± 0.42	2.15 ± 0.27
Median (Min. – Max.)	2.07 (1.22 – 2.71)	2.33 (1.62 – 2.75)	1.98 (1.30 – 2.89)	2.13 (1.66 – 2.72)
t(p)	t=3.299*,p=0.001*		t=1.339,p=0.186	
Left				
Mean ± SD.	1.97 ± 0.45	2.32 ± 0.35	2.05 ± 0.49	2.27 ± 0.34
Median (Min. – Max.)	1.90 (1.23 – 2.91)	2.36 (1.56 – 2.93)	2.07 (1.28 – 3.04)	2.26 (1.70 – 3.03)
t(p)	t=3.922*,p<0.001*		t=2.164*,p=0.034*	

SD: Standard deviation t: Student t-test

p: p value for comparing between cases and control in mild preeclampsia and severe preeclampsia.

*: Statistically significant at $p \leq 0.05$

There was significant difference among the cases with mild preeclampsia and the control group cases regarding atrial and ventricular diameter length where atrial and ventricular diameter where lower in the cases with mild preeclampsia.

There was significant difference among the cases with severe preeclampsia and the control group cases regarding atrial and ventricular diameter length where atrial and ventricular diameter where lower in the cases with severe preeclampsia except for right ventricular diameter length where no significant difference noted.

Table (3): Comparison between the two studied groups according to cardiothoracic ratio and tricuspid, mitral, aortic, and pulmonary valve annulus

	Mild		**Severe**	
	Cases (Grp I) (n = 40)	**Control (Grp IIIa) (n = 40)**	**Cases (Grp II) (n = 35)**	**Control (Grp IIIb) (n = 35)**
Cardiothoracic ratio				
Mean ± SD.	29.1 ± 4.73	32.1 ± 3.30	31.5 ± 5.62	31.4 ± 3.30
Median (Min. – Max.)	29.6 (20.1 – 40.5)	31.4 (27.2 – 40.1)	31.0 (19.4 – 42.4)	31.6 (25.3 – 38.9)
t(p)	t=3.310*,p=0.001*		t=0.092,p=0.927	
Tricuspid valve annulus (mm)				
Mean ± SD.	9.51 ± 2.24	9.37 ± 1.69	9.71 ± 2.14	9.49 ± 1.95
Median (Min. – Max.)	9.60 (1.0 – 13.50)	9.65 (6.60 – 12.50)	9.50 (5.40 – 15.60)	9.50 (5.90 – 13.0)
t(p)	t=0.310,p=0.757		t=0.462,p=0.645	
Mitral valve annulus (mm)				
Mean ± SD.	8.87 ± 2.28	8.77 ± 1.87	9.07 ± 2.10	8.92 ± 1.55
Median (Min. – Max.)	8.85 (1.0 – 14.70)	8.70 (5.80 – 13.50)	9.30 (4.60 – 13.10)	8.90 (6.0 – 12.60)
t(p)	t=0.209,p=0.835		t=0.343,p=0.732	
Aortic valve annulus (mm)				
Mean ± SD.	5.66 ± 1.05	5.68 ± 1.20	5.63 ± 1.21	5.65 ± 1.07
Median (Min. – Max.)	5.60 (3.60 – 7.70)	5.55 (3.50 – 8.60)	5.40 (3.40 – 8.40)	5.80 (3.40 – 8.10)

t(p)	t=0.089,p=0.929		t=0.094,p=0.925	
Pulmonary valve annulus (mm)				
Mean ± SD.	6.79 ± 1.08	7.03 ± 1.32	6.89 ± 1.48	6.80 ± 1.31
Median (Min. – Max.)	6.90 (4.60 – 9.30)	6.80 (5.0 – 11.30)	6.80 (4.60 – 10.30)	6.70 (4.30 – 9.40)
t(p)	t=0.921,p=0.360		t=0.256,p=0.798	

SD: Standard deviation t: Student t-test

p: p value for comparing between cases and control in mild preeclampsia and severe preeclampsia

*: Statistically significant at $p \leq 0.05$

Cardiothoracic ratio was significantly lower in cases with mild preeclampsia than in control group while there was no significant difference among cases with severe preeclampsia and control group. There was no significant difference between cases with mild and severe preeclampsia and control group regarding aortic, pulmonary, mitral and tricuspid valve annulus.

Discussion

Preeclampsia is a serious complication of pregnancy which is associated with maternal and fetal adverse effects.(12)

There is growing evidence that preeclampsia can cause fetal cardiac dysfunction and also long-term cardiovascular complications in children who were exposed in utero to preeclampsia.(13, 14).

1.Cardiothoracic ratio

In this study, fetal cardiothoracic ratio was significantly lower in cases with mild preeclampsia with median of 0.29 (0.26 – 0.31) while Youssef et al.,(15) study, which evaluated fetal cardiac structure and function in pregnancies complicated by preeclampsia and/or fetal growth restriction as compared with uncomplicated pregnancies, showed significantly higher fetal cardiothoracic ratio among cases with preeclampsia with median of 0.31 (0.29 - 0.33) for appropriate growth for gestational age fetuses of preeclamptic mothers than control group

However, in Zhou et al.,(16) study where the fetal cardiothoracic ratio was evaluated among women with normal pregnancy, preeclampsia without intrauterine growth retardation, and preeclampsia complicated with intrauterine growth retardation, there was no significant difference among the three groups of study.

2.Aortic and pulmonary valve annuli

In Balli et al.,(9) study assessing fetal cardiac function in cases with mild preeclampsia, assessment of fetal aortic and pulmonary valve annuli did not show significant difference between cases with mild preeclampsia and control group, this finding is similar to the finding in our study where no significant difference was noted among cases with mild and severe preeclampsia and control group.

3.Sphericity index

Regarding the sphericity index, this study found that it was higher in cases with preeclampsia than control group but this difference was only statistically significant in cases with mild preeclampsia.

While Semmler et al.,(17) study, which evaluated fetal cardiac function in pregnancies that subsequently developed preeclampsia, showed significant reduction in the fetal right ventricle sphericity index in preeclamptic cases but no difference in left ventricle sphericity index between cases and control groups.

Also Youssef et al.,(15) study showed significant reduction in left ventricle sphericity index and right ventricle sphericity index among fetuses with appropriate growth for gestational age in preeclamptic patients than normotensive group.

4. Interventricular septum and left ventricle posterior wall diameter

As for the interventricular septum measurement in systole and diastole, in this study there was no significant difference between the groups of study although interventricular septum in systole was lower in cases with preeclampsia and interventricular septum in diastole was higher in cases with preeclampsia.

This is comparable to the result from Lina Youssef et al.,(15) study where relative septal wall thickness was found to be higher in cases with preeclampsia with median of 0.68 (0.61– 0.76). (ventricular end-diastolic septal wall thicknesses were measured from a transverse 4-chamber view and relative septal wall thickness was calculated as 2 times septal wall thickness divided by the left ventricular diastolic diameter).

The left ventricular posterior wall diameter in systole and diastole were found to be lower in cases with preeclampsia than control group in our study but this only reached significant difference in cases with severe preeclampsia with median of 4.0 (3.60 – 6.05) mm for left ventricular posterior wall diameter in systole and 4.70 (3.70 – 5.75) mm for left ventricular posterior wall diameter in diastole.

This is comparable to Lv et al.,(18) study which assessed morphological changes of the fetal heart in cases of pregnancy induced hypertension, fetal ventricular perimeter and area in systole and diastole and the thickness of the ventricular septum were significantly greater in the hypertension group than in the normal group. However, the study showed that pregnancy induced hypertension exerts a greater effect on the right cardiac system than on the left cardiac system.

Our study showed that fetuses of mothers with preeclampsia showed larger and hypertrophied hearts as shown in higher sphericity index but lower atrial and ventricular diameter length which indicate increased cardiac contractility as response to pressure overload which resulted from placental resistance.

Limitations of the study were technical difficulties in obtaining the proper cardiac views specially when the fetuses were lying with back anterior and difficulties in recruiting the control group pregnant females to match the exact gestational age of the cases groups.

Funding

No funding was received to perform the study.

Conflict of interest

None

References

1. Jeyabalan A. Epidemiology of preeclampsia: impact of obesity. Nutr Rev. 2013;71 Suppl 1(0 1):S18-25.
2. Bell MJ. A historical overview of preeclampsia-eclampsia. J Obstet Gynecol Neonatal Nurs. 2010;39(5):510-8.
3. Ridder A, Giorgione V, Khalil A, Thilaganathan B. Preeclampsia: The Relationship between Uterine Artery Blood Flow and Trophoblast Function. Int J Mol Sci. 2019;20(13):3263.
4. van Kesteren F, Visser S, Hermes W, et al. Counselling and management of cardiovascular risk factors after preeclampsia. Hypertens Pregnancy. 2016;35(1):55-61.
5. Guida JPS, Surita FG, Parpinelli MA, Costa ML. Preterm Preeclampsia and Timing of Delivery: A Systematic Literature Review. Rev Bras Ginecol Obstet. 2017;39(11):622-31.
6. Cokkinos DV, Belogianneas C. Left Ventricular Remodelling: A Problem in Search of Solutions. Eur Cardiol. 2016;11(1):29-35.
7. Rocha LA, Rolo LC, Araujo Júnior E. How to perform a functional assessment of the fetal heart: a pictorial review. Ultrasonography. 2019;38(4):365-73.
8. Roberts JM, Escudero C. The placenta in preeclampsia. Pregnancy Hypertens. 2012;2(2):72-83.
9. Balli S, Kibar AE, Ece I, Oflaz MB, Yilmaz O. Assessment of fetal cardiac function in mild preeclampsia. Pediatr Cardiol. 2013;34(7):1674-9.
10. Ichizuka K, Matsuoka R, Hasegawa J, et al. The Tei index for evaluation of fetal myocardial performance in sick fetuses. Early Hum Dev. 2005;81(3):273-9.
11. Lees CC, Stampalija T, Baschat AA, et al. ISUOG Practice Guidelines: diagnosis and management of small-for-gestational-age fetus and fetal growth restriction. Ultrasound in Obstetrics & Gynecology. 2020;56(2):298-312.
12. Phipps EA, Thadhani R, Benzing T, Karumanchi SA. Pre-eclampsia: pathogenesis, novel diagnostics and therapies. Nature Reviews Nephrology. 2019;15(5):275-89.
13. Tan F, Yang J, Shen Y, et al. Evaluating fetal heart morphology in hypertensive disorders of pregnancy using the fetal heart quantitative technique. Transl Pediatr. 2022;11(11):1804-12.
14. Wojczakowski W, Kimber-Trojnar Ż, Dziwisz F, Słodzińska M, Słodziński H, Leszczyńska-Gorzelak B. Preeclampsia and Cardiovascular Risk for Offspring. J Clin Med. 2021;10(14):3154.
15. Youssef L, Miranda J, Paules C, et al. Fetal cardiac remodeling and dysfunction is associated with both preeclampsia and fetal growth restriction. Am J Obstet Gynecol. 2020;222(1):79.e1-.e9.

16. Zhou Q, Ren Y, Yan Y, Chu C, Gui Y, Li X. Fetal tissue Doppler imaging in pregnancies complicated with preeclampsia with or without intrauterine growth restriction. Prenat Diagn. 2012;32(11):1021-8.
17. Semmler J, Garcia-Gonzalez C, Sanchez Sierra A, Gallardo Arozena M, Nicolaides KH, Charakida M. Fetal cardiac function at 35-37 weeks' gestation in pregnancies that subsequently develop pre-eclampsia. Ultrasound Obstet Gynecol. 2021;57(3):417-22.
18. Lv M, Yu S, Li Y, Zhang X, Zhao D. Ultrasound of Fetal Cardiac Function Changes in Pregnancy-Induced Hypertension Syndrome. Evidence-Based Complementary and Alternative Medicine. 2022;2022:2019869.