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Maternal Cardiac Functional and Structural Changes in Preeclampsia: an Echocardiographic Study

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ABSTRACT

Background & objective: Preeclampsia is a pregnancy-induced multi-organ syndrome of acute cardiovascular manifestations with significant short and long-term sequelae. However, there is a relative lack of knowledge with respect to cardiac functional and structural changes in women with preeclampsia Therapeutic interventions used in the management of preeclampsia may cause iatrogenic adverse consequences due to this lack of knowledge. The present study was therefore designed to evaluate the echocardiographic changes in cardiac structural and functional indices in pregnant women with PE.

Methods: This cross-sectional study was carried out in the Department of Obstetrics and Gynaecology Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka Medical College Hospital (DMCH), and Shaheed Suhrawardy Medical College Hospital (SSMCH) in collaboration with National Institute of Cardiovascular Diseases (NICVD), Dhaka over a period of one year from July 2013 to June 2014. A total of 30 single-tone pregnant women of 20-40 weeks gestation with preeclampsia were taken as cases. An equal number of gestationally-matched healthy pregnant (HP) women of similar age cohorts having no history of preexisting hypertension were included as controls. Preeclampsia was defined as SBP ≥140 and/or DBP ≥ 90 mmHg after 20 weeks gestation in a woman with previously normal blood pressure and with proteinuria ≥1 + in the dipstick test. Pregnant women with systolic and diastolic blood pressures within the normal range (< 140 mmHg and > 90 mmHg respectively), trace or absence of proteinuria by dipstick test were defined as controls. All the subjects were investigated with ECG, standard two-dimensional, M-mode, and Doppler transthoracic echocardiography. The cardiac functional and structural changes were measured in terms of interventricular septal thickness (IVSTd), posterior wall thickness (PWTd), left ventricular internal diameter at the end of diastole (LVIDd), ejection fraction (EF), transmitral velocity (MV E/A ratio), MV deceleration time (MV DecT).

Result: Half of the women with preeclampsia were primigravidae and there was no association between gravidity and the occurrence of preeclampsia. Prepregnancy overweight or obesity (in terms of BMI) was found to be strongly associated with preeclampsia. One in 10 PE women had a previous history of preeclampsia as opposed to none in the HP women. A substantial proportion (56.7%) of PE women had a family history of hypertension in comparison to healthy pregnant women (16.3%). The women with PE had significantly higher SBP, DBP, & MAP than the HP women.

Parameters of diastolic dysfunction, like mitral E/A ratio was reduced and deceleration time was prolonged in PE with diastolic dysfunction (mean E/A ratio < 0.73 and mean DceT >178 ms respectively) than those in PE with normal diastolic function (mean E/A ratio 1.2 and mean DceT 192.4 ms respectively) healthy pregnant women (mean E/A ratio 1.3 and mean DecT 186.5 ms respectively). Over one-third (36.7%) of women with PE met the criteria of diastolic dysfunction compared to none in healthy pregnant women. The LVH appears to be a frequent occurrence in pregnancies complicated by preeclampsia (43.3%) as compared to none in healthy pregnant women. In the present study, the systolic function was assessed with the help of EF, which was well-preserved both in PE and HP with no significant intergroup difference.

Conclusion: Preeclampsia is associated with left ventricular diastolic dysfunction and hypertrophy preserving the systolic function. These structural and functional changes are primarily adaptive in nature for maintaining cardiac systolic function.

Key words: Preeclampsia, Maternal Cardiac Functional, Structural Changes, Echocardiographic Study etc.

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INTRODUCTION:

Preeclampsia is a multisystem disorder of unknown etiology, characterized by new onset of hypertension along with de novo proteinuria after 20 weeks of gestation.[1] The disease is responsible for considerable maternal and perinatal morbidity and mortality complicating

3-7% of pregnancies worldwide.[2] In Bangladesh, the incidence of preeclampsia is very high complicating about 10-15% of all pregnancies,[3] despite all efforts taken by the government. The pathological changes in preeclampsia are primarily ischemic in nature and are known to affect the blood vessels of the placenta, kidney, liver, and brain, whereas there is scant and conflicting information about the impact on the heart.[4-7] Cardiopulmonary morbidity is seen in a significant proportion of preeclampsia cases[8] as autopsy data have shown that preeclamptic women have a 10-fold higher prevalence of myocardial contraction band necrosis than deaths in pregnancy from other causes.[9] Epidemiological data have also highlighted a strong link between preeclampsia and premature cardiovascular disease morbidity and mortality.[10,11] In normal pregnancy, cardiac index (CI), heart rate (HR), intravascular volume, and global arterial and venous compliance increase with little changes in mean and pulse pressures, whereas total vascular resistance index (TVRI) decreases to accommodate markedly increased intravascular volume without a concomitant increase in mean arterial pressure.[12] Left ventricular mass index (LVMI) increases without changes in the ratio of wall thickness to cavity dimensions, indicative of preload-mediated physiological heart remodeling.[4]

The largest, prospective invasive study demonstrated that untreated preeclamptics present with high TVRI-low CI, whereas treated preeclamptics have a similar CI to normotensive controls.[13] A recent study using noninvasive methods confirmed the uniform low CI-high TVRI state in preeclampsia versus controls; the lowest CI and highest TVRI were seen in preeclampsia associated with fetal growth restriction.[14] There is evidence of an afterload-mediated left ventricular concentric remodeling in preeclampsia to minimize myocardial oxygen demand and thus preserve left ventricular performance.[4,7,15,16]

A recent study found that myocardial contractility is impaired in preeclampsia.[6] The author assessed longitudinal systolic function which is more sensitive and is impaired before radial function is affected. Assessment of left ventricular diastolic function is more important than systolic function. Diastolic dysfunction precedes the compromise of systolic function in 50% of cardiac diseases. Few studies have analyzed maternal diastolic function in pregnancies complicated by preeclampsia and demonstrated evidence of significant differences in diastolic function indices between cases and controls.[6,7,15]

Conventional clinical diagnostic and monitoring tools for assessing the cardiovascular system are limited in pregnant women to blood pressure, ECG, pulse oximetry, and rarely invasive pulmonary artery or cardiac output monitoring. Peripartum management of critically ill women with preeclampsia is hindered by a deficit in the knowledge regarding cardiovascular performance in preeclampsia and the absence of an effective cardiovascular assessment tool. Transthoracic echocardiography (TIE) is a simple, quick (may be done at bedside), accessible, non-invasive modality of investigation that has the potential to provide far greater diagnostic insight into the assessment of cardiac structural and functional changes associated with preeclampsia in a reproducible manner. So, the present study was undertaken to evaluate echocardiographic changes in the cardiac structural and functional indices in women with preeclampsia and to identify women at high cardiovascular risk even in the absence of other concomitant risk factors.

METHODS:

This cross-sectional study was carried out in the Department of Obstetrics and Gynaecology Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka Medical College Hospital (DMCH) and Shaheed Suhrawardy Medical College Hospital (ShSMCH) in collaboration with National Institute of Cardiovascular Diseases (NICVD), Dhaka over a period of one year from July 2013 to June 2014. Ethical clearance was taken from the Institutional Review Board of BSMMU and Ethical Review Committee of DMCH. For doing Echocardiography in NICVD, permission was taken from the Director of

NICVD. A total of 30 single-tone pregnant women of 20-40 weeks gestation with preeclampsia were taken as cases. An equal number of gestationally-matched healthy pregnant women of similar age groups who attended the antenatal clinic or admitted into the Obstetrics and Gynaecology Department of DMCH and ShSMCH and fulfilled the predefined eligibility criteria were included as controls. However, preexisting hypertension prior to current pregnancy, no first trimester BP record in the current pregnancy, women with known medical co-morbidities such as cardiovascular diseases (chronic hypertension, Ischemic heart disease etc.), chronic obstructive pulmonary disease (COPD), diabetes mellitus or GDM, endocrine disease (thyroid disease), connective tissue disease, renal or liver disease, or history of any congenital heart disease or chronic rheumatic heart disease, history of tobacco consumption or patients unwilling to take part in the study were excluded.

Preeclampsia was defined as SBP ≥140 and/or DBP ≥90 mmHg after 20 weeks gestation in a woman with previously normal blood pressure and with proteinuria ≥1 + with dipstick test. Pregnant women with systolic and diastolic blood pressures within normal range (<140 mmHg and > 90 mmHg respectively), no or trace proteinuria by dipstick test were defined as control. After selecting the study subjects, the purpose and procedure of the study were explained to them and written consent was taken. Initial evaluation of the patients was done by history followed by clinical examinations (pulse, blood pressure, ankle oedema, heart sound, chest auscultation, height, and weight measurement). The diagnosis was confirmed by measurement of blood pressure and the presence of proteinuria. Maternal blood pressure was measured manually from the brachial artery using a sphygmomanometer. All the subjects were investigated for ECG, standard two-dimensional, M-mode, and Doppler transthoracic echocardiography. The cardiac structural and functional changes were measured in terms of interventricular septal thickness (IVSTd), posterior wall thickness (PWTd), left ventricular internal diameter at the end of diastole (LVIDd), ejection fraction (EF), transmitral velocity (MV E/A ratio), MV deceleration time (MV DecT)

Data were processed and analyzed using the software SPSS (Statistical Package for Social Sciences), version 16.0. The results were reported as frequency and corresponding percentages, and the mean ± SD. The test statistics used to analyze the data were descriptive statistics, Chi-square (χ^2) Test, and Unpaired t-Tests. Data presented on a categorical scale were compared between case and control groups using a Chi-square (χ^2) Test, while the data presented on a continuous scale were compared between groups with the help of an Unpaired t-Test. The level of significance was set at 0.05 and $p < 0.05$ was considered significant.

RESULTS:

Table 1 shows the comparison of demographic and obstetric characteristics between the study groups. The mean maternal ages, gestational ages, and gravidity of the case and control groups were almost identical ($p = 0.611$, $p = 0.690$, and $p = 0.436$ respectively). However, the cases were significantly heavier than the controls in terms of BMI ($p=0.005$). Three (10%) cases had a past history of PE as opposed to none of the controls ($p = 0.119$). The cases demonstrated a significant presence of a family history of hypertension (56.7%) compared to their control counterparts (16.7%) ($p = 0.001$). The cases exhibited a significantly altered haemodynamic state (in terms of SBP and DBPs, and MAP) than their control counterparts ($p < 0.001$) (Table I).

Table I : Comparison of demographic and obstetric characteristics between groups

Characteristics	Group		p-value
	Case (n =30)	Control (n =30)	
Maternal age# (years)	25.5 ± 4.8	24.9 ± 4.2	0.611
Gestational age# (weeks)	33.7 ± 3.1	34.5 ± 2.5	0.690
Gravida*			
Primigravida	15(50.0)	18(60.0)	0.436
Multigravida	15(50.0)	12(40.0)	
BMI# (kg/m^2)	30.5 ± 5.7	27.2 ± 2.5	0.005
Previous history of PE*	3(10.0)	0(0.0)	0.119
Family history of HTN*	17(56.7)	5(16.3)	0.001
SBP# (mmHg)	167.0 ± 18.8	103.8 ± 9.6	< 0.001
DBP# (mmHg)	111.0 ± 16.2	68.5 ± 8.7	< 0.001
MAP# (mmHg)	129.7 ± 15.3	80.3 ± 8.3	< 0.001

*Data were analyzed using an **Unpaired t-Test** and were presented as **mean ± SD.**
*Data were analyzed using a Chi-squared (χ^2) Test; figures in the parentheses denote corresponding percentages. BMI = Body Mass Index; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; MAP = Mean Arterial Pressure

Table II : Comparison of echocardiographic structural indices of the study subjects

Parameter	Control (n = 30)	PE with normal diastolic function (n=19)	PE with diastolic dysfunction (n=11)	P-values (HP vs PE with normal diastolic function)	P-values (HP vs PE with diastolic dysfunction)
IVSTd (mm)	8.0 ± 1.4	10.1 ± 2.1	11.3 ± 1.8	0.001[s]	0.001[s]
PWTd (mm)	8.1 ± 1.4	10.1 ± 2.1	11.5 ± 1.6	0.001[s]	0.001[s]
LVIDd (mm)	45.3 ± 3.9	44.1 ± 3.9	43.8 ± 3.4	0.81[ns]	0.24 [ns]

Data were analyzed using Student's t-Test and were presented as Mean ± SD. S = Significant; NS = Non-significant. HP = Healthy pregnant women; PE = Preeclampsia.

Table III : Comparison of LVEF, MV E/A ratio and MV DecT among the study subjects with different diastolic functions

LVH*	Healthy Pregnant Women (n = 30)	PE with normal diastolic function (n=19)	PE with diastolic dysfunction (n=11)	P-values (HP vs PE with normal diastolic function)	P-values (HP vs PE with diastolic dysfunction)
EF%	65.4 ± 6.0	69.8 ± 6.1	67.4 ± 4.1	0.190	0.062
MV E/A ratio	1.3 ± 0.21	1.2 ± 0.20	0.72 ± 0.03	0.008	< 0.001
MV DecT (ms)	186.5 ± 21.6	192.4 ± 43.5	278.9 ± 53.3	0.52	< 0.001

Figures in the parentheses denote corresponding percentages.
*Fisher's Exact Test was done to analyze the data LVH = Left ventricular hypertrophy.

Table IV : Left ventricular structural remodeling of women with preeclampsia and healthy pregnant women

Parameter	Healthy Pregnant Women (n = 30)	PE with normal diastolic function (n=19)		PE with diastolic dysfunction (n=11)	P-values (HP vs PE with normal diastolic function)	P-values (HP vs PE with diastolic dysfunction)
Present		0	6(31.6)	7 (63.6)	0.002	< 0.001
Absent		30(100.0)	13(68.4)	4(36.4)		

Data were analyzed using an **Unpaired t-Test** and were presented as **Mean ± SD.**

Table II shows the echocardiographic structural indices of the study subjects. Out of 30 cases, 19(63.3%) had a normal diastolic function, and 11(36.7%) with diastolic dysfunction. The interventricular septal thickness (IVSTd) was observed to be significantly higher in PE with diastolic dysfunction than that in controls (11.3±1.8 mm vs. 8.0 ± 1.4 mm, p = 0.001). The posterior wall thickness at the end of diastole (PWTd) was also significantly higher in PE with diastolic dysfunction than that in controls (11.5 ± 1.6 mm vs. 8.1 ± 1.4 mm, p=0.001). The left ventricular internal diameter at the end of diastole (LVIDd) was significantly lower in PE with diastolic dysfunction than that in healthy pregnant women (43.8 ± 3.4 mm vs. 45.3 ± 3.8 mm, p = 0.240). As all the above echocardiographic structural indices were compared between healthy pregnant (HP) women and PE with normal diastolic function, similar results were found as was found when comparing HP women and PE with diastolic dysfunction.

Table III shows that there was no statistically significant difference among the three study groups (healthy pregnant women vs women with preeclampsia with or without diastolic dysfunction). An insignificant difference was found between healthy pregnant women and PE women with normal diastolic function (p = 0.190) as well as between HP women and PE women with diastolic dysfunction (p=0.062). The peak MV E/A ratio was significantly reduced in PE women with diastolic dysfunction than that in HP women with normal diastolic function (p<0.001). The E wave DecT was staggeringly higher in PE women with diastolic dysfunction (278.9 ms) in comparison to those found in PE with preserved diastolic function and HP women (192.4 and 186 ms respectively) (p<0.001), although no significant difference was evident between PE women with

ORIGINAL ARTICLE

normal diastolic function and HP women with respect to MV DecT (p = 0.520).

Table IV shows the left ventricular structural remodeling of the study subjects. LVH was significantly higher in PE with diastolic dysfunction compared to that in healthy pregnant women (p < 0.001). No LVH was found in healthy pregnant women. Preeclamptic women with normal diastolic function also had significantly higher LVH compared to healthy pregnant women (p = 0.002).

Fig.1 and 2 show the correlations between MAP and MV E/A ratio and MAP and MV DecT (ms) respectively. While a significantly negative correlation was observed between mean arterial pressure (MAP) and MV E/A ratio (r = -0.61, p = 0.001), a significantly positive correlation was seen between MAP & MV DecT (r = 0.41, p = 0.010).

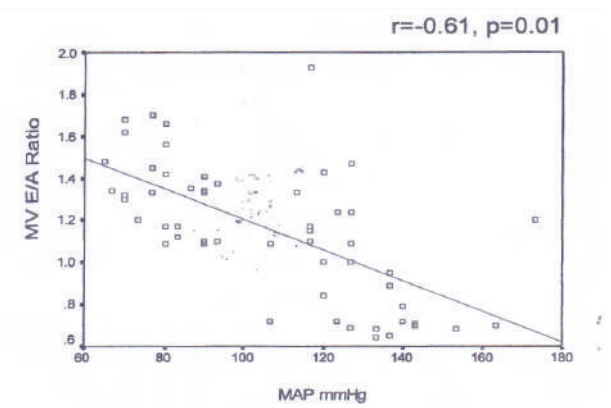

Figure 2: Correlation between Mean Arterial Pressure (MAP) and MV E/A ratio

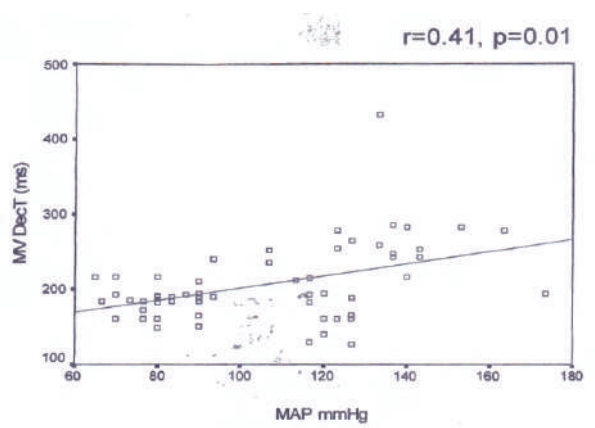

Figure 3: Correlation between Mean Arterial Pressure (MAP) & MV DecT

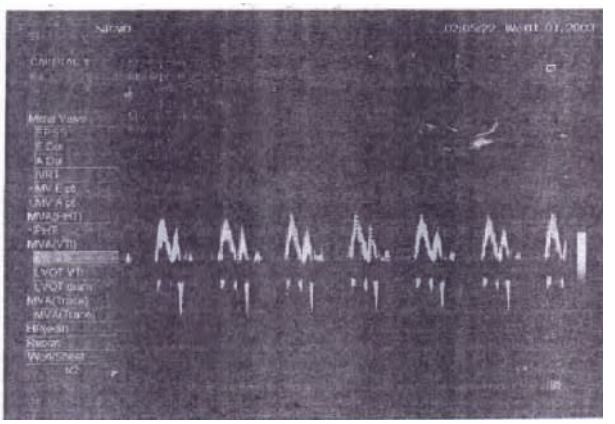

Figure: 4 Standard Doppler mitral ltiflqw pattern in a healthy pregnant woman, where peak MV E/A ratio is 1.32 and deceleration time is 160 ms

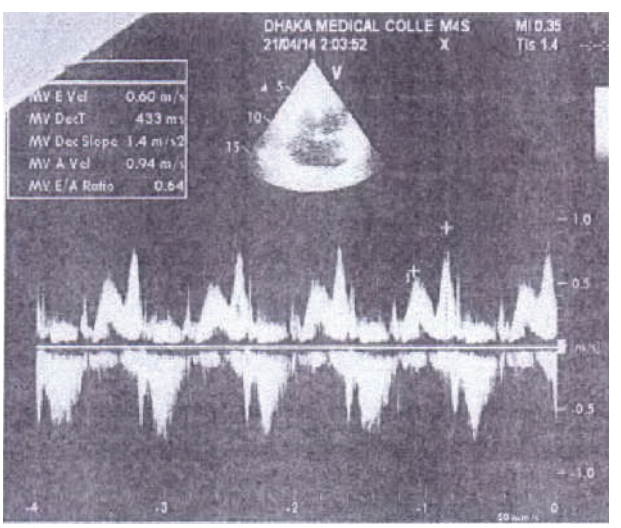

Figure: 5 Standard Doppler mitral inflow pattern in a preeclamptic woman where peak MV E/A ratio is 0.64 and deceleration time is 433 ms.

DISCUSSION:

The present study was intended to evaluate the echocardiographic changes in cardiac structural and functional indices in pregnancies complicated by preeclampsia and compare those indices with matched healthy pregnant women. Women with preeclampsia were matched with healthy pregnant women in terms of age, gestational age, and gravidity which ruled out the potential confounding effects of these variables on the outcome variables, cardiac structural, and functional indices. Cardiac investigation timing in relation to gestational age is also important, as some studies have demonstrated

a decrease in systolic function late in normal pregnancy.[17-19] Zentner & associates[20] demonstrated both systolic and diastolic functions to deteriorate by term in normal pregnancy.

Preeclampsia occurs with increased frequency among young, nulliparous women. However, the frequency distribution is bimodal, with a second peak occurring in multiparous women >35 years of age.[21] MacGillivray[22] in a study reported that nulliparous women are at increased risk of preeclampsia. The relative risk of developing preeclampsia in nulliparous women is 2.91, (95% CI:1.28-6.61).[23] However, in the present study, 50% of the women with preeclampsia were primigravidae and no association was found between gravidity and the occurrence of preeclampsia. In our study, elevated prepregnancy BMI was found to be strongly associated with preeclampsia, which supports the results of other studies reporting an increased incidence of preeclampsia in both overweight and obese women.[24-26] Regarding previous history of preeclampsia-eclampsia the relative risk of developing preeclampsia is 7.19, (95% CI:5.83-8.83).[27] In our study, 10% of PE women had a previous history of preeclampsia which supports the findings of the above-mentioned study. In the present study, a substantial proportion (56.7%) of PE had a family history of hypertension in comparison to healthy pregnant women (16.3%). Consistent with the findings of our study, a study demonstrated that women whose mothers had hypertension, preeclampsia, or eclampsia were at increased risk of severe preeclampsia. The risk was even greater when the women had a sister with a history of hypertension, preeclampsia, or eclampsia (OR 2.6, 95% CI = 1.6 – 4.2, p < 0.001).[28] Another study by Roes et al[29] demonstrated similar findings.

The heart is a biological pump with an intrinsic capacity to alter its structural and functional ability in response to its workload demands. During normal pregnancy, a number of hemodynamic changes take place, such as an increase in blood volume and stroke volume together with heart rate and a decrease in peripheral resistance and mean BP.[12,30] As a consequence of these changes there is a physiological cardiac remodeling which includes an increase in end-diastolic volume, left ventricular eccentric hypertrophy and functional changes in the left ventricle after the first half of pregnancy.[12,30] When pregnancy is complicated by preeclampsia i.e., increase in afterload, there is an accentuation of these physiological changes of which structural modification [increased left ventricular mass thickness and wall thickness] and functional changes especially the development of diastolic dysfunction merits special attention.

In the present study, the two populations (HP and PE) selected were representative of two different haemodynamic states, which were evident from the significant differences in SBP, DBP, and MAP. The diastolic dysfunction in PE was observed through the standard Doppler analysis of transmitral inflow parameters which appeared to be more significant in difference compared to healthy pregnant women. Parameters of diastolic dysfunction, like mitral E/A ratio was reduced and deceleration time was prolonged in PE with diastolic dysfunction (mean E/A ratio < 0.73 and mean DceT >178 ms respectively) compared to PE with normal diastolic function (mean E/A ratio 1.2 and mean DceT 192.4 ms respectively) and healthy pregnant women (mean E/A ratio 1.3 and mean DecT 186.5 ms respectively). In this study, over one-third (36.7%) of women with PE met the criteria of diastolic dysfunction compared to none in healthy pregnant women. Studies on maternal diastolic function in preeclampsia are scant. Although two studies.[6,7] analyzed diastolic function with relatively load-independent tissue Doppler indices, they interpreted the echocardiographic indices in isolation rather than using clinically validated diagnostic algorithms. Despite these limitations, both studies demonstrated evidence of significant differences in diastolic function indices between cases (women with PE) and controls (healthy pregnant women). The present study also demonstrated a significant alteration in diastolic function in preeclamptic women, the findings of which well corroborated with other studies. Among all those studies two prospective studies on cardiac function in preeclampsia,[15,16] demonstrated that women with preeclampsia are significantly associated with mild to moderate left ventricular diastolic dysfunction. As these studies used validated

diagnostic algorithms with the integration of multiple techniques, they seem to be more authentic.

Regarding cardiac remodeling, the study data indicate that most women with preeclampsia undergo adaptive responses with significant cardiac structural changes. The LVH appears to be a frequent occurrence in pregnancies complicated by preeclampsia (43.3%) as compared to none in healthy pregnant women. These changes are likely to be an adaptive response to reduce the wall stress associated with increased afterload. Similar results were found in several studies.[4,15,16] Simmons and associates[4] found that the significantly increased LVM was accompanied by an increase in cardiac work and concluded that heart remodeling in PE is a response to the increased systemic afterload in order to minimize myocardial oxygen demand and thus preserve left ventricular performance. A recent study found progression towards severe LV hypertrophy in association with advanced cardiac dysfunction in about 20% of preterm preeclamptic women.[16] This indicates that although most of the PE undergoes adaptive heart remodeling to increase after-load, a small subgroup demonstrates signs of overt decompensation.[15,16]

In our study, the systolic function was assessed with the help of EF, which was well-preserved both in PE and HP and was homogeneously distributed among the groups. This finding is in agreement with Simmons et al.[4] demonstrating no change in ejection phase indices and preservation of systolic function. Two other studies found a significant reduction in ejection phase indices in PE.[7,14] Recent studies have assessed longitudinal systolic function which is more sensitive to afterload and is impaired before radial function is affected.[31,32] Bamfo and associates[32] found that longitudinal LV systolic function tissue Doppler indices were reduced in preeclampsia and concluded that myocardial contractility is impaired in this condition.

CONCLUSION:

The findings of this study show that asymptomatic left ventricular diastolic dysfunction and structural changes are evident in women with preeclampsia without any change in systolic function. These cardiac structural changes are mainly adaptive in nature for maintaining cardiac systolic function. Early identification of these changes has public health implications, as these changes are associated with greater cardiovascular disease risk later in life, which may be prevented by early recognition and prophylactic intervention.

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