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Maternal cardiovascular dysfunction in women with early onset preeclampsia and late onset preeclampsia: A cross-sectional study

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ABSTRACT

Objectives: To compare the cardiovascular changes associated with early onset (EOPE) and late onset (LOPE) subtypes of preeclampsia.

Methods: A prospective matched cross-sectional study involving 50 women each with early and late onset subtypes of preeclampsia conducted in a tertiary hospital in South India. Cardiac function and remodelling were assessed by conventional 2D, M-mode and doppler echocardiography.

Results: Women with EOPE had a significantly more altered left ventricular (LV) geometry, global LV diastolic dysfunction, impairment in myocardial contractility (40% vs. 24%) and a higher total vascular resistance index (863.0 vs 704.0 dynes/s/cm^5/m^2) compared to LOPE. Stroke volume index (55.3 vs. 62.2 ml/m^2) and cardiac work index (520.7 vs. 584.9 mmHg × L/min/m^2) were higher in women with LOPE. However, the systolic function was found to be preserved in the LV in both the groups.

Conclusions: Women with EOPE have a more severe cardiac impairment than those with LOPE. The difference in the hemodynamic indices may provide a chance to tailor patient-specific treatment strategies to improve the pregnancy outcome as well as in early identification and initiation of preventive measures for those at risk of cardiovascular diseases later in life.

Key message: Adaptation of the heart in women with early onset subtype differs with that of late onset subtype of preeclampsia. Total vascular resistance is higher in early onset group compared to late onset group having a higher cardiac output. These differences in the hemodynamic indices may provide a chance to tailor patient-specific treatment strategies to improve the pregnancy outcome as well as in early identification and initiation of preventive measures for those at risk of cardiovascular diseases later in life.

1. Introduction

Pre-eclampsia affects 5–8% of all pregnancies, increases the risk of maternal and perinatal morbidity and mortality [1]. Cardiovascular complications are noted to occur in nearly 5% among them and it is considered at a risk factor for increase in the risk of cardiovascular disease in later in life [2,3]. Although it is well known that hypertension is the defining clinical feature of preeclampsia, the underlying hemodynamic explanation still remains controversial.

Pre-eclampsia is found to be associated with left ventricular (LV) diastolic dysfunction and increased LV mass when compared to normotensive pregnant women [2,4]. Recent studies suggested the cardiovascular states to be different in its two subtypes i.e. early onset (onset < 34 weeks) and late onset (onset after 34 weeks) [5]. Women with the early onset subtype have been found to have low cardiac output with high total vascular resistance whereas as those developing late onset subtype have a high cardiac output with low total vascular resistance [6].

So, our objective was to compare the cardiovascular changes associated with early onset and late onset subtypes of preeclampsia.

2. Methods

This cross-sectional study was carried out in the Women and Children's Hospital attached to Jawaharlal Institute of Postgraduate Medical Education & Research, Puducherry, India, from October 2014 to April 2016. We included women with preeclampsia diagnosed according to the American College of Obstetricians and Gynaecologists

Abbreviations: EOPE, Early Onset Pre-Eclampsia; LOPE, Late Onset Pre-Eclampsia; LV, Left Ventricle; TVR, Total Vascular Resistance

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(ACOG) Criteria 2013 [7]. Cases comprised of women diagnosed as preeclampsia between 28 and 34 weeks (Early Onset Pre-Eclampsia, EOPE, group A) and those who were diagnosed after 34 weeks were the controls (Late Onset Pre-Eclampsia, LOPE, group B). For each case in group A, one control in group B, matched for age and parity was recruited. Women with multiple pregnancies, those having chronic hypertension or medical co-morbidities such as anaemia, heart disease, renal disease and pre-gestational diabetes were excluded from the study. Ethical Clearance was obtained from the Institute Ethics Committee (Human Studies).

After taking an informed consent, baseline characteristics such as age, parity, pre-pregnancy body mass index, body surface area and gestational age at recruitment were noted. Systolic and diastolic blood pressure was measured before echocardiography. Standard 2-dimensional, M-mode and Doppler *trans*-thoracic echocardiographic evaluations were performed using a 2.5-MHz transducer on a Philips E7 scanner. This was done with the patient in the left lateral decubitus position and data acquired at end expiration from standard parasternal/apical views. Cardiac indices were normalized for body surface area, height, and end-diastolic left ventricle long or short axis lengths, as appropriate. All parameters were measured and evaluation of biventricular systolic function, left ventricular diastolic function, left ventricular remodelling and right ventricular systolic function was done according to the guidelines recommended by the American and European societies of Echocardiography. We graded the global diastolic dysfunction was graded using a diagnostic algorithm based on the recommendation of both the societies [8–10]. Flow mediated dilatation of the brachial artery was measured by the technique described in Tyldum et al. [6] Percentage change in the brachial artery diameter after cuff deflation was noted and compared between the two groups.

Statistical Analysis: Data was analysed using software STATA 13.1 (Stata Corp, Texas, USA). Student *t*-test and Chi -square test was used to the compare various factors with pattern of dysfunction in both the groups. A p value of $< .05$ is considered significant.

Sample size was calculated using nMaster software version2.0 (Vellore, India). To detect a difference of 22% in the prevalence of global diastolic dysfunction between women with two subtypes as demonstrated in the study by Melchoirre et al. [3]; with a power of 0.8 and a type I error probability of 0.05, 47 women were required in each group. So, we enrolled 50 women in each group in the study.

3. Results

We screened 105 women for the study, of which we excluded three women diagnosed to have rheumatic heart disease on echocardiography, one with severe anaemia and one with peripartum cardiomyopathy in her previous pregnancy. Finally, 50 women with EOPE (Group A) and 50 with LOPE (Group B) were included in the study (Fig. 1). Demographic characteristics of the women with EOPE and LOPE in the study are shown in Table 1. Among the multiparous women, history of preeclampsia in previous pregnancy was noted to be higher in group A than group B (13/19 (68.4%) vs 8/22 (36.4%), $p = .041$). More women in group A were receiving aspirin prophylaxis at the time of recruitment to study compared to the other group (11(22%) vs. 2(4%), $p = .007$). Majority of the women required antihypertensives after recruitment in the study (32(64%) vs 30(60%), $p = .06$). Eighteen women underwent caesarean section in both the groups. There were 10 still births (20%) and 9(18%) neonatal deaths in the EOPE group compared to 4(8%) neonatal deaths in the LOPE group. More fetuses were diagnosed to have intrauterine growth restriction in group A ($p < .001$) and the birth weight were found to be significantly lower in the EOPE group compared to LOPE group (1546.42 ± 700.60 vs. 2485.86 ± 568.91 grams, $p < .001$). Percentage change in brachial artery diameter was not significantly different between the groups (3.2% vs. 5.8%, $p = .11$).

3.1. Remodelling & hemodynamic indices

The LV remodelling indices were significantly higher in women with EOPE. Total Vascular Resistance Index (TVRI) was found to be higher whereas the stroke volume index and the cardiac indices were lower in the in the EOPE group compared to LOPE group. Proportion of women with LV concentric hypertrophy was higher in the EOPE compared to LOPE (50% vs 20%). Table 2 shows the hemodynamic and remodelling parameters in both the groups.

3.2. Systolic and diastolic function

Table 3 demonstrate the systolic and diastolic function parameter in both the groups. There were no significant differences between the LV ejection fraction and endocardial fractional shortening between both groups. Prevalence of impaired LV myocardial contractility was more in those with EOPE compared to LOPE (40% vs. 24%, $p = .002$). Some degree of diastolic dysfunction was noted in 82% women of EOPE group compared to 56% of LOPE group as shown in Fig. 1. In the EOPE group, there were 2(4%) with grade I, 35(70%) with grade II and 4(8%) had grade III diastolic dysfunction compared to LOPE group having 6 (12%) with grade I and 22(44%) grade II diastolic dysfunction ($p = .06$). Tricuspid annular plane systolic excursion (TAPSE) as marker of right ventricular longitudinal systolic function was significantly lower in the EOPE group than in the LOPE group ($p = .011$).

4. Discussion

Women with EOPE and LOPE were found to have a difference in the hemodynamic indices; with the vascular resistance being higher and the cardiac indices adjusted for body surface area being lower in the EOPE group compared to the LOPE group. EOPE group had more proportion of women with LV impaired myocardial contractility and severe diastolic dysfunction compared to LOPE.

Global systolic function of the LV was found to be preserved in both the groups studied. However, alteration of the ventricle morphology was noted in majority of women in both the groups; with more women in the EOPE group having LV concentric remodelling and increased LV mass indices. This may be suggestive of the compensatory changes, associated with the increase in strain related to increase in the afterload (as evidenced by increased TVRI and Cardiac Work Index(CWI)), which help to maintain the balance between the myocardial oxygen demand and supply. The LV end-systolic wall stress index in both the groups support this finding, although this was noted to be higher in LOPE group which have comparatively lower LVMI. This is supported by the previous studies which have observed that this may be appropriate response to the increase in after load preserving intrinsic myocardial contractility in preeclamptic women [3,11,12]. Thus, cardiac reserve is utilised more in women with EOPE than in women with LOPE, which increases the subsequent risk of pulmonary edema/heart failure and ischemic heart disease.

Women with EOPE had higher TVR compared to those with LOPE demonstrating greater rise in stroke volume, cardiac output and cardiac workload normalized for body surface area in our study. This is similar to the findings in the study by Valensise et al. [6] who noticed that these two groups to differ in the hemodynamic indices at 24 weeks' gestation, much before manifestation of preeclampsia, and these changes persisted even 1 year postpartum. These hemodynamic differences lead them to suggest the varied origins of both forms of preeclampsia; EOPE being the evolution of an extreme cardiovascular disorder secondary to defective trophoblastic invasion in placental development and LOPE probably linked to the maternal constitutional factors such as body mass index. However, we did not observe a difference between the body mass indexes in our study which was contrary to the findings noted in their study as well by others earlier [3,11]. This also raised the question that there might be other factors