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Original Article

Obstetrics and Gynaecology Section

# Comparison of Maternal Echocardiographic Findings in Women with Early Onset Preeclampsia and Late Onset Preeclampsia: A Prospective Observational Study

GOTER DOKE[1], DINA PABI[2], RINCHIN DORJEE MEGEJI[3], EK SHEHNA[4]




## ABSTRACT

**Introduction:** Preeclampsia is a leading cause of maternal and perinatal morbidity and mortality worldwide. Significant cardiovascular adaptations occur in preeclampsia, with Early Onset Preeclampsia (EOPE, onset before 34 weeks of gestation) associated with a more complex and severe haemodynamic profile compared to Late Onset Preeclampsia (LOPE, onset at or after 34 weeks). Recent evidence indicates that EOPE and LOPE represent distinct pathophysiological entities characterised by different haemodynamic states, necessitating subtype-specific cardiovascular risk assessment during the antenatal period.

**Aim:** To compare echocardiographic findings in women with EOPE versus those with LOPE and to characterise differences in biventricular systolic and diastolic function between the two subtypes.

**Materials and Methods:** A prospective observational study was conducted in 80 antenatal women (40 with EOPE and 40 with LOPE) at a tertiary care centre in Arunachal Pradesh from June 2021 to September 2022. Standard two-dimensional, M-mode, and Doppler transthoracic echocardiography was performed for all participants. Biventricular systolic function, Left Ventricular (LV) diastolic function, LV geometry, and Right Ventricular (RV) systolic function were assessed according to American and European Society of Echocardiography guidelines.

**Results:** Impairment in LV Ejection Fraction (LVEF) was significantly more prevalent in EOPE compared with LOPE (42.5% versus 20%, p-value=0.03). Indices of LV diastolic dysfunction, including mitral E/A ratio, septal E/E', and lateral E/E', were significantly higher in EOPE (p-value=0.005, 0.015, and 0.011, respectively). Overall diastolic dysfunction was more frequent in EOPE than in LOPE (80% versus 55%, p=0.017). Tricuspid annular plane systolic excursion (TAPSE) was significantly lower in EOPE compared with LOPE (2.11±0.286 cm versus 2.45±0.523 cm, p-value <0.001), indicating RV longitudinal systolic dysfunction in EOPE. Relative LV wall thickness was significantly higher in EOPE (0.53±0.18 versus 0.45±0.12, p-value=0.026).

**Conclusion:** Women with EOPE demonstrate significantly greater LV diastolic dysfunction and biventricular myocardial contractility impairment compared with LOPE. Echocardiography performed during the antenatal period can identify preeclamptic women at higher cardiovascular risk, particularly those with early onset disease, enabling patient-specific management and long-term cardiovascular surveillance.


**Keywords:** Biventricular function, Echocardiography, Hypertensive disorders of pregnancy, Left ventricular diastolic dysfunction, Tricuspid annular plane systolic excursion

## INTRODUCTION

Preeclampsia is the most common and severe hypertensive disorder of pregnancy, affecting 5-8% of all pregnancies globally and representing a major cause of maternal and perinatal morbidity and mortality [1]. The condition is associated with LV diastolic dysfunction, increased LV mass, altered chamber geometry, and pericardial effusion compared with normotensive pregnancy [2]. Asymptomatic global LV dysfunction and subclinical myocardial injury have been demonstrated to be significantly more prevalent in acute preeclampsia than in uneventful pregnancy [3].

Preeclampsia is further classified based on gestational age at onset: EOPE is defined as an onset before 34 weeks of gestation, and LOPE as an onset at or after 34 weeks. Haemodynamic studies have consistently identified two distinct phenotypes. EOPE is characterised by a low Cardiac Output (CO) state with high Systemic Vascular Resistance (SVR), arising from failed placental vascular remodelling resulting in placenta-mediated pathology of greater complexity and severity. LOPE, conversely, tends to arise in association with maternal constitutional risk factors such as elevated body mass index and family history of hypertension and is characterised by relatively higher CO and lower SVR [4]. These distinct aetiologies support the classification of EOPE and LOPE as different forms of the disease requiring individualised clinical management.

Women with EOPE carry a substantially higher risk of acute cardiovascular complications and of developing premature cardiovascular disease in later life compared with women with LOPE [5,6]. A recent systematic review and meta-analysis reported that preeclampsia is associated with a two-fold increased risk of stroke, a 2.5-fold increased risk of heart failure, and a two-fold increased risk of cardiovascular mortality in later life [7]. Despite this evidence, relatively few studies have [4,7,8] directly compared echocardiographic parameters between EOPE and LOPE. The present study was therefore undertaken to compare echocardiographic findings, including biventricular systolic and diastolic function and LV geometry, in women with EOPE versus those with LOPE.

## MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Obstetrics and Gynaecology in collaboration with the Department of Cardiology at a tertiary care hospital in Arunachal Pradesh, India from June 2021 to September 2022. Ethical clearance was obtained from the Institutional Ethics Committee (IEC) prior

to commencement of the study (No. TRIHMS/ETHICS/01/ 2019-20/13). All participants provided written informed consent prior to enrolment.

**Inclusion criteria:** Patients who fulfilled the definition of preeclampsia as per the 2020 American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin [9].

- SBP ≥140 mmHg or DBP ≥90 mmHg on two occasions at least four hours apart after 20 weeks of gestation.
- Coexistence of one or more of: proteinuria ≥300 mg/24 h or dipstick 2+ on two random samples at least four hours apart; or evidence of multisystem end-organ dysfunction with or without proteinuria.

**Exclusion criteria:**

- Chronic hypertension;
- Pre-existing cardiac disease;
- Renal disease;
- Severe anaemia (haemoglobin <7 g/dL);
- Multiple pregnancy

**Sample size calculation:** Here, the sample size formula used to estimate the difference between two means for equal group sizes ($\kappa = 1$):

$n = (z_{\alpha/2}+z_{\beta})^2(\sigma_1^2+\sigma_2^2) /\delta^2$

| | |
|---|---|
| n | Required sample sizes in Group-1 and Group-2 |
| $\sigma_1^2$, $\sigma_2^2$ | Known (or estimated) variances for each group — can differ |
| $\delta$ | Minimum detectable difference $\mu_1-\mu_2$ |
| $z\alpha/2$ | Critical z for significance level $\alpha$ (two-tailed: 1.96 at $\alpha$=0.05) |
| $Z\beta$ | Critical z for power 1–$\beta$ ( 0.842 for 80% ) |

The sample size of 80 (40 per group) was calculated based on the study by Vaddamani S et al., which demonstrated a significant difference in mean LV Relative Wall Thickness (RWT) between EOPE (0.52±0.19) and LOPE (0.42±0.13) groups [8]. Using a two-sample t-test with a power of 80% (beta error 0.20) and a type I error probability of 0.05 (two-tailed), the minimum required sample size was 40 women per group.

A total of 80 antenatal women were enrolled: 40 with Group A EOPE and 40 with Group B LOPE.

### Study Procedure

A structured proforma was maintained for each participant. Blood pressure was measured during the antenatal period in the left arm in the sitting position with the arm at heart level, recording Korotkoff phase I (systolic) and phase V (diastolic) sounds. Standard two-dimensional, M-mode, and Doppler transthoracic echocardiography was performed using a 2.5-MHz transducer on a Philips E7 scanner, with the patient in the left lateral decubitus position. Biventricular systolic function, LV diastolic function, LV geometry, and RV systolic function were assessed according to guidelines of the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI) [10]. LV diastolic dysfunction was graded from one to three using standard doppler criteria including mitral E/A ratio, tissue doppler septal and lateral E/E', and tricuspid regurgitation velocity was also assessed using American Society of Echocardiography (ASE) and the EACVI guidelines [10,11]. Degree of Impairment in LVEF was graded as normal, mild, moderate and severe [11]. RV systolic function was assessed by TAPSE. LV geometry was evaluated using the RWT [10]. Perinatal outcome of both groups was also evaluated.

## STATISTICAL ANALYSIS

Data were analysed using IBM Statistical Package for the Social Sciences (SPSS) Statistics for Windows, Version 28.0 (IBM Corp., Armonk, NY, USA). Continuous variables (age, gestational age, CO, Total Vascular Resistance (TVR), echocardiographic parameters) were compared using the independent samples Student t-test. Categorical variables (parity, diastolic dysfunction grading, pattern of contractility impairment) were compared using the Chi-square test. A p-value <0.05 was considered statistically significant.

## RESULTS

A total of 80 antenatal women were enrolled from June 2021 to September 2022: 40 with EOPE (Group A) and 40 with LOPE (Group B).

**Maternal characteristics:** [Table/Fig-1] presents baseline maternal characteristics. The maternal age was higher in LOPE (range 21-39 years). The proportion of nulliparous women was 45% in EOPE and 37.5% in LOPE. A history of preeclampsia in a previous pregnancy was more common in EOPE (40%) than in LOPE (25%), though this difference did not reach statistical significance. The proportion of women on a single antihypertensive agent (labetalol or nifedipine) was higher in EOPE (85%) compared with LOPE (75%).

| Factors | EOPE n=40 (%) | LOPE n=40 (%) |
|---|---|---|
| **Maternal age (years)** | | |
| 20-24 | 9 (22.5) | 7 (17.5) |
| 25-29 | 17 (42.5) | 15 (37.5) |
| 30-34 | 11 (27.5) | 11 (27.5) |
| 35-40 | 3 (7.5) | 7 (17.5) |
| **Parity** | | |
| Nulliparous | 18 (45) | 15 (37.5) |
| Multiparous | 22 (55) | 25 (62.5) |
| **History of preeclampsia in prior pregnancy** | | |
| Yes | 16 (40) | 10 (25) |
| No | 24 (60) | 30 (75) |
| **Antihypertensive use** | | |
| None | 4 (10) | 8 (20) |
| Single agent (labetalol/nifedipine) | 34 (85) | 30 (75) |
| Two or more agents | 2 (5) | 2 (5) |

**[Table/Fig-1]:** Baseline maternal characteristics.

**Clinical and haemodynamic parameters:** [Table/Fig-2] shows maternal clinical parameters. Heart rate and respiratory rate were marginally higher in LOPE, whereas SBP (151.75±10.59 versus 148.75±9.92 mmHg) and mean arterial pressure (MAP: 115.8±8.49 versus 114.9±8.85 mmHg) were slightly higher in EOPE. None of these differences reached statistical significance (p-value >0.05). DBP was identical between groups (p-value=1.0).

| Parameter | EOPE (n=40) Mean±SD | LOPE (n=40) Mean±SD | p-value |
|---|---|---|---|
| Heart rate (beats/min) | 80.6±6.34 | 81.5±5.23 | 0.491 |
| Respiratory rate (/min) | 15.95±1.6 | 16.2±1.85 | 0.521 |
| Systolic BP (mmHg) | 151.75±10.59 | 148.75±9.92 | 0.195 |
| Diastolic BP (mmHg) | 98±8.53 | 98±9.39 | 1.0 |
| Mean arterial pressure (mmHg) | 115.8±8.49 | 114.9±8.85 | 0.659 |

**[Table/Fig-2]:** Maternal clinical parameters.

[Table/Fig-3] presents maternal haemodynamic indices. CO (7.87±2.37 versus 7.46±2.27 L/min) and stroke volume (96.55±28.04 versus 92.65±27.56 mL) were higher in LOPE, while TVR was higher in EOPE (1362.01±437.1 versus 1265.93±350.55 dyne/s/cm$^5$). None of these differences was statistically significant (p-value >0.05).

| Parameter | EOPE (n=40) Mean±SD | LOPE (n=40) Mean±SD | p-value |
|---|---|---|---|
| Stroke volume (mL) | 92.65±27.56 | 96.55±28.04 | 0.532 |
| Cardiac output (L/min) | 7.46±2.27 | 7.87±2.37 | 0.431 |
| Total Vascular Resistance (TVR) (dyne/s/cm$^5$) | 1362.01±437.1 | 1265.93±350.55 | 0.282 |

**[Table/Fig-3]:** Maternal haemodynamic indices.

**Left Ventricular (LV) systolic and diastolic function:** [Table/Fig-4] summarises LV systolic and diastolic parameters. Mean RWT was significantly higher in EOPE (0.53±0.18 versus 0.45±0.12, p-value=0.026). Mean LVEF was lower in EOPE compared with LOPE (p-value =0.055). Combined mild and moderate impairment of LV contractility was observed in 42.5% of EOPE women versus 20% of LOPE women (p-value=0.03). Normal LV systolic function was present in 57.5% of EOPE and 80% of LOPE women. No severe impairment was observed in either group.

| | Parameter | EOPE (n=40) Mean±SD / n (%) | LOPE (n=40) Mean±SD / n (%) | p-value |
|---|---|---|---|---|
| Left Ventricular (LV) remodelling indices | Relative Wall Thickness (RWT) | 0.53±0.18 | 0.45±0.12 | 0.026 |
| Left Ventricular (LV) radial systolic function | LV Ejection Fraction (LVEF) (%) | 57.99±8.26 | 61.14±6.06 | 0.055 |
| | Endocardial fractional shortening (%) | 30.63±8.006 | 32.21±6.79 | 0.344 |
| Degree of impairment in LVEF | Normal contractility | 23 (57.5) | 32 (80) | 0.03 |
| | Mild impairment | 12 (30) | 7 (17.5) | |
| | Moderate impairment | 5 (12.5) | 1 (2.5) | |
| | Severe impairment | 0 | 0 | |
| Mitral inflow velocities (Diastolic function of left heart) | Mitral E/A | 1.50±0.467 | 1.24±0.333 | 0.005 |
| | Septal E/E' | 10.14±3.75 | 8.13±3.46 | 0.015 |
| | Lateral E/E' | 10.13±3.50 | 8.14±3.30 | 0.011 |
| Grades of Left Ventricular (LV) diastolic dysfunction | Normal diastolic function | 8 (20) | 18 (45) | 0.017 |
| | Grade 1 diastolic dysfunction | 3 (7.5) | 5 (12.5) | |
| | Grade 2 diastolic dysfunction | 25 (62.5) | 17 (42.5) | |
| | Grade 3 diastolic dysfunction | 4 (10) | 0 | |

**[Table/Fig-4]:** Left Ventricular (LV) systolic and diastolic function.

Mitral E/A ratio (1.50±0.467 versus 1.24±0.333, p-value=0.005), septal E/E' (10.14±3.75 versus 8.13±3.46, p-value=0.015), and lateral E/E' (10.13±3.50 versus 8.14±3.30, p-value=0.011) were all significantly higher in EOPE, indicating greater LV filling pressures. Overall, 80% of EOPE versus 55% of LOPE women demonstrated some degree of diastolic dysfunction (p-value=0.017).

**Right Ventricular (RV) function:** [Table/Fig-5] presents RV parameters. Right Ventricular Systolic Pressure (RVSP) was marginally higher in LOPE compared with EOPE, without statistical significance (p=0.530). Tricuspid annular plane systolic excursion (TAPSE), an indicator of RV longitudinal systolic function, was significantly lower in EOPE than in LOPE (p-value <0.001), indicating RV systolic dysfunction in women with EOPE.

**Perinatal outcomes:** [Table/Fig-6] presents perinatal outcomes. Mean birth weight was significantly lower in EOPE (1398.52±423.04 g versus 2636.85±281.07 g, p-value <0.0001). Extreme low birth weight (<1000 g) and very low birth weight (1000-1499 g) neonates were found only in the EOPE group. Low birth weight (1500-2499 g) was significantly more common in EOPE (40%) than LOPE (22.5%). NICU admission was significantly higher in EOPE (60%) compared with LOPE (25%, p-value=0.002).

| Parameter | EOPE (n=40) Mean±SD | LOPE (n=40) Mean±SD | p-value |
|---|---|---|---|
| RVSP (mmHg) | 27.5±7.39 | 28.5±6.75 | 0.530 |
| TAPSE (cm) | 2.11±0.286 | 2.45±0.523 | <0.001 |

**[Table/Fig-5]:** Right Ventricular (RV) function.

| Parameter | EOPE (n=40) | LOPE (n=40) | p-value |
|---|---|---|---|
| Mean birth weight±SD (g) | 1398.52±423.04 | 2636.85±281.07 | <0.0001 |
| ELBW (<1000 g) | 7 (17.5) | 0 | - |
| VLBW (1000–1499 g) | 17 (42.5) | 0 | |
| LBW (1500–2499 g) | 16 (40) | 9 (22.5) | |
| Normal birth weight (≥2500 g) | 0 | 31 (77.5) | |
| NICU admission | 24 (60) | 10 (25) | 0.002 |

**[Table/Fig-6]:** Perinatal outcomes.
LBW: Low birth weight; VLBW: Very low birth weight; ELBW: Extreme low birth weight; NICU: Neonatal intensive care unit.

## DISCUSSION

Preeclampsia is a serious multisystem disorder and a major risk factor for maternal and neonatal complications including placental abruption, intrauterine growth restriction, and perinatal mortality. EOPE is associated with a ten-fold increase in perinatal mortality compared with LOPE [3,4]. The underlying pathophysiology of EOPE is more severe and complex, being predominantly related to placental insufficiency, whereas LOPE is more commonly associated with maternal constitutional factors such as obesity and metabolic syndrome [4,5].

Several studies have confirmed abnormalities in biventricular systolic and diastolic function and in cardiac chamber geometry in preeclampsia, with these changes being consistently more pronounced in EOPE compared with LOPE [3,8,12]. Furthermore, these cardiac changes have been shown to persist into the postpartum period, representing a risk factor for premature cardiovascular sequelae [5]. A recent meta-analysis by Inversetti A et al., reported that women with a prior history of preeclampsia carry a more than two-fold increased risk of stroke (ES 1.75, 95% CI 1.52-2.02), a 2.5-fold increased risk of heart failure (ES 2.47, 95% CI 1.89-3.22), and a two-fold increased risk of cardiovascular death (ES 2.04, 95% CI 1.76-2.38) compared with women without preeclampsia [7]. These findings underscore the importance of early identification and close cardiovascular surveillance of women with preeclampsia, particularly those with early onset disease.

In the present study, MAP was comparatively higher in the EOPE group than in the LOPE group, and CO was lower in EOPE due to reduced intravascular volume, whereas it was high to normal in LOPE. These findings are consistent with the haemodynamic phenotypes described by Valensise H et al., and are in agreement with the findings of Vaddamani S et al., who similarly reported higher MAP (117.4±6.94 mmHg in EOPE versus 113.3±8.73 mmHg in LOPE, p-value=0.013) and lower CO in EOPE [4,8]. RWT was significantly higher in EOPE (0.53±0.18 versus 0.45±0.12, p-value=0.026), indicating early preclinical ventricular geometric alteration in this group. This is consistent with study demonstrating higher RWT in EOPE at 24 weeks of gestation, reflecting adverse LV remodelling in placenta-mediated disease [13].

The present study found significantly higher mitral E/A ratio and E/E' values in EOPE compared with LOPE (p-value=0.005, 0.015, and 0.011 respectively), consistent with the findings of Vaddamani S et al., (E/A 1.5 versus 1.3, p-value=0.03; E/E' 9.9 versus 8.13, p-value=0.015) [9]. Elevated E/A and E/E' ratios indicate increased LV filling pressure. Overall diastolic dysfunction was observed in 80% of EOPE versus 55% of LOPE women (p-value=0.017) in the present study, a finding comparable to Vaddamani S et al., (78% in EOPE and 56% in LOPE, p-value=0.06) [8] and consistent with a recent Indian study by Pillai AA et al., confirming higher rates

of diastolic dysfunction in EOPE using both 2009 and 2016 ASE criteria [12]. Impaired diastolic function has been posited as the earliest echocardiographic manifestation of cardiac involvement in preeclampsia, preceding other chamber-level changes [3].

The LV systolic dysfunction was significantly more common in EOPE, with combined mild, mild, and moderate impairment present in 42.5% of EOPE versus 20% of LOPE women (p-value=0.03), in agreement with Vaddamani S et al., (40% versus 22%, p-value=0.009) [8]. These findings are further supported by Paudel A et al., who demonstrated significantly lower LV global longitudinal strain in preeclamptic women (-18.0±2.6% versus -19.8±2.1%, p-value=0.001) despite preserved LVEF, suggesting that subclinical LV systolic dysfunction may be underestimated by LVEF alone [14].

The present study also demonstrated a significant difference in RV function between the two subtypes. TAPSE was significantly lower in EOPE (2.11±0.286 cm) compared with LOPE (2.45±0.523 cm, p-value <0.001), comparable to the findings of Vaddamani S et al., (TAPSE 2.184 cm in EOPE versus 2.504 cm in LOPE, p-value=0.003) [8]. RV systolic dysfunction in preeclampsia is believed to arise from pressure overload secondary to decompensated LV dysfunction, leading to RV remodelling and elevated pulmonary arterial pressures, thereby progressively impairing contractility. A recent cross-sectional study by Alimi H et al., similarly demonstrated significantly reduced RV fractional area change and RV strain indices in preeclamptic women compared with normotensive pregnant controls [15]. RV dysfunction therefore has important prognostic significance and is predominantly observed in severe EOPE [3,8].

Perinatal outcomes were significantly worse in EOPE, with substantially lower mean birth weight, a high prevalence of extreme and very low birth weight neonates exclusive to the EOPE group, and significantly higher NICU admission rates (60% versus 25%, p-value=0.002). These findings reflect the greater severity of placental insufficiency in EOPE and are consistent with the published literature [4,8].

Taken together, the present study demonstrated that EOPE and LOPE represent distinct cardiovascular phenotypes, with EOPE being associated with significantly greater impairment of biventricular systolic and diastolic function, adverse LV geometry, higher TVR, and worse perinatal outcomes. Echocardiography performed during the antenatal period is a valuable, non-invasive tool for characterising cardiac involvement in preeclampsia and stratifying cardiovascular risk. Women identified with diastolic dysfunction or biventricular impairment during pregnancy should be referred for long-term cardiovascular follow-up given the evidence of persistent postpartum cardiac changes and substantially elevated long-term cardiovascular risk.

### Limitation(s)

The present study had several limitations. First, the sample size of 80 women was relatively small, limiting the power to detect smaller differences between subgroups and to perform multivariate analysis adjusting for potential confounders such as BMI, gestational age at echocardiography, and severity of hypertension. Second, as an observational study, temporal relationships between haemodynamic changes and clinical outcomes cannot be established. Third, echocardiography was performed at a single time point during the antenatal period; serial assessments and postpartum follow-up would provide greater insight into the trajectory of cardiac changes. Lastly, the study was conducted at a single tertiary centre in Arunachal Pradesh, and findings may not be generalisable to all populations.

Future prospective multicentre studies with larger sample sizes and longitudinal follow-up, incorporating speckle tracking echocardiography, are warranted.

## CONCLUSION(S)

Women with EOPE demonstrated significantly higher TVR and more pronounced echocardiographic abnormalities- including greater LV diastolic dysfunction, impaired biventricular myocardial contractility, increased relative LV wall thickness, and reduced TAPSE- compared with women with LOPE. EOPE is therefore associated with a more severe form of cardiovascular impairment than LOPE. Echocardiography performed during the antenatal period is a valuable non-invasive tool to identify this high-risk subset of preeclamptic women, enabling timely patient-specific cardiovascular management and long-term surveillance for premature cardiovascular disease.

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**PARTICULARS OF CONTRIBUTORS:**
1. Associate Professor, Department of Obstetrics and Gynaecology, Tomo Riba Institute of Health and Medical Sciences, Naharlagun, Arunachal Pradesh, India.
2. Assistant Professor, Department of Obstetrics and Gynaecology, Tomo Riba Institute of Health and Medical Sciences, Naharlagun, Arunachal Pradesh, India.
3. Professor, Department of Cardiology, Tomo Riba Institute of Health and Medical Sciences, Naharlagun, Arunachal Pradesh, India.
4. Final Year DNB Student, Department of Obstetrics and Gynaecology, Tomo Riba Institute of Health and Medical Sciences, Naharlagun, Arunachal Pradesh, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Goter Doke,
Associate Professor, Department of Obstetrics and Gynaecology, Tomo Riba Institute of Health and Medical Sciences, Naharlagun-791110, Arunachal Pradesh, India.
E-mail: dokegoter@gmail.com

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