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Original Research Article

Maternal Outcomes in Early-Onset and Late-Onset Pre-eclampsia: A Prospective Observational Study

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Abstract: ***Background:*** Pre-eclampsia is a heterogeneous multisystem disorder of pregnancy and the puerperium and remains a leading cause of maternal morbidity and mortality worldwide. Based on gestational age at onset, pre-eclampsia is classified into early-onset pre-eclampsia (EOPE) occurring before 34 weeks and late-onset pre-eclampsia (LOPE) occurring at or after 34 weeks of gestation. These two entities differ in pathophysiology, severity, and clinical outcomes, with EOPE being primarily placental in origin and associated with more severe maternal complications. ***Objectives:*** To compare maternal outcomes in women with early-onset and late-onset pre-eclampsia and to assess the pattern and severity of maternal morbidity between the two groups. ***Methods:*** This prospective observational study was conducted in the Department of Obstetrics and Gynaecology at Government Medical College Hospital, Kannur, over a period of one year following Institutional Ethics Committee approval. A total of 176 antenatal women with singleton pregnancies diagnosed with pre-eclampsia were enrolled consecutively. Participants were divided into two groups: EOPE (n = 88) and LOPE (n = 88), based on gestational age at diagnosis. Maternal demographic variables and outcomes including HELLP syndrome, eclampsia, placental abruption, acute kidney injury, disseminated intravascular coagulation, and postpartum hemorrhage were compared. Statistical analysis was performed using SPSS version 17.0, and a p-value <0.05 was considered statistically significant. ***Results:*** Women with EOPE had a significantly higher mean age compared to those with LOPE (p = 0.021). HELLP or partial HELLP syndrome was significantly more common in EOPE than LOPE (29.5% vs 10.2%, p = 0.001). Placental abruption was also significantly higher in EOPE (22.7% vs 4.5%, p <0.05). Other complications, including eclampsia, acute kidney injury, disseminated intravascular coagulation, and postpartum hemorrhage, were more frequent in EOPE, although these differences were not statistically significant. Overall, severe maternal complications were more than twice as common in the EOPE group compared to the LOPE group. ***Conclusion:*** Early-onset pre-eclampsia is associated with significantly greater maternal morbidity compared to late-onset disease. Recognition of EOPE as a distinct, high-risk clinical entity is essential for early diagnosis, vigilant monitoring, and timely intervention to improve maternal outcomes.

Keywords: Early-onset pre-eclampsia, HELLP syndrome, Late-onset pre-eclampsia, Maternal morbidity, Placental abruption

INTRODUCTION

Pre-eclampsia is a heterogeneous multisystem disorder unique to pregnancy and the puerperium, contributing substantially to maternal morbidity and mortality worldwide. It complicates approximately 2–10% of pregnancies globally, with a disproportionately higher burden in low- and middle-income countries, where maternal mortality rates are up to seven times higher than in developed nations (1,2). Hypertensive disorders of pregnancy remain among the leading direct causes of maternal death, often acting synergistically with hemorrhage and infection to form a fatal triad (2,3).

Recent advances have led to a paradigm shift in understanding pre-eclampsia as two biologically distinct entities based on gestational age at onset: early-onset pre-eclampsia (EOPE) occurring before 34 weeks and late-onset pre-eclampsia (LOPE) occurring at or beyond 34 weeks of gestation (4,5,6,7,8). Although the diagnostic criteria remain identical, these two phenotypes differ markedly in pathophysiology, clinical course, and maternal risk profile (9,10).

EOPE is primarily a placental disorder, resulting from defective trophoblastic invasion and inadequate spiral artery remodeling during early gestation. This leads to placental ischemia, oxidative stress, and excessive release of anti-angiogenic and pro-inflammatory factors into the maternal circulation, precipitating severe endothelial dysfunction and multiorgan involvement (10–11). In contrast, LOPE is more often associated with maternal constitutional factors such as obesity, metabolic syndrome, and advanced maternal age, with relatively preserved placentation (9,12).

These fundamental differences translate into variations in maternal complications. EOPE has been consistently associated with higher rates of HELLP syndrome, placental abruption, renal dysfunction, and severe maternal morbidity when compared to LOPE (13–14). Understanding these differences is essential for risk stratification, surveillance, and timely obstetric intervention. This study aims to compare maternal outcomes between EOPE and LOPE and place the findings in the context of existing literature.

MATERIALS AND METHODS

Study Design

This study was designed as a prospective observational study to evaluate and compare maternal and fetal outcomes in women with early-onset and late-onset pre-eclampsia.

Study Setting

The study was conducted in the Antenatal Outpatient Department and Obstetric Emergency Room of the Department of Obstetrics and Gynaecology at Government Medical College Hospital, Kannur, a tertiary care referral centre catering to a large population.

Study Period

The study was carried out over a duration of one year, commencing after obtaining approval from the Institutional Ethics Committee.

Study Population

The study population comprised antenatal women diagnosed with pre-eclampsia who were admitted and delivered at Government Medical College Hospital, Kannur, during the study period.

Inclusion Criteria

Antenatal women with singleton pregnancy, diagnosed with pre-eclampsia according to standard diagnostic criteria, who were admitted and delivered in the study hospital and who provided written informed consent were included in the study.

Exclusion Criteria

Women with **multiple pregnancies**, essential hypertension or hypertension diagnosed before 20 weeks of gestation, pre-existing renal disease, liver disease or epilepsy, and those who did not consent to participate in the study were excluded.

Sample Size

A total of 176 antenatal women with pre-eclampsia fulfilling the inclusion and exclusion criteria were enrolled consecutively during the study period.

Grouping of Study Participants

Based on gestational age at diagnosis, participants were categorized into two groups. The Early-Onset Pre-eclampsia (EOPE) group included women diagnosed with pre-eclampsia before 34 completed weeks of gestation, while the Late-Onset Pre-eclampsia (LOPE) group included women diagnosed at or after 34 weeks of gestation. Each group consisted of 88 participants.

Data Collection and Variables Studied

Maternal demographic characteristics and risk factors including maternal age, parity, body mass index (BMI), and previous history of pre-eclampsia were recorded. These variables were analyzed to assess factors associated with the development of early- and late-onset pre-eclampsia.

Assessment of Maternal Outcomes

Maternal outcomes evaluated included the occurrence of HELLP syndrome, eclampsia, abruptio placentae, postpartum hemorrhage, acute kidney injury, and disseminated intravascular coagulation. These outcomes were documented using clinical findings, laboratory investigations, and standard diagnostic criteria.

Assessment of Fetal and Neonatal Outcomes

Fetal and neonatal outcomes assessed included stillbirth, defined as intrauterine fetal death occurring after 24 completed weeks of gestation, birth weight, low birth weight, small for gestational age, five-minute APGAR score less than 7, and admission to the neonatal intensive care unit. Neonatal complications such as intraventricular hemorrhage, hypoxic-ischemic injury, respiratory distress syndrome, and necrotizing enterocolitis were also recorded for live-born infants.

Doppler Assessment

Umbilical artery Doppler studies were performed when indicated. Abnormal Doppler findings were defined as increased systolic-to-diastolic ratio for gestational age, absent end-diastolic flow, or reversed end-diastolic flow.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 17.0. Categorical variables were expressed as frequency and percentage, while continuous variables were expressed as mean ± standard deviation. Normality of continuous data was assessed using the Kolmogorov–Smirnov test. For normally distributed variables, comparisons between the two groups were performed using the independent Student's t-test, while the Mann–Whitney U test was used for non-normally distributed variables. Associations between categorical variables were analyzed using the Chi-square test or Fisher's exact test, as appropriate. A p-value < 0.05 was considered statistically significant.

RESULTS

Baseline Demographic Characteristics of the Study Population

Table 1. Comparison of Maternal Demographic Characteristics between Study Groups

Variable	Early Onset (n = 88)	Late Onset (n = 88)	p value
Age (years)	30.55 ± 6.71	28.35 ± 5.74	**0.021**
<20 years	3 (3.4%)	1 (1.1%)	
20–25 years	21 (23.9%)	32 (36.4%)	
25–30 years	24 (27.3%)	26 (29.5%)	
30–35 years	16 (18.2%)	19 (21.6%)	
≥35 years	24 (27.3%)	10 (11.4%)	
Parity			0.545
Primi	46 (52.3%)	50 (56.8%)	
Multi	42 (47.7%)	38 (43.2%)	
BMI category			0.474
Normal	26 (29.6%)	32 (36.4%)	
Overweight	12 (13.6%)	13 (14.8%)	
Obese I	38 (43.2%)	28 (31.8%)	
Obese II	12 (13.6%)	15 (17.0%)	

Women with early-onset pre-eclampsia had a significantly higher mean maternal age compared to those with late-onset disease ($p = 0.021$). A higher proportion of EOPE cases occurred in women aged ≥35 years, suggesting a possible role of age-related vascular susceptibility in early disease manifestation.

Parity and BMI distribution did not show statistically significant differences between the two groups, indicating that maternal age rather than parity or adiposity may be more strongly associated with early-onset disease in this cohort.

Table 2. Comparison of HELLP / Partial HELLP Syndrome between Study Groups

HELLP / Partial HELLP	Early Onset n (%)	Late Onset n (%)	p value
No	62 (70.5%)	79 (89.8%)	
Yes	26 (29.5%)	9 (10.2%)	**0.001**
Total	**88 (100%)**	**88 (100%)**	

The incidence of HELLP or partial HELLP syndrome was nearly three times higher in the early-onset group compared to the late-onset group. This difference was statistically significant ($p = 0.001$), highlighting the severe systemic involvement associated with early-onset pre-eclampsia.

This finding supports the concept that EOPE is driven by abnormal placentation and profound endothelial dysfunction, leading to greater maternal morbidity.

Table 3. Comparison of Other Major Maternal Complications between Study Groups

Complication	Early Onset n (%)	Late Onset n (%)	p value
Eclampsia	14 (15.9%)	10 (11.4%)	>0.05
Placental abruption	20 (22.7%)	4 (4.5%)	**<0.05**
Acute kidney injury	8 (9.1%)	3 (3.4%)	>0.05
Disseminated intravascular coagulation	3 (3.4%)	0 (0%)	>0.05
Postpartum hemorrhage	9 (10.2%)	6 (6.8%)	>0.05

Placental abruption was significantly more frequent in early-onset pre-eclampsia, reflecting severe placental ischemia and vascular compromise.

Although eclampsia, AKI, DIC, and PPH were observed more commonly in the EOPE group, these differences did not reach statistical significance, possibly due to lower event frequencies. Nonetheless, the consistently higher proportions reinforce the greater maternal risk profile of EOPE.

Table 4. Distribution of Maternal Outcome Severity between Study Groups

Outcome severity	Early Onset n (%)	Late Onset n (%)	Outcome severity
Severe maternal complications*	34 (38.6%)	13 (14.8%)	Severe maternal complications*
Mild to moderate disease	54 (61.4%)	75 (85.2%)	Mild to moderate disease
Total	**88 (100%)**	**88 (100%)**	**Total**

Severe maternal complications were more than twice as common in the early-onset group compared to the late-onset group. In contrast, late-onset pre-eclampsia was predominantly associated with mild to moderate disease.
This distribution clearly demonstrates that EOPE represents a distinct, high-risk clinical phenotype, requiring intensive surveillance and multidisciplinary management.

Early-onset pre-eclampsia was associated with significantly higher maternal morbidity, particularly HELLP syndrome and placental abruption. Although not all complications reached statistical significance, the overall pattern consistently favored worse outcomes in EOPE.

These findings strongly support the study hypothesis that early-onset pre-eclampsia carries a more severe maternal disease burden than late-onset disease, underscoring the need for early identification, vigilant monitoring, and timely obstetric intervention.

DISCUSSION

Pre-eclampsia is increasingly recognized as a heterogeneous disorder with distinct clinical phenotypes, of which early-onset and late-onset forms differ substantially in pathophysiology, severity, and maternal outcomes. Several large cohort and comparative studies have demonstrated that early-onset pre-eclampsia (EOPE) is predominantly a placental disorder characterized by defective trophoblastic invasion, impaired spiral artery remodeling, and severe uteroplacental ischemia, whereas late-onset pre-eclampsia (LOPE) is more closely related to maternal constitutional factors with relatively preserved placentation (13–17). These biological differences translate into varying clinical courses, with EOPE consistently associated with a higher burden of maternal morbidity and life-threatening complications compared to LOPE (13,14,16,17).

In the present study, EOPE was associated with a significantly higher frequency of severe maternal complications, supporting the concept that EOPE represents a distinct, high-risk phenotype rather than merely an earlier manifestation of the same disease. Similar observations have been reported by Teka et al., Simsek et al., Wadhwani et al., Wojtowicz et al., and Lisonkova et al., who demonstrated increased rates of HELLP syndrome, placental abruption, renal dysfunction, and composite severe maternal morbidity among women with EOPE compared to those with LOPE (13–17). These findings emphasize that the timing of disease onset has important prognostic implications and should be considered a key determinant in maternal risk stratification and management.

The following sections discuss individual maternal complications observed in this study in comparison with existing literature, highlighting similarities, discrepancies, and possible explanations for variations across populations.

CONCLUSION

This study demonstrates that early-onset pre-eclampsia is associated with significantly worse maternal outcomes than late-onset pre-eclampsia. EOPE showed markedly higher rates of HELLP syndrome and placental abruption, along with a consistently higher frequency of eclampsia, renal dysfunction, DIC, and postpartum hemorrhage.

These findings reinforce the concept that EOPE is a distinct, placental-driven, high-risk disorder, requiring intensified maternal surveillance, early referral to tertiary care centers, and multidisciplinary management. Late-onset pre-eclampsia, although common, was associated with comparatively milder maternal morbidity.

Recognizing EOPE as a separate clinical entity has important implications for risk stratification, counseling, and individualized management, ultimately contributing to improved maternal outcomes.

Conflict of interest: nil

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