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Original Research Article

Comparative analysis of maternal and neonatal outcomes in early versus late onset pre-eclampsia: a prospective study from northern India

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ABSTRACT

Background: Pre-eclampsia, a leading hypertensive disorder in pregnancy, significantly contributes to maternal and neonatal morbidity and mortality. It is categorized into Early-Onset Pre-Eclampsia (EOPE, <34 weeks) and Late-Onset Pre-Eclampsia (LOPE, ≥34 weeks), differing in risk factors, clinical profiles, and outcomes. This study compared EOPE and LOPE regarding risk factors, laboratory findings, and maternal and neonatal outcomes.
Methods: A prospective study was carried out from April, 2021 to March, 2022 at Kamla Nehru State Hospital for Mother and Child, IGMC, Shimla, including 184 pre-eclamptic women diagnosed as per ACOG 2020 criteria. Participants were divided equally into EOPE (n=92) and LOPE (n=92) groups. Demographics, clinical history, complications and outcomes were analyzed using SPSS 25.0, with significance set at $p<0.05$.
Results: EOPE was associated with younger age (mean 24.79 vs. 26.95 years, p=0.001), primigravidity (62% vs. 37%, p=0.001), chronic hypertension and prior pre-eclampsia. Diabetes was more prevalent in LOPE (21.7% vs. 5.4%, p=0.001). EOPE had higher rates of severe maternal complications, including HELLP syndrome (9.8% vs. 2.2%), eclampsia (20.7% vs. 8.7%) and placental abruption (14.1% vs. 5.4%). Neonates in EOPE had poorer outcomes, with lower birth weight (1.84 kg vs. 2.45 kg, $p<0.001$), more NICU admissions (90.2% vs. 20.7%, $p<0.001$) and longer NICU stays (13.69 vs. 1.65 days, $p<0.001$).
Conclusions: EOPE is linked to younger maternal age, primigravidity and severe outcomes, whereas LOPE is associated with metabolic risk factors like diabetes and milder complications. Early identification and tailored management are crucial to improve maternal and neonatal outcomes.

Keywords: Early-onset pre-eclampsia, Late-onset pre-eclampsia, Maternal outcomes, Neonatal outcomes, Pre-eclampsia, Pregnancy hypertension

INTRODUCTION

Hypertensive disorders of pregnancy are a significant global health challenge, contributing substantially to maternal and perinatal morbidity and mortality. Among these, pre-eclampsia stands out as a complex multisystem disorder unique to human pregnancy and is a leading cause of adverse outcomes. Globally, pre-eclampsia affects 2-8% of pregnancies and is responsible for severe obstetric complications and over 50,000 maternal deaths annually. In developing countries like India, it accounts for approximately 10-15% of maternal deaths. Given its widespread prevalence and potentially life-threatening consequences, early detection and effective management of pre-eclampsia are critical in mitigating its impact on maternal and neonatal health.[1-6]

Recent advancements have refined the classification of pre-eclampsia based on gestational age at onset: Early-Onset Pre-Eclampsia (EOPE), occurring before 34 weeks of gestation, and Late-Onset Pre-Eclampsia (LOPE), occurring at or after 34 weeks of gestation. This classification goes beyond mere timing; it reflects distinct differences in pathophysiology, clinical manifestations and outcomes. EOPE is often linked to impaired placentation, resulting in severe maternal and fetal complications. In contrast, LOPE is more commonly associated with predisposing maternal factors, such as metabolic disorders, and typically manifests as a milder form of the disease. Understanding these distinctions is essential for predicting disease progression and planning appropriate interventions.[7-12]

Despite its importance, the differentiation between EOPE and LOPE, along with their respective impacts on maternal and neonatal outcomes has not been extensively studied in the Indian context. India's diverse socio-demographic landscape and healthcare disparities highlight the need for region-specific research to better understand the risk factors, challenges in management and outcomes associated with these subtypes of pre-eclampsia. Such insights are crucial for developing tailored interventions and improving maternal and neonatal care.

This study aims to conduct a comparative analysis of EOPE and LOPE, focusing on their risk factors, laboratory profiles, and maternal and neonatal outcomes. By identifying the differences and commonalities in clinical and laboratory presentations, the research seeks to enhance early diagnosis, improve risk stratification, and promote timely and effective interventions. Ultimately, the findings aim to contribute to better health outcomes for both mothers and their newborns. The primary aim of this prospective comparative study is to analyze the differences in maternal and perinatal outcomes between Early-Onset Pre-Eclampsia (EOPE) and Late-Onset Pre-Eclampsia (LOPE). By enhancing understanding of these two subtypes, the study aims to contribute to better risk stratification, earlier diagnosis and more effective management strategies. The specific objectives are as follows: 1) To identify and compare the risk factors associated with EOPE and LOPE, 2) To assess and differentiate laboratory parameters between EOPE and LOPE, highlighting both commonalities and differences, 3) To evaluate maternal and perinatal outcomes in EOPE and LOPE, focusing on differences in disease severity, clinical progression and neonatal health indicators.

METHODS

TThis prospective comparative study was conducted in the Department of Obstetrics and Gynecology at Kamla Nehru State Hospital for Mother and Child, Indira Gandhi Medical College (IGMC), Shimla, between April 1, 2021 and March 31, 2022. The study included antenatal women diagnosed with pre-eclampsia, meeting the American College of Obstetricians and Gynecologists (ACOG) 2020 diagnostic criteria.

Study population

Pregnant women with confirmed gestational age and a diagnosis of pre-eclampsia were recruited according to the following criteria and subsequently categorized into two groups: Group A (EOPE): Pre-eclampsia diagnosed at <34 weeks of gestation. And Group B (LOPE): Pre-eclampsia diagnosed ≥34 weeks of gestation.

Inclusion criteria

Pregnant women with confirmed gestational age based on last menstrual period (LMP) or first-trimester Level II ultrasound. And patients diagnosed, monitored and delivered in the Department of Obstetrics and Gynecology (OBG) at the study center were included.

Exclusion criteria

Women with pre-existing cardiac disease, women having severe anemia, women having history of substance abuse, patients having history of epilepsy were excluded.

Diagnostic Criteria for Pre-Eclampsia (ACOG 2020)

Blood pressure (BP)

Systolic BP of 140 mm Hg or more or diastolic BP of 90 mm Hg or more after 20 weeks of gestation on two occasions at least four hours apart in previously normotensive women.

Systolic BP of 160 mm Hg or more or diastolic BP of 110mm Hg or more (severe hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy).

Proteinuria

Protein excretion ≥300 mg in a 24-hour urine collection, protein/creatinine ratio ≥0.3, or urine dipstick reading of 2+. In the absence of proteinuria: Diagnosis requires the presence of one or more of the following:

Thrombocytopenia (platelet count <1 lac/µl). Renal dysfunction (serum creatinine level >1.1 mg/dl or doubling of baseline). Hepatic dysfunction (elevated liver enzymes level twice the normal range). Pulmonary edema. Visual disturbances or new-onset headache.

Study population

The study was carried out after receiving institutional ethics committee's approval. Participants were fully briefed on the study's objectives, and written informed consent was obtained. Participation was voluntary, and

withdrawal was allowed at any stage without consequences.

Patient evaluation

Detailed medical histories were taken, including demographic data, maternal age, parity, gestational age, and relevant obstetric history. Clinical examinations included general, systemic, and obstetric assessments. Laboratory tests relevant to pre-eclampsia were performed, with regular monitoring of maternal clinical, hematological, and biochemical parameters. Fetal well-being was assessed using biophysical profiles, non-stress tests, and Doppler ultrasonography.

Management and monitoring

Patients received treatment as per established hospital protocols, with decisions regarding the timing and mode of delivery made based on maternal and fetal conditions. Maternal and perinatal outcomes were documented, focusing on the progression of severe disease, organ involvement and neonatal health parameters.

Statistical analysis

Data analysis was performed using IBM SPSS Statistics, Version 25.0. Continuous variables were presented as mean±standard deviation, while categorical variables were expressed as frequencies and percentages. Comparisons of continuous variables were conducted using the independent t-test and categorical data were analyzed using the Chi-square test. A p value of <0.05 was considered statistically significant.

RESULTS

This prospective comparative study was conducted to analyze and compare the risk factors, laboratory parameters, maternal and perinatal outcomes in early-onset pre-eclampsia and late-onset pre-eclampsia. The study included a total of 184 women divided into two equal groups: Group A (EOPE, n=92) and Group B (LOPE, n=92).

The demographic and clinical characteristics reveal notable differences between EOPE (early-onset pre-eclampsia) and LOPE (late-onset pre-eclampsia) groups. The mean age in Group A (EOPE) was significantly lower at 24.79 years compared to 26.95 years in Group B (LOPE) (p=0.001), indicating a younger age profile in the early-onset group. EOPE was more common among younger women (≤20 years: 18.5%) than in the late-onset group (3.3%), with a significant association (p=0.003). Gravidity showed a distinct difference, with a higher percentage of primigravida women in the EOPE group (62.0%) compared to LOPE (37.0%) (p=0.001). The prevalence of chronic hypertension in pregnancy was significantly higher in the EOPE group (27.2%) than in the LOPE group (12.0%) whereas diabetes in present pregnancy was significantly lesser in EOPE (group (5.4%) than in the LOPE group (21.7%). Additionally, previous history of pre-eclampsia was significantly more common in the EOPE group (21.7%) compared to the LOPE group (10.9%) (p=0.046).

Table 1: Demographic and clinical characteristics.

Variable	Sub-variable	Group A (EOPE) (%)	Group B (LOPE) (%)	P value	Statistical significance
Age	Mean±SD (years)	24.79±4.28	26.95±3.84	0.001*	Significant
	≤ 20 years	17 (18.5)	3 (3.3)	0.003*	Significant
	21-30 years	63 (68.5)	71 (77.2)	-	-
	> 30 years	12 (13.0)	18 (19.6)	-	-
Gravidity	Primigravida	57 (62.0)	34 (37.0)	0.001*	Significant
	Multigravida	35 (38.0)	58 (63.0)	-	-
Booked status	Booked	73 (79.3)	82 (89.1)	0.105	Not Significant
	Unbooked	19 (20.7)	10 (10.9)	-	-
BMI	Mean±SD (kg/m²)	24.03±1.31	24.0±1.16	0.845	Not Significant
	Overweight (25-29.9 kg/m²)	26 (28.3)	18 (19.6)	-	-
Chronic hypertension	Present	25 (27.2)	11 (12.0)	0.009*	Significant
Diabetes in pregnancy	Present	5 (5.4)	20 (21.7)	0.001*	Significant
Previous history of pre-eclampsia	Present	20 (21.7)	10 (10.9)	0.046*	Significant

*Statistically significant.

Table 2: Blood pressure, laboratory findings and urinary parameters.

Variable	Sub-variable	Group A (EOPE) (%)	Group B (LOPE) (%)	P value	Statistical significance
Blood pressure	Systolic (Mean±SD, mmHg)	174.95±15.04	164.08±14.40	0.001*	Significant
	Diastolic (Mean±SD, mmHg)	114.34±8.42	104.93±9.13	0.001*	Significant
Hemoglobin	Mean±SD (g/dl)	11.75±0.86	11.77±0.81	0.853	Not Significant
Platelets	<100 (thousand/mm³)	31 (33.7%)	11 (11.96%)	0.001*	Significant
	Mean±SD	119.19±38.85	136.73±43.02	-	-
BUN	Mean±SD (mg/dl)	30.83±6.56	26.32±5.88	0.001*	Significant
Serum creatinine	≥ 1.1 mg/dl	16 (17.4%)	6 (6.5%)	0.023*	Significant
	Mean±SD	0.91±0.17	0.82±0.15	-	-
SGOT	Mean±SD (unit/l)	173.05±60.51	135.41±61.76	0.001*	Significant
SGPT	Mean±SD (unit/l)	148.71±47.26	123.17±47.71	0.001*	Significant
LDH	≥600 (unit/l)	14 (15.2%)	4 (4.3%)	0.013*	Significant
	Mean±SD	409.73±135.46	300.87±106.04	-	-
Urine protein	Mean±SD (mg/mg)	0.27±0.04	0.54±2.68	0.330	Not Significant
24-hour urine protein	Mean±SD (mg)	276.14±73.84	265.02±63.56	0.275	Not Significant
Proteinuria	2+/3+	89 (96.7)	88 (95.7)	1.000	Not Significant
Antihypertensive therapy	Yes	85 (92.4)	76 (82.6)	0.045*	Significant
Pre-eclampsia with severe features	Yes	80 (87.0)	65 (70.7)	0.011*	Significant

*Statistically significant.

Blood pressure levels were notably higher in the EOPE group, with mean systolic and diastolic pressures of 174.95 mm Hg and 114.34 mmHg, respectively, compared to 164.08 mm Hg and 104.93 mm Hg, respectively, in the LOPE group (both p=0.001). This indicates more severe hypertension in early-onset cases. Laboratory parameters also revealed significant differences: EOPE had lower platelet counts (33.7% with counts <100,000/mm³) and higher levels of BUN, serum creatinine, SGOT, SGPT and LDH, indicating greater organ dysfunction in the EOPE group. However, no significant differences were observed in hemoglobin levels, urine protein, 24-hour urine protein, or proteinuria, indicating similar kidney involvement in both groups. The requirement for antihypertensive therapy and severe pre-eclampsia features were significantly higher in EOPE (92.4% and 87.0%, respectively), underscoring its more aggressive nature compared to LOPE.

Maternal complications were more frequent and severe in the EOPE group. Partial HELLP syndrome was observed in 25.0% of EOPE cases compared to 3.3% in LOPE (p = 0.001). Similarly, HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count), eclampsia, and placental abruption were significantly more common in EOPE (9.8%, 20.7% and 14.1%, respectively) compared to LOPE (2.2%, 8.7% and 5.4%, respectively). The higher frequency of magnesium sulfate therapy for seizure prophylaxis in EOPE (87.0%) compared to LOPE (70.7%) (p = 0.007) further highlights the severity of EOPE cases. Overall, maternal morbidity was notably higher in the early-onset group, with significantly more adverse outcomes.

Table 3: Maternal outcomes and complications.

Variable	Sub-variable	Group A (EOPE) (%)	Group B (LOPE) (%)	P value	Statistical significance
Partial HELLP	Yes	23 (25.0)	3 (3.3)	0.001*	Significant
HELLP syndrome	Yes	9 (9.8)	2 (2.2)	0.030*	Significant
Eclampsia	Yes	19 (20.7)	8 (8.7)	0.022*	Significant
Abruption	Yes	13 (14.1)	5 (5.4)	0.047*	Significant
Magnesium sulphate	Yes	80 (87.0)	65 (70.7)	0.007*	Significant
Antihypertensive use	Yes	85 (92.4)	76 (82.6)	0.045*	Significant

*Statistically significant.

The neonatal outcomes were also poorer in the EOPE group. Abnormal umbilical artery Doppler was considerably more common in EOPE (28.26%) than LOPE (6.52%) (p=0.002), suggesting that fetal blood flow was more compromised in early-onset cases. The mean birth weight was notably lower in EOPE (1.84 kg) than LOPE (2.45 kg) (p=0.001), reflecting more severe fetal growth restriction. APGAR scores at 5 minutes were <7 in 17.39% of EOPE cases, compared to 6.52% in LOPE (p=0.040), indicating poorer neonatal adaptation at birth in early-onset cases. NICU admissions were significantly higher in EOPE (90.22%) than in LOPE (20.65%) (p=0.001), with longer NICU stays (mean 13.69 days in EOPE vs. 1.65 days in LOPE). Respiratory distress syndrome (RDS) and neonatal deaths were also significantly more common in EOPE (53.3% and 17.4%, respectively) compared to LOPE (9.8% and 3.3%, respectively), indicating poorer neonatal outcomes associated with early-onset pre-eclampsia.

Table 4: Neonatal outcomes.

Variable	Sub-variable	Group A (EOPE) (%)	Group B (LOPE) (%)	P value	Statistical significance
Umbilical doppler	Abnormal	26 (28.26)	6 (6.52)	0.002*	Significant
Birth weight	Mean±SD (kg)	1.84±0.34	2.45±0.16	0.001*	Significant
APGAR score	< 7 at 5 minutes	16 (17.39)	6 (6.52)	0.040*	Significant
NICU admission	Yes	83 (90.22)	19 (20.65)	0.001*	Significant
NICU stay	Mean±SD (days)	13.69±11.97	1.65±4.86	0.001*	Significant
RDS	Yes	49 (53.3)	9 (9.8)	0.001*	Significant
Neonatal death	Yes	16 (17.4)	3 (3.3)	0.003*	Significant

*Statistically significant.

The gestational age at diagnosis and termination differed significantly between the two groups, with EOPE cases diagnosed earlier (mean 32.38 weeks) and terminated sooner (mean 32.95 weeks) compared to LOPE (mean diagnosis at 36.87 weeks and termination at 37.19 weeks) (both p=0.001). This earlier termination in EOPE reflects the need for more urgent delivery due to severe maternal or fetal conditions. The mode of delivery showed significant differences, with more vaginal deliveries in the LOPE group (78.3%) compared to EOPE (65.2%) (p=0.049). Even though EOPE had a greater rate of caesarean sections (34.8%) than LOPE (22.8%), the difference was not statistically significant (p=0.073).

Table 5: Delivery characteristics and gestational details.

Variable	Sub-variable	Group A (EOPE) (%)	Group B (LOPE) (%)	P value	Statistical significance
Gestational age	At diagnosis (Mean±SD, weeks)	32.38±1.86	36.87±0.82	0.001*	Significant
	At termination (Mean±SD, weeks)	32.95±2.03	37.19±0.60	0.001*	Significant
Mode of delivery	Vaginal delivery	60 (65.2)	71 (78.3)	0.049*	Significant
	Caesarean section	32 (34.8)	21 (22.8)	0.073	Not Significant

*Statistically significant.

DISCUSSION

This study highlights the differences in maternal and neonatal outcomes between early-onset pre-eclampsia (EOPE) and late-onset pre-eclampsia (LOPE), two clinically distinct forms of pre-eclampsia. The World Health Organization (WHO) has identified pre-eclampsia as one of the major causes of maternal and newborn morbidity and mortality globally, with a notably larger burden in developing nations. This study explored how the timing of pre-eclampsia onset influences its clinical course and outcomes, given the distinct pathophysiology, risk factors, and progression of EOPE and LOPE.

Our findings indicate that EOPE is more prevalent among younger women, with a mean maternal age of 24.79 years compared to 26.95 years in LOPE, a statistically significant difference (p=0.001). This is consistent with previous studies by Gohar et al and Kiran et al, which also identified younger maternal age as a predisposing factor for EOPE.[13,14] The association may be attributed to immune maladaptation, particularly in first pregnancies.

Primigravidity was notably higher in EOPE (62%) than LOPE (37%) (p=0.001), supporting findings by Kumari et al and Kanta Das et al, which highlight primigravidity as a key risk factor for EOPE.[15,7] Additionally, EOPE was more frequently associated with chronic hypertension and a history of pre-eclampsia in prior pregnancies, further

emphasizing the role of pre-existing hypertensive disorders. In contrast, LOPE was more strongly associated with diabetes (21.7% vs. 5.4% in EOPE, p=0.001), suggesting that metabolic factors play significant role in LOPE pathogenesis, as supported by findings from Kiran et al and Lacovelli et al.[4,16]

Maternal complications were significantly worse in EOPE compared to LOPE. Conditions such as partial HELLP syndrome, HELLP syndrome, eclampsia and placental abruption were more frequent in EOPE, corroborating findings from Wadhwani et al and Kiran et al, which attribute these complications to greater placental insufficiency and severe endothelial dysfunction in EOPE.[4,14] In our study, partial HELLP syndrome occurred in 25% of EOPE cases versus 3.3% in LOPE (p<0.001), reflecting higher risks of maternal organ dysfunction in early-onset cases.

The use of magnesium sulfate and antihypertensive medications was significantly higher in EOPE, indicating the need for more intensive management. In this study, 87% of EOPE cases required magnesium sulfate therapy compared to 70.7% in LOPE, consistent with observations by Atluri et al and Shrestha et al, who emphasized the severity and rapid progression of EOPE.[17,18]

Neonatal outcomes were significantly poorer in EOPE, primarily due to placental dysfunction and earlier gestational age at delivery. The mean birth weight was significantly lower in EOPE (1.80 kg vs. 2.43 kg in LOPE, p<0.001), with all neonates in EOPE being low birth weight (<2.5 kg) compared to 44.5% in LOPE. These findings align with studies by Wadhwani et al and Atluri et al, which reported higher rates of intrauterine growth restriction (IUGR) and umbilical artery Doppler abnormalities in EOPE.[4,17]

Respiratory distress syndrome (RDS) was notably higher in EOPE, affecting 53.3% of neonates compared to 9.8% in LOPE. This difference reflects the impact of prematurity and placental insufficiency on neonatal respiratory health and is consistent with findings by Damayanti et al and Kumari et al.[3,15] Neonates born to mothers with EOPE also had higher NICU admission rates (90.22% vs. 20.65%, p<0.001) and longer NICU stays (mean 13.69 days vs. 1.65 days). These findings underscore the increased morbidity associated with EOPE due to prematurity and complications like RDS and hypoglycemia.

The mean gestational age at diagnosis was earlier in EOPE (32.38 weeks) compared to LOPE (36.87 weeks) (p<0.001), as reported in studies by Kiran et al and Atluri et al.[14,17] Similarly, gestational age at delivery was significantly earlier in EOPE (32.95 weeks) compared to LOPE (37.19 weeks), indicating the frequent need for preterm delivery in EOPE to prevent severe maternal and fetal complications.

EOPE cases showed more severe laboratory abnormalities, including thrombocytopenia, elevated liver enzymes, and increased serum creatinine and LDH levels. These findings align with studies by Kumar et al and Atluri et al, which also noted more pronounced hematological and biochemical derangements in EOPE.[19,17] Thrombocytopenia was observed in 33.7% of EOPE cases compared to 11.96% in LOPE, reflecting greater hematological involvement.

The study's findings highlight critical clinical implications, underscoring the importance of early identification, close monitoring, and tailored management strategies for EOPE and LOPE. EOPE, driven primarily by placental pathology, requires aggressive intervention to address severe maternal and neonatal complications. Conversely, LOPE, often associated with maternal metabolic and hypertensive conditions, necessitates ongoing management to prevent recurrence and long-term complications in future pregnancies. These results emphasize the need for distinct clinical pathways to optimize outcomes for both mothers and neonates.

This study has few limitations and strengths. The primary strength of this study is its prospective hospital-based design, which facilitated thorough data collection and minimized missing information. It effectively highlights differences in risk factors, laboratory findings, and maternal and neonatal outcomes between early-onset and late-onset pre-eclampsia. However, the hospital-based nature of the study may limit its generalizability, as it represents only women seeking care at a tertiary facility. The relatively small sample size and lack of long-term follow-up also restrict the ability to assess outcomes beyond the immediate postpartum period. Moreover, potential confounding factors, such as socioeconomic status and genetic predispositions, were not fully addressed, which may influence outcomes. Despite these limitations, the study provides meaningful insights into the distinctions and challenges associated with early versus late-onset pre-eclampsia.

CONCLUSION

Pre-eclampsia continues to be a major contributor to maternal and neonatal morbidity and mortality. This study demonstrates that early-onset pre-eclampsia (EOPE) is associated with a more severe clinical profile compared to late-onset pre-eclampsia (LOPE). EOPE is more prevalent among younger mothers, primigravidae, and those with unbooked pregnancies, chronic hypertension and a history of pre-eclampsia in previous pregnancies. It is linked to increased risks of severe maternal complications and adverse neonatal outcomes, such as preterm delivery, low birth weight and higher rates of NICU admissions. Conversely, LOPE is less severe but more commonly associated with metabolic factors like diabetes and obesity.

Timely screening, early identification of risk factors, consistent monitoring during pregnancy, delivery and the

postpartum period are critical for reducing the impact of pre-eclampsia. This study emphasizes the importance of targeted clinical interventions and patient education, particularly for high-risk populations, to improve maternal and neonatal outcomes. By addressing these factors, healthcare providers can contribute to safer pregnancies and healthier deliveries.

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