

## Original Research Article

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# Fetal and neonatal outcomes in early onset versus late onset pre-eclampsia-a comparative study

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## ABSTRACT

**Background:** Pre-eclampsia is typed as two different entities: early-onset preeclampsia occurring at less than 34 weeks of gestation, and late-onset occurring at 34 or more weeks of gestation. The aim of this study is to compare the fetal and neonatal outcomes in early versus late onset preeclampsia.

**Methods:** 208 patients diagnosed with pre-eclampsia in Shri Sathya Sai medical college and research institute over a period of three years (From January 2016 to January 2019) were retrospectively studied. Patients were classified as early onset and late onset pre-eclampsia based on the gestational age of onset. Data on fetal and neonatal outcomes were collected and analysed using Chi square and Fisher's test and compared.

**Results:** Early onset and late onset pre-eclampsia were 34.6% and 65.3%. The incidence of oligohydramnios, SGA, low APGAR at 5 minutes of birth were high in early onset type. 64.9% of early onset type required NICU admission whereas only 38.23% new born of mothers with late onset type required NICU admissions. 10.8% of babies of patients with early onset type were still born. The incidence of NICU admissions, requirement of respiratory support, duration of NICU stay were significantly high in early onset type.

**Conclusions:** Patients with early onset pre-eclampsia are found to have higher rates of specific fetal and neonatal morbidity when compared to the late onset type.

Prudent and close scrutinizing and follow up and delaying delivery in stable and appropriately selected patients with pre-eclampsia would be advantageous for neonates.

**Keywords:** Early onset, Fetal outcome, Late onset pre-eclampsia, Neonatal outcome

## INTRODUCTION

Hypertensive disorders complicate 5 to 10% of all pregnancies. Pre-eclampsia is present in 2 to 8% of women worldwide.<sup>1</sup> It is still a leading cause of maternal morbidity and mortality. Hypertensive disorders remain as the second direct cause for maternal death worldwide.<sup>2</sup>

They still remain one among the most significant and intriguing unsolved challenges in obstetrics.

Preeclampsia is a pregnancy condition which can affect any organ system and is being identified as two different entities: early-onset preeclampsia occurring at less than

34 weeks of gestation, and late-onset disease occurring at 34 or more weeks of gestation.<sup>3</sup>

The pathophysiology of the two diseases is also found to be different. A few publications have discussed the associated maternal morbidities, perinatal outcomes, clinical and laboratory features of both the pre-eclampsia types.<sup>4-6</sup> In general, in a population there is representation of both the forms with majority of them present with late onset type and few with early onset type.<sup>7</sup>

Although they may share some risk factors and overlapping presenting features, early-onset and late

onset pre-eclampsia are found to have different effects for the fetus and neonate.

However, the consequences of early-onset compared with late-onset preeclampsia on fetal and neonatal health have not been adequately quantified in South Indian population. Hence, we intended to carry out a study to examine and compare the risk factors and fetal and neonatal outcomes in early-onset vs late-onset preeclampsia. Also, this study will help to optimise the prognosis and management of both the types of pre-eclampsia. The aim of the present study was to compare the differences in fetal and neonatal outcomes in both the types of pre-eclampsia.

## METHODS

### Study type

The study type was retrospective observational study.

### Study place

The study carried out at Shri Sathya Sai medical college and research institute, Chennai.

### Study period

The study was carried out from January 2016 to January 2019.

### Selection criteria

#### Inclusion criteria

Patients with pre-eclampsia, eclampsia, any age, parity satisfying the criteria for pre-eclampsia, chronic hypertension with super imposed pre-eclampsia were included in the study.

#### Exclusion criteria

Women with pre-existing cardiac disease, pre-existing diabetes, pre-existing renal disease, pre-existing liver disease, chronic hypertension without proteinuria were excluded from the study.

### Definition of exposure

Blood pressure more than or equal to 140/90 mmHg after 20 weeks of gestation with proteinuria  $\geq 300$  mg/24 hours or  $\geq 1+$  in dipstick.<sup>8</sup>

Women with a diagnosis of preeclampsia (including eclampsia, superimposed pre-eclampsia) during any pregnancy visit or hospitalization in a tertiary care hospital were identified and studied retrospectively by analysis of case records and outpatient database over a period of 3 years (From January 2016 to January 2019).

Patients were classified as early onset and late onset pre-eclampsia based on the gestational age of onset.

Data on fetal and neonatal outcomes- incidence of umbilical artery Doppler abnormality, oligohydramnios, SGA, low 5 minutes APGAR, NICU admissions, duration of NICU stay, requirement of assisted ventilation, stillbirths, neonatal deaths were collected and analysed.

### Procedure

208 patients diagnosed with pre-eclampsia in Shri Sathya Sai medical college and research institute over a period of three years (From January 2016 to January 2019) were retrospectively studied. Patients were classified as early onset and late onset pre-eclampsia based on the gestational age of onset. Data on fetal and neonatal outcomes were collected and analysed using Chi square and Fisher's test and compared.

### Statistical analysis

The data collected was analysed using Chi square (using SPSS statistical tool) and Fisher's test and compared. The significance of difference in fetal and neonatal outcomes in early onset and late onset type was determined based on the calculation of p value. P value less than 0.05 was considered significant.

## RESULTS

The overall preeclampsia rate was 6.3%. Early onset and late onset were 34.6% and 65.4% respectively and the rate increased with increasing gestational age. In younger age group of patients (<30 years), late onset pre-eclampsia was more prevalent than early onset type (Table 1).

**Table 1: Demographic data.**

Risk factors	Early onset (%)	Late onset (%)
<b>Age (&lt;30 years)</b>	64 (34.78)	120 (65.21)
<b>Male fetus</b>	20 (17.85)	92 (82.14)
<b>Blood group (A positive)</b>	10 (50)	10 (50)

**Table 2: Demographic data according to age.**

Age (years)	No. of patients (total)	<34 weeks, n, (%)	$\geq 34$ weeks, n, (%)
<b>&lt;20</b>	16	4 (5.5)	12 (8.8)
<b>21-25</b>	80	28 (38)	52 (38.2)
<b>26-30</b>	88	32 (44.4)	56 (41.2)
<b>31-35</b>	20	4 (5.5)	16 (11.8)
<b>&gt;35</b>	4	4 (5.5)	0
<b>Total</b>	208	72	136

The presence of oligohydramnios, small for gestational age foetuses and low APGAR at 5 minutes of birth was significantly higher in early onset pre-eclampsia than late onset type (66.6% vs 33.3%) ( $p<0.05$ ) (Table 3). Adverse fetal and neonatal outcomes were more commonly associated with early onset than late onset type.

The rate of stillbirths was significantly higher in early onset compared to late onset type (10.8% vs 0.5%). Umbilical artery Doppler abnormality was significantly more in early onset type when compared to late onset type (28.2% vs 9.1%) (Table 3).

**Table 3: Fetal outcomes comparison between early and late onset pre-eclampsia.**

Variables	Early onset (%)	Late onset (%)	P value
<b>Oligohydramnios</b>	16 (66.7)	8 (33.3)	0.022
<b>SGA</b>	48 (66.7)	24 (33.3)	0.016
<b>5 min Apgar &lt;7</b>	24 (66.7)	12 (33.3)	0.031
<b>Still births</b>	8 (10.8)	1 (0.5)	0.029
<b>Umbilical artery Doppler abnormalities</b>	20 (28.2)	12 (9.1)	0.035

The requirement of respiratory support was more in early onset type than late onset type and the difference was found to be statistically significant (24.5% vs 2.4%). NICU admission (64.9% vs 38.23%) and duration of NICU stay was significantly higher in early onset type (Table 4). Neonatal deaths among babies of mothers with early onset preeclampsia was more than late onset type though not statistically significant ( $p=0.089$ ).

**Table 4: Neonatal outcomes comparison between early and late onset pre-eclampsia.**

Variables	Early onset pre-eclampsia	Late onset pre-eclampsia	P value
<b>NICU admission (%)</b>	47 (64.9)	52 (38.23)	0.036
<b>Duration of NICU stay (days)</b>	12.98±10.6	5.95±4.16	0.032
<b>Requirement of respiratory support (%)</b>	18 (24.5)	3 (2.4)	0.025
<b>Low birth weight (%)</b>	48 (66.7)	24 (33.3)	0.017
<b>Neonatal deaths</b>	10	5	0.089

## DISCUSSION

Present study has shown that there is an increase in pre-eclampsia rates and early onset pre-eclampsia has a significantly increased risk of severe fetal and neonatal

morbidity. Chronic hypertension is more strongly associated with early onset than late onset pre-eclampsia.<sup>9</sup>

Early onset pre-eclampsia poses a great challenge to treating clinicians in terms of need to balance the risk of perinatal and neonatal morbidity due to early delivery with the risk of worsening maternal condition associated with expectant management. Meta analyses have shown that expectant management is associated with lower incidence of neonatal morbidity with no significant difference in maternal outcomes.<sup>10</sup> Hence, early interventions for maternal reasons in early onset type could have led to significant fetal and neonatal morbidity in present study.

### Compared with previous studies in this topic

Lisonkova et al, conducted a population-based study in 2013 and concluded that the overall pre-eclampsia rate was 3.1% and the rates increased with increasing gestation whereas in present study the pre-eclampsia rate was 6.3%.<sup>9</sup>

Madazli et al, studied the perinatal outcomes comparison between the two groups in which the incidences of small-for-gestational age, oligohydramnios, Apgar score<7 at 5 min were significantly higher in women with early onset pre-eclampsia when compared with late onset pre-eclampsia ( $p<0.01$ ) which was the same in present study.<sup>11</sup>

Weitzner et al studied a positive correlation between gestational age at pre-eclampsia diagnosis and gestational age at delivery which is the same in our study.<sup>12</sup>

Lacobelli et al concluded that foetal and neonatal outcomes after adjustment for gestational age at delivery showed no difference between early- and late-onset preeclamptic women. In contrary, this study has shown a significant difference in various fetal and neonatal parameters.<sup>13</sup>

A study by Madazli et al has shown that the incidences of small-for-gestational age, oligohydramnios, Apgar score <7 at 5 min, stillbirth and early neonatal death rates were significantly higher in women with early onset type compared to late onset pre-eclampsia. In our study, there is no significant difference in the neonatal death rates in both the types whereas the other outcome parameters showed a similar result.<sup>14</sup>

Büyükeren et al concluded that the frequency of Small for gestational age foetuses was higher in the early-onset subgroup when compared to the late-onset preeclampsia group which is the same as our study.<sup>15</sup>

As this study is a retrospective analysis, it has its own limitations. Gestational age of onset of pre-eclampsia was determined based on hospital database records. This study was conducted in a tertiary care hospital. Hence

more population based larger studies are needed. The strength of the study is that it includes a cohort sample of specific geographic area which is representative of a regional population in which study on this area is sparse. The gestational age was based on time of onset rather than time of delivery. Present study has quantified the effect of early and late onset pre-eclampsia on fetal and neonatal morbidity.

## CONCLUSION

Prudent and close scrutinizing and follow up and delaying delivery in stable and appropriately selected patients with pre-eclampsia would be advantageous for neonates.

Patients with early onset pre-eclampsia are found to have significantly higher rates of specific fetal and neonatal morbidity when compared to the late onset type.

Hence, both preeclampsia types should be treated as different entities from a prognostic perspective.

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