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## Pregnancy Outcome in Early versus Late Onset Preeclampsia

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### ABSTRACT

**Aims:** To determine the pregnancy outcome of early and late onset preeclampsia.

**Methods:** This was a cross sectional analytical study conducted in the department of Obstetrics and Gynaecology, Manipal Teaching Hospital from July to October 2021. All cases of preeclampsia diagnosed according to International Society of Study of Hypertension in Pregnancy 2018, were included. Early and late onset preeclampsia cut-off used was 34 weeks. Preeclampsia diagnosed before 34 were classified as early onset and after 34 weeks as late onset preeclampsia. Maternal and perinatal outcomes were analyzed using Statistical Package for Social Sciences version 21.

**Results:** The prevalence of early onset and late onset preeclampsia were 4.3% and 8.3% of all deliveries. Early to late onset preeclampsia were 1:2. Renal involvement, placental abruption, IUGR, low birth weight, low Apgar and perinatal morbidity were significantly more in early onset; pre-term labor and use of MgSO<sub>4</sub> and antihypertensives were also more in early onset.

**Conclusion:** Late onset preeclampsia was more common than early onset preeclampsia but the maternal and perinatal outcome were poor for early onset as compared to late onset preeclampsia.

**Key words:** early onset; late onset; preeclampsia; pregnancy outcome

### INTRODUCTION

Hypertensive disorders in pregnancy (HDP) complicates about 2.73% of all pregnancies worldwide.<sup>1</sup> In Nepal, it ranges from 1.8% to 3.3%.<sup>2-5</sup> It is a major

cause of maternal and perinatal morbidity and mortality.<sup>1,3,5</sup> In Nepal, it is one of the important causes of maternal mortality, with 17% of the maternal deaths occurring because of it.<sup>6</sup>

Preeclampsia (PE) can be divided into early and late onset preeclampsia depending on the time of onset. Early-onset PE is usually defined as one that develops before 34 weeks of gestation, and late onset as one that develops at or after 34 weeks of gestation.<sup>7</sup> Although the diagnostic criteria and the presenting features may be same for both entities, it has been seen that the risk factors, maternal and perinatal outcome are different for these two entities with poorer outcome for early onset disease.<sup>8-12</sup>

Classification based on clinical and laboratory parameters as mild and severe PE is not recommended currently as it can be misleading to less experienced clinicians and as PE is an evolving disease and change from one form to another is possible.<sup>14</sup> New method of classifying PE based on the onset of disease as early and late onset is more predictive of adverse pregnancy outcome.<sup>9</sup> Hence this study was conducted with the aim of finding out prevalence of early and late onset PE and to compare their maternal and perinatal outcome.

## **METHODS**

This was a cross sectional analytical study conducted in the department of Obstetrics and Gynaecology of Manipal Teaching Hospital from July 2021 to October 2021. The study was conducted after ethical clearance was obtained (MEMG/454/IRC). Informed consent was taken from women or person nearest to her in case she was not able to consent prior to enrolment in the study.

Sample size calculation for comparing the proportion in finite population was done using online software for sample size calculation.<sup>13</sup>

Sample size was calculated using the following

formula,  $n = (Z_{\alpha/2} + Z_{\beta})^2 \times \{p_1(1-p_1) + p_2(1-p_2)\} / (p_1 - p_2)^2$ , where  $Z_{\alpha/2}$  is the critical value of the Normal distribution at  $\alpha/2$  (e.g. for a confidence level of 95%,  $\alpha$  is 0.05 and the critical value is 1.96),  $Z_{\beta}$  is the critical value of the Normal distribution at  $\beta$  (e.g. for a power of 80%,  $\beta$  is 0.2 and the critical value is 0.84) and  $p_1$  and  $p_2$  are the expected sample proportions of the two groups.

Sample size of 21 in each group was determined using the software and taking proportion in early onset (group 1) as 30% (27-34%) and proportion in late onset (group 2) as 70% (73-66%) as shown in previous studies.<sup>11,12</sup> So, minimum of at least 21 patients was considered in each group at the beginning of the study.

Among women with HDP delivering at our centre, only those with PE were taken in the study. PE was diagnosed using the revised guidelines of International Society for the Study of hypertension in pregnancy 2018 (ISSHP).<sup>14</sup> PE was diagnosed if there was development of de novo hypertension with systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg after 20 weeks' gestation accompanied by proteinuria and/or evidence of maternal acute kidney injury (AKI), liver dysfunction, neurological features, hemolysis or thrombocytopenia, or fetal growth restriction.<sup>14</sup> Only those women whose gestational age at onset of hypertension in pregnancy was known, was taken in the study. Women with chronic hypertension, preexisting renal disease, known connective tissue disorder,

diabetes mellitus or any other chronic illness were excluded. Women lost to follow up till delivery were excluded.

Women with PE were divided into categories – early onset or late onset depending on the onset of disease. If hypertension develops prior to 34 weeks then they were classified as early onset and if it developed at or after 34 weeks as late onset PE.

Maternal outcome variables were proteinuria, hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome, eclampsia, abruptio placentae, postpartum hemorrhage, acute kidney injury, venous thromboembolism, cerebrovascular accident, pulmonary edema, and disseminated intravascular coagulopathy, induction of labour and mode of delivery; and perinatal outcome variables were intrauterine growth restriction (IUGR), low birth weight (LBW), stillbirth after 28 weeks, Apgar scores, neonatal intensive care unit (NICU) admission and neonatal morbidity and mortality.

Preformed proforma, Excel chart sheet and SPSS version 21 were used for data recording and analysis. Descriptive data were presented as frequency, percentage, mean and standard deviation. Inferential statistical tests were Student's t-test, Chi-squared test or Fisher's exact test. A p-value less than 0.05 was considered statistically significant.

## **RESULTS**

Of 541 deliveries that occurred during the study period, there were total of 129 women with hypertensive disorders in pregnancy. According to ISSHP, there were 68 women with PE. Hence the prevalence of PE was 12.6% of all deliveries. Amongst them, 23 (33.8%) had early

onset and 45 (66.2%) had late onset PE. The prevalence of early onset PE was 4.3% and that of late onset PE was 8.3% of all deliveries. Residences like rural or urban ( $p=0.914$ ) and gravidity ( $p=0.098$ ) were not significantly different whereas the mean age ( $27.9\pm 3.3$  vs  $26.1\pm 3.7$ ,  $p=0.047$ ) and mean gestational week at onset ( $30.4\pm 2.9$  vs  $38.0\pm 2.1$ ,  $p<0.001$ ) were different in early onset ( $n=23$ ) and late onset ( $n=45$ ) respectively.

Proteinuria ( $p=0.003$ ), renal involvement ( $p=0.003$ ), abruptio ( $p=0.003$ ), IUGR ( $p=0.017$ ) and severe PE ( $p<0.001$ ) were significantly increased in early onset pre-eclampsia; and liver involvement ( $p=0.546$ ), neurological ( $p=0.804$ ), hematological involvement ( $p=0.192$ ), HELLP syndrome ( $p=0.327$ ) and eclampsia were not significantly different in early and late onset pre-eclampsia. [Table-1]

There was not much difference in the rate of labour induction ( $p=0.667$ ) and mode of delivery ( $p=0.848$ ) in early and late onset PE. There was no case of postpartum haemorrhage (PPH) in both groups but mean blood loss ( $p=0.123$ ) was slightly more ( $306\pm 71$ ml vs  $279\pm 63$ ml) in early onset PE. Requirement of antihypertensives was necessary in almost 95.7% cases ( $p=0.058$ ) of early onset PE and MgSO<sub>4</sub> requirement was similar ( $p=0.459$ ) in two groups. [Table-2]

Lower mean gestational week at birth ( $32.9\pm 3.5$  vs  $38.3\pm 1.8$ ), higher pre-term delivery (78.3% vs 8.9%), lower mean birth weight ( $1613 \pm 645$ g vs  $2781 \pm 652$ g) and

more low birth weight all were highly significant in early onset group ( $p < 0.001$ ); and Apgar score below 7 ( $p = 0.019-0.015$ ), neonatal morbidity {12 (52.2%) vs 10 (22.2%),  $p = 0.012$ } and intrauterine fetal death ( $p = 0.011$ ) were significantly more in early onset group. [Table-3]

Table-1: Maternal Organ System Involvement in Early and Late Onset PE

Maternal Organ System Involvement	Early onset PE (n= 23)	Late Onset PE (n=45)	p-value
Proteinuria	14 (60.9%)	11 (24.4%)	0.003
Renal Involvement	5 (21.7%)	0 (0.0%)	0.003
Liver Involvement	12 (52.2%)	20 (44.4%)	0.546
Neurological Involvement	5 (21.7%)	11 (24.4%)	0.804
Eclampsia	2 (8.7%)	5 (11.1%)	1.000
Haematological Involvement	6 (26.1%)	6 (13.3%)	0.192
HELLP syndrome	3 (13.0%)	2 (4.4%)	0.327
Abruption placenta	5 (21.7%)	0 (0.0%)	0.003
IUGR	11 (47.8%)	9 (20.0%)	0.017
Severity of PE			
Mild	3 (13%)	27 (60%)	< 0.001
Severe	20 (87%)	18 (40%)	

Table-2: Maternal Obstetric Outcome of Early and Late Onset PE

Maternal Obstetric Outcome	Early onset PE (n= 23)	Late Onset PE (n = 45)	p-value
Mode of delivery			0.848
Vaginal	5 (21.7%)	12 (26.7%)	
Assisted vaginal delivery	0 (0.0%)	1 (2.2%)	
Cesarean section	18 (78.3%)	32 (71.1%)	
Induction of labour	6 (26.1%)	14 (31.1%)	0.667
Mean blood loss (ml ± SD)	306 ± 71	279 ± 63	0.123
Use of MgSO <sub>4</sub>	7 (30.4%)	10 (22.2%)	0.459
Use of Antihypertensives	22 (95.7%)	35 (77.8%)	0.058

Table-3: Perinatal Outcome of Early and Late Onset PE

Perinatal Outcome	Early onset PE (n= 23)	Late Onset PE (n = 45)	p-value
Mean gestational weeks	32.9 ± 3.5	38.3 ± 1.8	< 0.001
Preterm delivery	18 (78.3%)	4 (8.9%)	< 0.001
Mean Birth weight (grams))	1613 ± 645	2781 ± 652	< 0.001
Birth weight			< 0.001
<1000 gm	4 (17.4%)	0 (0.0%)	
1000-1500gm	6 (26.1%)	1 (2.2%)	
1500 –2500 gm	11 (47.8%)	10 (22.2%)	
>2500 gm	2 (8.7%)	34 (75.6%)	
Apgar Score <7 at one minute	8 (34.8%)	5 (11.1%)	0.019
Apgar Score <7 at five minutes	5 (21.7%)	1 (2.2%)	0.015
NICU Admission	12 (52.2%)	10 (22.2%)	0.012
Perinatal Mortality	6 (26.1%)	2 (4.4%)	0.015

## DISCUSSION

In our study, the prevalence of PE was 12.6% of all deliveries during the study period. This is higher compared to another study.<sup>11</sup> The prevalence of early onset PE was 4.3% and that of late onset PE was 8.3% of all deliveries. Among women with PE in our study, 33.8% were early onset and 66.2% were late onset PE. Similar findings were reported by Shankar P et al and Gohar S et al with 32 to 34.6% early onset and 65.3 to 67.7% late onset PE among cases of PE.<sup>11,14</sup> Some studies reported a slightly lower proportion of cases of early onset PE.<sup>12,16</sup> Hence, late onset PE is more common form of disease compared to early onset PE as in other studies.<sup>11,12,14,16</sup>

Mean age of women with early onset PE was slightly more than that of late onset PE. Both types of the diseases were more common in 20 to 35 years of age, same as that in study conducted by Gomathy E et al.<sup>12</sup> Early onset PE was more common in multigravida while late onset in primigravida contrary to finding of Gomathy et al, where, both were found to be more common in primigravida, which is a known risk factor for PE.<sup>12</sup> Early and late onset were both common in multigravida in another study.<sup>15</sup> The difference in the findings could be due to different study setting.

The mean gestational age at onset of early onset PE was 30 weeks and that of late onset PE was 38 weeks in our study. Many other studies have also found the gestational age at onset for early onset PE to be 30 weeks.<sup>8-10,16</sup> Gestational age at onset for late onset disease was reported to be 36-37 weeks in other studies similar to our study.<sup>9,10,15,16</sup>

In terms of involvement of different organ syst-

em, it was found that early onset disease showed increased involvement specifically of renal system and presence of proteinuria. These findings were similar to that of other studies.<sup>9,10,17</sup> Proteinuria was more common in late onset disease in another study.<sup>11</sup> This could be because, in this study only proteinuria was used as diagnostic criteria instead of all organ system involvement unlike in our study. Involvement of hepatic and haematological system was noted to be almost similar in both groups unlike in other studies.<sup>9,11,17</sup> This is because, the latest ISSHP 2018 guidelines have decreased liver and haematological parameters for diagnosing PE. Therefore, even with slight increase in the liver enzymes or decrease in platelet count, women were diagnosed as PE – as noted in both groups. Further analysis of the levels of liver enzymes or platelet levels in two groups were not done. Hence it cannot be inferred from this study, in which group the involvement of the liver and haematological system was more severe. Neurological system involvement and eclampsia was same in both the groups as in another study.<sup>10</sup> Some other studies have reported increased involvement of neurological system and eclampsia.<sup>9,17</sup> This could be due to difference in the type of study population and study site. Likewise, the use of MgSO<sub>4</sub> was similar in both groups in our study contrary to findings of other studies.<sup>9,17</sup> However, the use of antihypertensives was more in early onset disease compared to late onset in our study which is as same as in other studies.<sup>9-11</sup> MgSO<sub>4</sub> may have been used for other severe features of disease and not just for neurolog-

ical system involvement. Severe PE was more common in early onset disease in our study and hence also the use of MgSO<sub>4</sub>. Similarly, severe PE was more common in early as compared to late onset PE in other studies as well.<sup>9,10,17</sup> Eclampsia was more common in early disease in another study where severe PE was comparatively more in early onset group.<sup>10</sup>

All cases of abruptio placenta occurred in early onset PE in our study. There were also significantly more IUGR in early onset PE compared to late onset PE. Other studies also reported significantly increased occurrence of abruptio and IUGR in early onset PE.<sup>9,10,17</sup> However, Gohar S et al. found that occurrence of IUGR was same in early and late onset PE.<sup>15</sup> Mean gestational age at onset of early PE was later, at 32 weeks in their study, which could be the reason for IUGR not being more common in the early onset PE in their study.

Operative delivery by cesarean section was same in early as well as late onset PE in our study same as shown in other studies.<sup>10-12,16</sup> Study by Aksornphusitaphong A et al reported high cesarean section rate in early onset disease while Gohar S et al reported more number of cesarean section in late onset PE.<sup>8,15</sup> Hence, it is not just the onset of PE that decides which mode pregnancy termination is done but also other factors like severity of the disease, organ system involvement, occurrence of preterm labour and other obstetric factors that may be present.

Preterm delivery was more common in early onset PE (78.3%) compared to late onset PE (8.9%). In about 21.7% women with early onset PE, pregnancy could be continued and delivered at term. Preterm delivery occurred in 100% women with early onset PE in one study, while

in another it occurred in 60% cases of PE.<sup>8,15</sup>

Overall preterm delivery was more common in early onset PE compared to late onset PE.<sup>8,15</sup> Mean gestational age at delivery for early onset PE was 33 weeks and that for late onset disease was 39 weeks similar to other studies.<sup>8-10</sup> The gestational age at delivery was lower in early onset compared to late onset PE as in other studies.<sup>8-10,12,15</sup>

The perinatal outcome of early onset PE was poorer than that of late onset PE in our study. Mean birth weight was lower in early onset disease. Low birth weight, Apgar score less than seven at one and five minutes, NICU admission for neonatal morbidity and perinatal mortality was significantly higher in early onset PE compared to late onset PE in our study. Similarly, other studies also presented poor perinatal outcome in early onset compared to late onset PE.<sup>8-12,15-17</sup>

There was disparity in the number of patients in the two groups during the study period. This could make analysis slightly biased. A larger study involving multiple study sites and larger patient population would give more robust results to make stronger recommendations.

## CONCLUSIONS

Early onset PE is more common than the late onset PE. Maternal and perinatal outcomes were poor in early onset as compared to late onset PE.

## REFERENCES

1. Abalos E, Cuesta C, Carroli G, Qureshi Z, Widmer M, Vogel JP, Souza JP, WHO Multicountry Survey on Maternal and Newborn Health Research Network. Preeclampsia, eclampsia and adverse maternal and perinatal

- outcomes: a secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health. *Br J Obstet Gynaecol.* 2014;121:14-24. [[PubMed](#) | [Full Text](#) | [DOI](#)]
2. Das S, Das R, Bajracharya R, Baral G, Jabegu B, Odland JØ, Odland ML. Incidence and risk factors of pre-eclampsia in the Paropakar Maternity and Women's Hospital, Nepal: A retrospective study. *Int J Environ Res Pub Health.* 2019;16(19):3571 [[PubMed](#) | [Full Text](#) | [DOI](#)]
  3. Joshi R, Thakur A, Chhetry M, Uprety DK. Maternal and Fetal Outcome of Pregnancies Complicated with Hypertension in a Tertiary Care Hospital in Eastern Nepal. *Asian Res J Gynaecol Obstet.* 2020;3:32-8. [[Full Text](#)]
  4. Singh AC, Rana SS. Fetal Outcome in Hypertensive Disorders of Pregnancy. *Med J Shree Birendra Hosp.* 2013;12(1):8-10. [[Full Text](#) | [DOI](#)]
  5. Bilano VL, Ota E, Ganchimeg T, Mori R, Souza JP. Risk factors of pre-eclampsia/eclampsia and its adverse outcomes in low-and middle-income countries: a WHO secondary analysis. *PloS One.* 2014;9(3):e91198. [[PubMed](#) | [Full Text](#) | [DOI](#)]
  6. Suvedi BK, Pradhan A, Barnett S, Puri M, Chitrakar SR. Nepal Maternal Mortality and Morbidity Study 2008/2009: Summary of Preliminary Findings. Kathmandu: Government of Nepal. 2009. [[Full Text](#)]
  7. Raymond D, Peterson E. A critical review of early-onset and late-onset preeclampsia. *Obstet Gynecol Surv.* 2011;66(8):497-506. [[PubMed](#) | [DOI](#)]
  8. Aksornphusitaphong A, Phupong V. Risk factors of early and late onset pre-eclampsia. *J Obstet Gynaecol Res.* 2013;39(3):627-31. [[PubMed](#) | [Full Text](#) | [DOI](#)]
  9. Wojtowicz A, Zembala-Szczerba M, Babczyk D, Kołodziejczyk-Pietruszka M, Lewaczyńska O, Huras H. Early-and late-onset preeclampsia: a comprehensive cohort study of laboratory and clinical findings according to the New ISHHP criteria. *Int J Hypertens.* 2019;2019:Article ID 4108271. [[PubMed](#) | [Full Text](#) | [DOI](#)]
  10. Wadhvani P, Saha PK, Kalra JK, Gainer S, Sundaram V. A study to compare maternal and perinatal outcome in early vs. late onset preeclampsia. *Obstet Gynecol Sc.* 2020;63(3):270-7. [[PubMed](#) | [Full Text](#) | [DOI](#)]
  11. Shankar P, Karthikeyan K, Nalini AP, Sindhura M, Kim G. Maternofetal outcomes in early versus late onset pre-eclampsia: a comparative study. *Int J Reprod Contracep Obstet Gynecol.* 2019;8(2):549 [[Full Text](#) | [DOI](#)]
  12. Gomathy E, Akurati L, Radhika K. Early-onset and late-onset preeclampsia-maternal and perinatal outcomes in a rural tertiary health center. *Int J Reprod Contracept Obstet Gynecol.* 2018;7(6):2266-9. [[Full Text](#) | [DOI](#)]
  13. Comparing Two Proportions - Sample Size - Select Statistical Consultants (select-statistics.co.uk); Available at: <https://select-statistics.co.uk/calculators/sample-size-calculator-two-proportions/>
  14. Brown MA, Magee LA, Kenny LC, Karumanchi SA, McCarthy FP, Saito S, Hall DR, Warren CE, Adoyi G, Ishaku S. Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations for international practice. *Hypertension.* 2018;72(1):24-43 [[PubMed](#) | [Full Text](#) | [DOI](#)]
  15. Gohar S, Syed W. Comparison of adverse fetomaternal outcome in early and late onset preeclampsia. *JPMI: J Postgrad Med Inst.* 2021;35(1). [[Full Text](#) | [DOI](#)]
  16. Aziz A. The differences of characteristic, management, maternal and perinatal outcomes among early and late onset preeclampsia. *Open Access Lib J.* 2016;3(06):1. [[Full Text](#) | [DOI](#)]
  17. Atluri S, Manoli NS. Comparative study of maternal and perinatal outcome in early onset and late onset preeclampsia. *J Evidence Based Med Healthcare.* 2017;4(9):499-504. [[DOI](#)]
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