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Original Research Article

Comparative Study of Maternal and Perinatal Outcomes in Early and Late Onset Preeclampsia in Tertiary Health Care Center

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Abstract:

Introduction: Hypertension during pregnancy is a major health problem. Hypertensive disorder of pregnancy (Gestational Hypertension (GHT), Pre-eclampsia (PE) & Eclampsia (E) occurs in approximately 10-15% of all pregnancies. It accounts for approximately a quarter of all antenatal admissions. In addition, it is strongly associated with foetal growth retardation and prematurity, this contributes largely to perinatal mortality and morbidity.

Material and Methods: This prospective study of 246 women with preeclampsia conducted at B.J.M.C and SGH, Pune, between November 2020 to May 2022. Outcome of mother was noted in form of stay in hospital, duration of stay, ICU care, blood transfusion, near miss mortality and maternal mortality and fetal outcome in form of NICU care, Neonatal death, stillbirth, and Intra-uterine death were noted.

Result: Out of the total 246 cases of pre-eclampsia studied, early onset pre-eclampsia was seen in 30.1% cases while late onset pre-eclampsia was seen in 69.9% cases. Maternal complications like abruption (9.5% vs 1.7%), HELLP (9.5% vs 1.2%) and acute kidney injury (6.8% vs 0.6%) was significantly higher in cases of EO-PE ($p<0.01$). Total 28.4% women from EOPE developed complications vs 3.4% from LOPE.

Conclusion: Study concluded that late onset preeclampsia (LO-PE) was more common than early onset preeclampsia (EO-PE). However, EO-PE is associated with higher LSCS rates, maternal morbidities and mortality as compared to LO-PE. Incidence of pre-term birth, NICU stay, and perinatal mortality was also higher in EO-PE cases. Hence EO-PE needs early diagnosis, timely intervention, and treatment to reduce maternal and perinatal complications.

Keywords: Preeclampsia, Early Onset Preeclampsia, Late Onset Preeclampsia, Maternal Morbidity, HELLP Syndrome.

Introduction

According to new terminology (ACOG 2014), preeclampsia without evidence of end-organ damage is termed preeclampsia without severe features [1]. However, the presence of end-organ damage defines severe preeclampsia.

In recent years, a new disease classification based on onset timing consisting of early-onset preeclampsia (EO-PE) occurring before 34 weeks of gestation and late-onset preeclampsia (LO-PE) occurring at or after 34 weeks of gestation has gained attention [2-4]. The diagnostic criteria are the same for EO-PE and LO-PE; in fact, this simple division has better prognostic implications than mild vs. severe terminology [5]. The concept of early and late PE is more modern, and it is widely accepted that these two entities have different etiologies and should be regarded as different forms of the disease [6,7]. Early-onset PE (before 34 weeks) is commonly associated with abnormal uterine artery Doppler, fetal growth restriction (FGR), and adverse maternal and neonatal outcomes [8]. In contrast, late-onset PE (after 34 weeks) is mostly associated with normal or slight increased uterine resistance index, a low rate of foetal involvement, and more favourable perinatal outcomes [8,9]. This prospective study thus aimed to examine the effects of EO-PE and LO-PE on composite maternal and perinatal outcomes and identified the similarities and differences in laboratory parameters and clinical presentations of these two groups.

Material and Method: This study is a prospective observational study, conducted at B.J.M.C and Sassoon General Hospital Pune. All patients

admitted according to inclusion criteria were included in study after written informed consent.

On admission- history, clinical examination, referral notes, chain of events were noted in case record form with opinion of senior obstetrician and other faculties like physician, intensivist, anaesthetist, surgeon, regarding multidisciplinary management of patient. Blood investigations like hemogram, CBC, liver function tests, renal function tests, coagulation profile were done in all cases. Radiological investigations like chest x-ray, ultrasonography, CT scan and MRI was done as advised by senior faculty and noted in case record form.

Cases were diagnosed as having pre-eclampsia as per standard definition. Pre-eclampsia was divided into two groups as per timing of diagnosis i.e. early (<34 weeks) and late pre-eclampsia (>34 weeks). After evaluating the patient thoroughly, the complications were noted down. Maternal and foetal parameters were collected and need for admission in NICU, ICU, blood transfusion, re-suturing, surgical intervention was noted in case record form.

Lastly, the outcome of mother was noted in form of stay in hospital, duration of stay, ICU care, blood transfusion, near miss mortality and maternal mortality and foetal outcome in form of NICU care, Neonatal death, stillbirth, and Intra-uterine death were noted.

Statistical analysis: All the data was noted down in a pre-designed study proforma. Qualitative data was represented in the form of frequency and percentage. Association between qualitative variables was assessed by Chi-Square test. Quantitative data was represented using Mean ± SD. Analysis of Quantitative data between the two groups was done using unpaired t-test if data passed 'Normality test' and by Mann-Whitney Test if data failed 'Normality test'. A p-value < 0.05 was taken as level of significance. Results were graphically represented where deemed necessary.

Results: Out of the total 246 cases of pre-eclampsia studied, early onset pre-eclampsia was seen in 30.1% cases while late onset pre-eclampsia was seen in 69.9% cases.

Table 1: Distribution of study groups as per demographic characteristics and obstetrics details

Parity	**EOP N=74 (30.1%)**	**LOP N=172 (69.9%)**
Primigravida	68(91.9%)	107 (62.2%)
Multigravida	6(8.1%)	65(37.8%)
Mean age(years)	20.97	23.63
Gestation age at diagnosis (weeks)	30.68(30%)	36.63 (70%)

In both the groups of pre-eclampsia, majority of the cases were primigravida (91.9% in EO-PE and 62.2% in LO-PE; p-0.34). Mean age of the cases with early onset PE was significantly less than cases with late onset PE (20.97 vs 23.63; p<0.01). Mean age of diagnosis for EO-PE was 30.68 weeks while for that of LO-PE was 36.63 weeks (p<0.01).

Table 2: Distribution of study groups as per presenting symptoms, investigations, and term of delivery

Symptoms	**Group**		**Total**
	EOP	**LOP**	
Headache	30(40.5%)	54(31.4%)	84(34.1%)
Nausea/ Vomiting	24(32.4%)	37(21.5%)	61(24.8%)
Dyspnoea	22(29.7%)	35(20.3%)	57(23.2%)
Visual Disturbances	17(23.0%)	17(9.9%)	34(13.8%)
Vaginal Bleeding	11(14.9%)	5(2.9%)	16(6.5%)
Deranged LFT	47(63.5%)	88(51.2%)	135(54.9%)
Low platelet	45(60.8%)	66(38.4%)	111(45.1%)
High creatinine	25(33.8%)	30(17.4%)	55(22.4%)
Pre-term (<37 weeks)	60(81.1%)	101(58.7%)	161(65.4%)
Term	14(18.9%)	71(41.3%)	85(65.4%)

Most common presenting symptoms in PE cases was headache (34.1%), nausea/ vomiting (24.8%) and dyspnoea (23.2%). The study groups were comparable regarding these symptoms; however, incidence of visual disturbances was significantly more in EO-PE group (23% vs 9.9%; p<0.01). Incidence of thrombocytopenia (60.8% vs 38.4%) and derangement of renal functions, as measured by high creatinine levels (33.8% vs 17.4%) was significantly more in cases of EO-PE. Incidence of pre-term delivery was 81.1% in EO-PE cases as compared to 58.7% in LO-PE cases (p-0.34).

Table 3: Distribution of study groups by management

Management	Group		Total
	EOP	LOP	
Labetalol	53	110	163
	71.6%	64.0%	66.3%
Magnesium Sulphate	49	81	130
	66.2%	47.1%	52.8%
Nifedipine	34	42	76
	45.9%	24.4%	30.9%
Labetalol+ Nifedipine	31	33	64
	41.9%	19.2%	26.0%
Induction of Labour	52	112	164
	70.3%	65.1%	66.7%

Above table showed the management details for both groups. Need of magnesium sulphate in EO-PE was 66.2% vs 47.1% in LO-PE. Antihypertensive drugs like labetalol were required in 71.6% in EO-PE vs 64.0% in LO-PE, Nifedipine in 45.9% in EO-PE vs 24.4% in LOP, both labetalol and nifedipine in 41.9% in EO-PE vs 19.2% in LO-PE. Induction of labour was required in 70.3% cases of early onset as compared to 65.1% cases of late onset group.

Table 4: Distribution of study groups by maternal outcome

Maternal Outcome	Group		Total
	EOP	LOP	
ICU Admission	19 25.7%	7 4.1%	26 10.6%
BT	16 21.6%	6 3.5%	22 8.9%
Near Miss	5 6.8%	1 0.6%	6 2.4%
Maternal Mortality	4 5.4%	0 0.0%	4 1.%
Abruption	7 9.5%	3 1.7%	10 4.1%
HELLP	7 9.5%	2 1.2%	9 3.7%
AKI	5 6.8%	1 0.6%	6 2.4%
ICH	2 2.7%	0 0.0%	2 0.8%
Mild PIH	40 54.1%	129 75.0%	169 68.7%
Sever PIH	34 45.9%	43 25.0%	77 31.3%
LSCS	50 67.6%	82 47.7%	132 53.7%
Vaginal	24 32.4%	90 52.3%	114 46.3%

Incidence of ICU admissions (25.7% vs 4.1), requirement of BT (21.6% vs 3.5%) was significantly more in EO-PE cases. Maternal near miss was seen in 6.8% and 0.6% cases while maternal mortality was 5.4% and 0% in early versus late PE cases. Out of 4 maternal mortalities in EO-PE, 2 cases were due to aspiration pneumonitis and 1 case was due to DIC and 1 was due to ICH. Overall unfavourable maternal outcome was significantly associated with early onset pre-eclampsia.

Table 5: Distribution of study groups by fetal complications

Fetal Complications	Group		Total
	EOP	LOP	
LBW	71	126	197
	95.9%	73.3%	80.1%
IUGR	25	11	36
	33.8%	6.4%	14.6%
Sepsis	9	4	13
	12.2%	2.3%	5.3%
Birth asphyxia	19	6	25
	25.7%	3.5%	10.2%
RDS	12	3	15
	16.2%	1.7%	6.1%
MAS	6	3	9
	8.1%	1.7%	3.7%
IUFD	2	0	2
	2.7%	0.0%	0.8%
Still Birth	2	1	3
	2.7%	0.6%	1.2%
Neonatal Death	2	1	3
	2.7%	0.6%	1.2%

Overall unfavourable fetal outcome was significantly associated with early onset pre-eclampsia. Incidence of LBW (95.9% vs 73.3%), IUGR (33.8% vs 6.4%), sepsis (12.2% vs 2.3%), RDS (16.2% vs 1.7%), meconium aspiration syndrome (8.1% vs 1.7%) and perinatal mortality including IUFD, still births and neonatal deaths (8.1% vs 1.2%), IUFD (2.7% vs 0), still birth (2.7% vs 0.6%), neonatal death (2.7% vs 0.6%) were all significantly higher in babies born to EO-PE mothers ($p<0.01$).

Discussion:

The concept of early and late PE is more modern, and it is widely accepted that these two entities have different aetiologies and should be regarded as different forms of the disease [6,7]. Early-onset PE (EO-PE) i.e., before 34 weeks is commonly associated with abnormal uterine artery Doppler, fetal growth restriction (FGR), and adverse maternal and neonatal outcomes [8]. In contrast, late-onset PE (LO-PE) i.e., after 34 weeks is mostly associated with normal or slight increased uterine resistance index, a low rate of fetal involvement, and more favourable perinatal outcomes [8,9]

The present hospital based comparative study thus aimed to examine the effects of EO-PE and LO-PE on composite maternal and perinatal outcomes and identified the similarities and differences in laboratory parameters and clinical presentations of these two groups. Study included 246 consecutive cases diagnosed as pre-eclampsia during the study period. Cases were thoroughly investigated and managed as per standard hospital protocol. These cases were followed up till delivery to record the maternal and neonatal outcomes in the two groups.

Out of the total 246 cases of pre-eclampsia studied, early onset pre-eclampsia was seen in 30.1% cases while late onset pre-eclampsia was seen in 69.9% cases. Gomathy E et al., [10] showed that the incidence of EO-PE (27.6%) was lower than LO-PE (72.4%). Gohar S et al., [11] studied 254 PE cases. Out of 254 patients, 172 (67.7%) patients had LO-PE while 82 (32.3%) presented with EO-PE.

Mean age of the cases with early onset PE was significantly less than cases with late onset PE (20.97 vs 23.63; $p<0.01$). In both the groups of pre-eclampsia, majority of the cases were primigravida (91.9% in EO-PE and 62.2% in LO-PE; p-0.34). In a study by Nadkarni et al., [12] majority of women in the study group were in the age group 21-25 years.

Gohar S et al.,[11] observed that most of the patients were primigravida in both groups, 43 (52.4%) in EO-PE and 122 (70.93%) in LO-PE. In a study by Nandkarni et al.,[12], primigravida women constituted 49% of the total subjects in the study group. In present study, requirement of Caesarean section was 67.6% in EO-PE group as compared to 47.7% in LO-PE group ($p<0.01$). Similar results were observed by Gohar S et al.,[11] where LO-PE group had more caesarean sections (n=62, 36.02%) than EO-PE (n=16, 19.53%) with a p-value of ≤ 0.05. Mean gestational age at diagnosis for EO-PE was 30.68 weeks while for that of LO-PE was 36.63 weeks ($p<0.01$). Mean gestational age at delivery was significantly lower in EO-PE cases as compared to LO-PE cases (32.44 vs 37.36; $p<0.01$).

Wadhwani P et al., [13] observed mean gestational age at diagnosis was 30 weeks and 36.5 weeks in

EO-PE and LO-PE respectively. The mean gestational age at delivery was 32.6 and 37.3 weeks for EO-PE and LO-PE respectively. Sever pre-eclampsia was seen in 45.9% cases of early onset PE as compared to 25.0% in late onset PE ($p<0.01$). Overall unfavourable maternal outcome was significantly associated with early onset pre-eclampsia. Incidence of pre-term delivery was 81.1% in EO-PE cases as compared to 58.7% in LO-PE cases (p-0.34). Need of magnesium sulphate in EO-PE was 66.2% vs 47.1% in LO-PE. Antihypertensive drugs like labetalol were required in 71.6% in EO-PE vs 64.0% in LO-PE, Nifedipine in 45.9% in EO-PE vs 24.4% in LOP, both labetalol and nifedipine in 41.9% in EO-PE vs 19.2% in LO-PE. Induction of labour was required in 70.3% cases of early onset as compared to 65.1% cases of late onset group.

Maternal complications like abruption (9.5% vs 1.7%), HELLP (9.5% vs 1.2%) and acute kidney injury (6.8% vs 0.6%) was significantly higher in cases of EO-PE ($p<0.01$). Incidence of ICU admissions (25.7% vs 4.1), requirement of BT (21.6% vs 3.5%) was significantly more in EO-PE cases. Maternal near miss was seen in 6.8% and 0.6% cases while maternal mortality was 5.4% and 0% in early versus late PE cases. Shrestha J et al.,[14] study found that renal involvement, placental abruption, IUGR, low birth weight, low Apgar and perinatal morbidity were significantly more in early onset; pre-term labour and use of MgSO4 and antihypertensives were also more in early onset. Study concluded that maternal outcome was poor for early onset as compared to late onset preeclampsia.

Overall unfavourable foetal outcome was significantly associated with early onset pre-eclampsia. Mean birth weight was significantly lower in babies delivered to EO-PE mothers as compared to LO-PE mothers (1.69 vs 2.13 Kg; $p<0.01$). Incidence of LBW (95.9% vs 73.3%), IUGR (33.8% vs 6.4%), sepsis (12.2% vs 2.3%), RDS (16.2% vs 1.7%), meconium aspiration syndrome (8.1% vs 1.7%) and perinatal mortality including IUFD, still births and neonatal deaths was (8.1% vs 1.2%), IUFD (2.7% vs 0), still birth (2.7% vs 0.6%), neonatal death (2.7% vs 0.6%) were all significantly higher in babies born to EO-PE mothers ($p<0.01$). Need for resuscitation was observed in 18.9% EO-PE babies as compared to 10.5% LO-PE babies ($p<0.01$). Mean NICU stay was significantly more in babies born to EO-PE mothers as compared to LO-PE babies (8.84 vs 5.39; $p<0.01$).

Ness RB and Sinai., [8] in their study observed that incidence of small-for-gestational age, Apgar score <7 at 5 min, stillbirth and early neonatal death rates were significantly higher in women with EO-PE compared to LO-PE ($p < 0.01$). Gomathy E et al.,[10] showed that complications in perinatal outcomes such as low birth weight (<2500 gram) are more in EO-PE (98.3%) compared to LO-PE (45.2%) and asphyxia is more on EO-PE (11.7%) compared to LO-PE (1.3%). Stillbirth in EO-PE (15%) is more than LO-PE group (3.2%).

Thus, to summarize, late onset preeclampsia (LO-PE) is more common than early onset preeclampsia (EO-PE). However, EO-PE is associated with higher LSCS rates, maternal morbidities like abruption, HELLP, AKI and mortality due to aspiration pneumonitis, DIC and ICH as compared to LO-PE. Incidence of pre-term birth, NICU stay, and perinatal mortality was also higher in EO-PE cases.

In Conclusion, late onset preeclampsia (LO-PE) was more common than early onset preeclampsia (EO-PE). However, EO-PE is associated with higher LSCS rates, maternal morbidities and mortality as compared to LO-PE. Incidence of pre-term birth, NICU stay, and perinatal mortality was also higher in EO-PE cases. Hence EO-PE needs early diagnosis, timely intervention, and treatment to reduce maternal and perinatal complications.

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