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Comparison of maternal outcomes in early onset versus late onset pre-eclampsia - A prospective observational study

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Abstract

Background: Early-onset preeclampsia is usually defined as preeclampsia that develops before 34 weeks of gestation, whereas late-onset preeclampsia develops at or after 34 weeks of gestation. Although the diagnostic criteria for EOP and LOP are the same, there are some uncertainties about the maternal and fetal outcomes. It is thought that EOP poses a high risk to both mother and fetus, whereas LOP may present with less severe clinical symptoms.

Aim: To compare the maternal outcomes of EOP and LOP and to find the prognostic implications of the two groups.

Methods: This hospital based prospective observational study was conducted in the Department of Obstetrics & Gynaecology, SMS Medical College, Jaipur from May 2020 to May 2021.

Results: 150 primigravida were recruited in the study 75 in EOP group and 75 in LOP group. Percentage of women developing severe pre-eclampsia was significantly higher in EOP group (67.7%) than in LOP group (32.3%) and significantly more women underwent a cesarean section delivery in EOP group (58.7%) as compared to LOP group (33.3%). Postpartum Hemorrhage (PPH) (17.3%) was the most common complication that occurred in all the participants followed by Antepartum Hemorrhage (APH) [14%]. While the proportion of participants who had PPH, HELLP, DIC (Disseminated Intravascular Coagulation) and ATN (Acute Tubular Necrosis) was more in the LOP group and the proportion of participants who had APH, Eclampsia and pulmonary edema was more in EOP group, the intergroup difference was not statistically significant (p value >0.05).

Conclusion: With detailed analysis of the study, it can be concluded that severity of PE is inversely proportional to the POG of development of pre-eclampsia and rate of cesarean section increases with the early onset of pre-eclampsia.

Keywords: EOP, LOP. PE

Introduction

Pre-eclampsia is a disorder of pregnancy affecting multiple organs and complicating 2-8% of pregnancies. [1] Risk factors include maternal co-morbidities such as obesity and chronic hypertension, paternal factors, and genetic factors which can be recognised early and preclude the development of complications owing to the emergent nature of this disease. Diagnostic criteria include new onset hypertension (BP 140/90 mmHg on 2 occasions 4 hrs apart) and proteinuria (+1 on dipstick), with or without end organ damage causing significant maternal and perinatal morbidity and mortality which warrants advanced competencies to manage this disease.

The International Society for the Study of Hypertension in Pregnancy (ISSHP) currently defines pre-eclampsia (PE) as the occurrence of hypertension in combination with proteinuria, developing after 20 weeks gestation in a previously normotensive, non-proteinuric patient [3]. This society has re-classified PE in its 2014 update according to the time of onset of disease as early-onset pre-eclampsia (EOP) and late-onset pre-eclampsia (LOP). Early-onset pre-eclampsia is usually defined as pre-eclampsia that develops before 34 weeks of gestation, whereas late-onset pre-eclampsia develops at or after 34 weeks of gestation.

Although the causes of pre-eclampsia are unclear, multiple authors have suggested that the pathophysiology of EOP differs from that of LOP. Early-onset disease appears to be mediated by the placenta. LOP, on the other hand, is mediated by maternal factors and a maternal overreaction to pregnancy [4].

Although the diagnostic criteria for EOP and LOP are the same, there are some uncertainties about the maternal and fetal outcomes [5]. It is thought that EOP poses a high risk to both mother and fetus [6,7], whereas LOP may present with less severe clinical symptoms.

With this background, the present study was conducted to compare the maternal and perinatal outcomes of EOP and LOP and to find the prognostic implications of the two groups.

Materials and methods

This hospital based prospective observational study was conducted in the Department of Obstetrics & Gynaecology, SMS Medical College, Jaipur from May 2020 to May 2021.On calculating,125 pregnant women were required as sample size which was further enhanced to 150 pregnant women as final sample size for present study expecting 20% dropout / loss to follow-up / attrition in follow up period.

After proper counselling regarding the purpose of the study, a written informed consent was taken from the women.

Pre-eclampsia was defined according to American College of Obstetrics and Gynecology criteria [1]. Patients with or without severe features of pre-eclampsia were recruited. Only subjects with confirmed gestation and disease onset timing (pre-eclampsia) were included. 75 eligible patients were consecutively recruited in each group.

Inclusion criteria

- Primigravidas between the age of 18-35 years with live Singleton pregnancy with Pre-eclampsia (BP ≥ 140/90 mmHg on 2 occasions 4 hrs. apart) with or without severe features, willing to participate in the study.

Exclusion criteria

Pregnant women with

1. Autoimmune diseases

2. Endocrine disorders like Diabetes Mellitus and Hypothyroidism
3. Ischemic heart disease
4. Chronic renal disease
5. Patients on treatment with drugs that may influence lipid profile.
6. Morbid obesity (BMI >40 kg/m^2)

Study participants who developed PE before 34 weeks of gestation were identified as having EOP and those who developed PE after 34 weeks of gestation were identified as having LOP.

All Patients with PE were admitted and baseline hematological investigations [Complete Blood count, Viral Markers, Random blood sugar, Blood group (ABO-Rh), urinalysis] along with Kidney function tests, Liver function tests, Thyroid function test and ultrasonography for fetal well-being, gestational age and colour doppler study were done.

Features of severe PE were noted and participants were managed accordingly, if one or more of the following criteria were present:

1. Blood pressure of 160 mm Hg systolic or higher or 110 mm Hg diastolic or higher on two occasions at least 6 hours apart while the patient is on bed rest
2. Oliguria of less than 500 ml in 24 hours
3. Cerebral or visual disturbances
4. Pulmonary edema or cyanosis
5. Epigastric or right upper-quadrant pain
6. Impaired liver function as indicated by abnormally elevated blood concentrations of liver enzymes (to twice normal concentration), severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both
7. Thrombocytopenia

Renal insufficiency

Mode of delivery (normal vaginal or by cesarean section) was also taken into account. Any complication in the ante partum, intra partum and post-partum period was noted. Maternal outcome was recorded.

Statistical analysis

Continuous variables were summarized as mean and were analysed by using unpaired t test. Nominal / Categorical variables were summarized as proportions and was analysed by using chi square/ Fischer exact test. P value < 0.05 was considered as significant.

Results

Our study was conducted from May 2020 to May 2021 where a total of 150 primigravida booked at Zenana Hospital were followed till delivery for the development of pre-eclampsia. Features of severity were also correlated to the onset of the disease.

Table 1: Description of baseline parameters of study participants

All Parameters	EOP Mean ± SD	LOP Mean ± SD	p-value	S/NS
Age (Years)	21.92 ± 2.36	22.15 ± 2.66	0.840	NS
Religion				
Hindu	47 (62.7%)	52 (69.3%)	0.388	NS
Muslim	28 (37.3%)	23 (30.7%)		
Residence				
Rural	44 (58.7%)	39 (52%)	0.411	NS
Urban	31 (41.3%)	36 (48%)		
BMI (kg/m^2)	22.81±2.21	23.95±2.16	<0.001	S
Systolic Blood Pressure (mmHg) on admission	152.51±8.9	151.34±7.8	0.396	NS
Diastolic Blood Pressure (mmHg) on admission	96.78±6.33	97.43±6.12	0.524	NS

The average age of patients admitted in our study was 22.11 ± 2.61 years ranging from 18-35 years. We selected Primigravidas for the present study as nulliparity does not only have high risk of pre-eclampsia but is the

most common maternal risk factor which can easily be assessed just by the history. Nearly half of the women belonged to rural area while the other half belonged to urban area with no significant difference observed in terms of residence and religion. This study excluded the women with BMI >40 kg/m2. However, the mean BMI of women with EOP was 22.81 ± 2.21 kg/m2, women with LOP had a significantly higher BMI (23.95 ± 2.16 kg/m2) [p-value< 0.001] as is well documented in many studies that overweight and obese women have a higher incidence of development of PE. [Table 1]

Table 2: Association between gestational age (POG of onset) and severity of pre-eclampsia

Onset of Pre-eclampsia (POG in weeks)	Mild	Severe	Total	Chi-square Test (χ^2)	p-value
Early (<34 weeks)	31 (36.5%)	44 (67.7%)	75 (50%)	14.362	<0.001
Late (≥ 34 weeks)	54 (63.5%)	21 (32.3%)	75 (50%)		
Total	85 (100%)	65 (100%)	150(100%)		

In our study, out of 75 women who developed PE before 34 weeks of gestation (EOP), 67.7% had severe form of PE which was significantly higher than 32.3% of females developing severe PE amongst women developing PE after 34 weeks (LOP). [Table 2]

Table 3: Association Between Mode of Delivery and onset of pre-eclampsia (n = 150)

Mode of Delivery	Pre-eclampsia			Chi-Squared Test	
	EOP	LOP	Total	$\chi 2$	p-value
VD	31 (41.3%)	50 (66.7%)	81 (54%)	9.688	0.001
LSCS	44 (58.7%)	25 (33.3%)	69 (46%)		
Total	75 (100.0%)	75 (100.0%)	150 (100.0%)		

Overall, out of 150 women included in our study 69 (46%) underwent LSCS. Percentage of women delivering by LSCS was significantly higher in women developing PE before 34 weeks (58.7%) compared to 33.3% women with LOP delivered by LSCS. This result shows that cesarean rate increasing with the early onset of disease. [Table 3]

Table 4: Association of Maternal Complications developed and Onset of Pre-eclampsia

Complication	EOP (n=75) [n/%]	LOP (n=75) [n/%]	TOTAL (n=150) [n/%]
APH	12 (16%)	9 (12%)	21 (14%)
Eclampsia	9(12%)	9 (12%)	15(10%)
Hellp	8(10.7%)	10(13.3%)	18(12%)
DIC	2(2.7%)	3(4%)	5(3.3%)
ATN	2(2.7%)	3(4%)	5(3.3%)
Intra-cranial Hemorrhage	1(1.3%)	0(0)	1(0.6%)
Pulmonary Edema	5(6.7%)	5(6.7%)	10(6.6%)
Chorioamnionitis	0(0)	1(1.3%)	1(0.6%)
Retinopathy	1(1.3%)	0(0)	1(0.6%)
PPH	10(14.7%)	16(19.5%)	26(17.3%)
Total	50(66.7%)	53(70.7%)	103(68.7%)

The comparison of all the antepartum, intrapartum and postpartum complications in early and late onset preeclamptic participants are shown in Table 4.

Postpartum Hemorrhage (PPH) [17.3%] was the most common complication that occurred in the participants followed by Antepartum Hemorrhage (APH) which occurred in 21 participants, a little over half of whom had EOP. While the proportion of participants who had PPH, HELLP, DIC (Disseminated Intravascular Coagulation) and ATN (Acute Tubular Necrosis) was more in the LOP group and the proportion of participants who had APH, Eclampsia and pulmonary edema was more in EOP group, the intergroup difference was not statistically significant (p value >0.05).

Discussion

In our study out of 150 primigravida booked and equally divided into EOP and LOP group. Females in both the groups were comparable in terms of age and had equal representation from urban and rural population and had no significant difference in terms of religious representation. Systolic and diastolic BP was recorded at admission and there was no significant difference between the 2 groups.

In our study significantly higher number of females (67.7%) who developed pre-eclampsia before 34 weeks (EOP) had severe features as compared to females (32.3%) who developed pre-eclampsia at or after 34 weeks (LOP). This observation is similar to the findings of study by Wadhwani P et al. [8], where significantly more women with EOP than those with LOP developed severe features and required treatment with antihypertensive drugs and magnesium sulfate. Lisonkova S et al. [9] in their study on temporal trends in early and late onset pre-eclampsia found that severity of disease was relatively lower in women with late onset pre-eclampsia.

Our study shows significantly higher number, 44 (58.7%) out of 75 women in EOP group delivered by cesarean section while only 25 (33.3%) out of 75 women in LOP group delivered by cesarean section. Demonstrating that women with early onset pre-eclampsia required surgical intervention for delivery thus leading to more surgery related complications. Our results were similar to study by Pettit et al. [10], where cesarean section rate was highest (70%) in the EOP group. But Wadhwani P et al. [8] in their study found that even though number of women undergoing cesarean section in EOP group was more than LOP group but the difference was not significant.

Maternal complications were seen in 50 (66.7%) out of 75 women in EOP group and in 53 (70.7%) out of 75 women in LOP group in our study and there was no significant difference between the 2 groups. While the proportion of participants who had PPH, HELLP syndrome, DIC and ATN was more in the LOP group and the proportion of participants who had APH, Eclampsia and pulmonary edema was more in EOP group, but the intergroup difference was insignificant. In study by Wadhwani P et al. [8], the most common maternal complications were HELLP syndrome, abruptio placentae, and eclampsia in both groups but no significant intergroup difference was noted in adverse maternal outcomes. Consistent with the present study, the rate of antepartum hemorrhage was significantly higher in the study conducted by Lisonkova et al. [9]. Another study published by Pettit et al. [10] concluded that pre-eclampsia causes significant maternal organ dysfunction (acute kidney injury, abnormal liver function, thrombocytopenia, and neuronal complications) regardless of gestational age at onset.

Conclusion

In conclusion, females with early onset and late onset PE are prone to develop adverse maternal outcomes

irrespective of gestational age of onset of disease. Women who develop PE early tend to have disease with severe features concluding the inverse proportion of onset of PE with its severity. Present study concluded cesarean section to be a valid option for women with EOP owing to low bishop's score and severity, demanding urgent delivery. Our study thus confirms timing of onset of PE to be one of the important modalities to be considered while evaluating women with PE.

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