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A Comparative Study of Early Versus Late Onset Pre-Eclampsia

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Abstract

Background: It is a comparative study of early onset pre-eclampsia (EOP) and late onset pre-eclampsia (LOP). Aim of Study: To compare clinical features and maternal and perinatal outcomes in patients with early onset and late onset pre-eclampsia.

Methods: This prospective longitudinal study was performed at tertiary referral hospital. All patients meeting the inclusion criteria were divided in two groups, the EOP and the LOP group, according to gestational age at onset of disease. The distinction criteria for early versus late onset disease were set as 34 week gestational age. Clinical features and maternal and perinatal outcomes were compared between the two groups.

Result: Mean gestational age at onset (p-value 0.00) was significantly lower in EOP group and systolic blood pressure (p-value0.031) was statistically significantly higher in the EOP group than in LOP Group. Maternal complications were higher in EOP group (25%) than LOP group (8.33%) but they were not statistically significant.EOP Group had a higher adverse birth outcome than in LOP group. EOP group had higher rates of NICU admissions (40%), still birth (13.33%), SGA (20%), neonatal mortality (10%) and lower APGAR scores at 1 min(48.33%) and 5 min (33.33%) compared to LOP group.

Conclusion: Early onset pre-eclampsia (EOP) is a distinct and more severe clinical entity with significantly higher rates of fetal and neonatal morbidity and mortality as compared to late onset pre-eclampsia(LOP). Therefore, early recognition and timely intervention can improve the maternal and fetal outcome.

Keywords: LOP,EOP, NICU, Pre-eclampsia.

Introduction

Preeclampsia is a multiorgan disease process of unknown aetiology characterized by de novo development of hypertension and proteinuria after 20 weeks of gestation, sometimes progressing into a multiorgan cluster of varying clinical features.[1]The incidence of preeclampsia is 2 to 10% of all pregnancies in the world. According to WHO the incidence is 7 times greater in developing countries

compared to developed countries.[2]Now pre-eclampsia is being characterized as two different disease on the basis of gestational age:-

Early onset pre-eclampsia (EOP)- is usually defined as pre-eclampsia developing before 34 wks of gestation.

Late onset pre-eclampsia (LOP)- develops at or after 34 wks of gestation.[3]

Even though the presenting features overlap, there are differences in maternal and perinatal outcome, prognosis and complications. Early and late onset preeclampsia have different etiologies and should be considered as different diseases.[4] There are also important differences in the mechanisms of the disease in the two forms: EOP is linked with compromised trophoblastic differentiation and placental hypoxia and LOP is related to preexisting maternal conditions that somehow could affect endothelial integrity. Although poor placentation plays a much greater role in the pathophysiology of the EOP, endothelial dysfunction seems to be presented in early and late forms of this disease. The elevated concentration of placental debris in maternal circulation of patients that develop pre-eclampsia after 34 weeks of pregnancy is probably due to a reduction in the serum clearance of those substances, which are in its majority metabolized by healthy endothelial cells.[5] EOP is commonly associated with abnormal uterine artery doppler, fetal growth restriction (FGR), and adverse maternal and neonatal outcomes.[6-7] In contrast, LOP is mostly associated with normal or slight increased uterine resistance index, a low rate of fetal involvement, and more favourable perinatal outcomes.[7-8]

These observations may contribute to increased knowledge about both the clinical entities, identification of possible risk factors and may contribute to improvements in clinical management. Therefore, our objective was to evaluate similarities and differences on clinical findings in patients with EOP and LOP.To this end, we also compared maternal and perinatal outcomes for EOP and LOP patients.

Aim and objectives:

To compare clinical findings and maternal and perinatal outcomes in patients with early onset pre-eclampsia and late onset pre-eclampsia.

Inclusion criteria

- Singleton viable pregnancies
- Women with pre-eclampsia / eclampsia

Exclusion criteria

- Chronic hypertension
- Diabetes mellitus / gestational diabetes mellitus
- Renal disease
- Liver disease
- Autoimmune disease

Methodology

It is a prospective & longitudinal observational study conducted at Department of Obstetrics and Gynaecology, SMS Medical College & associated Hospitals, Jaipur, India, from June 2018 to October 2019. Approval of the Local Ethics Committee was obtained before beginning this study and informed consent was obtained from all participating patients. Patients who chose to participate were clinically evaluated and the final diagnosis of preeclampsia was derived according to American College of Obstetrics and Gynaecology (ACOG) criteria.[9] All patients meeting the inclusion and exclusion criteria were divided into two groups, EOP and LOP according to gestational age at the onset of the disease. The distinction criterion for early versus late onset was set as 34 weeks of gestation. 60 women with early onset pre-eclampsia (EOP) and 60 women with late onset pre-eclampsia (LOP) admitted in hospital were taken as

sample population. Gestational age was confirmed by first trimester or early second trimester sonographic findings. Evaluated maternal demographic characteristics included age, booking status, residence, socioeconomic status, literacy and gravidity. Clinical findings were the presence of prodromal symptoms (headache, nausea, vomiting, upper abdominal pain and visual disturbance), gestational age (weeks) when HTN developed, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure at admission (MAP), pre-tibial edema and previous history of pre-eclampsia. Maternal complications evaluated were Abruption, Pulmonary oedema, Acute renal failure, DIC, PPH. Birth outcomes like admissions to neonatal intensive care unit (NICU), low APGAR score (<7 at 1min and 5 min), Still birth (SB), Birth weight (gm),SGA and Neonatal Mortality were evaluated.Data was collected and statistically analyzed using Epi-info software. P-value<0.05 was considered statistically significant.

Observation and discussion

In our study, majority of women were in age group of 25 years or below in both groups. The mean age in EOP Group was 26.53±4.57 year and in LOP Group 25.6±3.64 year which was not statistically significant. 56.67% patients in EOP group and 40% patients in LOP group belonged to booked category. In EOP Group 53.33% patients and in LOP Group 50% patients belonged to urban area. Majority of women belonged to lower middle socioeconomic status in both groups. More number of patient in study were literate with 75% in EOP group and 83.33% in LOP group.

Table 1: Distribution of patient according to gravidity of patients

Gravidity	EOP group		LOP group	
	No	Percentage	No	Percentage
G1	31	51.67	35	58.33
G2	15	25.00	14	23.33
G3	7	11.67	7	11.67
G4 and beyond	7	11.67	4	6.67
Total	60	100.00	60	100.00

p-value = 1.000(ns)

51.67% in EOP group and 58.33% women in LOP Group were primigravida which was not statistically significant. Parra-Cordero M et al (2012)[10] had 47.1% primigravida in early onset preeclampsia and 52.8% in late onset preeclampsia. Kucukgoz Gulec U et al (2013)[3] had 43.6 % primigravida in early onset preeclampsia and 43% in late onset preeclampsia. Junus K et al (2014)[11] in their study found 67% primigravida in early onset preeclampsia and 55% in late onset preeclampsia.

Table 2: Distribution of cases according to clinical characteristics

Parameters	EOP group	LOP group	p-value
1 – Age	26.53±4.57	25.61±3.64	0.225(ns)
2- Prodromal symptoms	11	10	1.00(ns)
3- Gestational age (weeks) at HTN develop	30.28±1.78	36.86±2.25	0.00(s)
4-Systolic blood pressure (mmHg)	156.5±19.99	150±11.54	0.031(s)
5- Diastolic blood pressure (mmHg)	102.1±14.75	98.87±7.32	0.131(ns)
6 – MAP	119.8±15.66	115.7±8.14	0.075(ns)
7- Pre-tibial edema	33(55.00%)	34(56.67%)	1.00(ns)
8- History of previous pre eclampsia	4	0	0.127(ns)

Mean gestational age at onset was significantly earlier(p-value 0.00) and systolic blood pressure(p-value0.031) was statistically significantly higher in the

EOP group than in the LOP group. There were no statistically significant differences between the groups with respect to maternal age, prodromal symptoms, diastolic blood pressure, mean arterial pressure and pre-tibial edema. EOP group had higher ratio of history of previous preeclampsia.

Ni Y et al (2016)[12] study had mean maternal age 30.62 ± 4.4 years in EOP and 30.81 ± 3.348 years in LOP group. Mean gestational age at onset was significantly earlier in the EOP(31.37 ± 2.56 weeks) group than in the LOP group(37.63 ± 1.73) ($P < 0.05$).No statistically significant differences were seen on admission between the two groups in maternal age, the rate of the prior pregnancy with hypertensive disorder, systolic blood pressure and diastolic blood pressure. Kucukgoz U et al (2013)[3] found mean maternal age 30.4±7.9 years in EOP and 29.2±7.4years in LOP and The mean gestational age(p-value <0.001),Diastolic blood pressure(p-value0.018) and the previous preeclamptic (p- value0.016) was significantly higher in the EOP group than in the LOP group.There were no statistically significant differences between the groups with respect to maternal age, systolic blood pressure, mean arterial blood pressure on admission, the degree of pre-tibial edema and the presence of prodromal symptoms . W´ojtowicz A et al (2019)[13] study found mean maternal age 30.7 ± 5.5 years in EOP and 30.1 ± 5.3 in LOP. Mean gestational age was significantly lower in the EOP group than in the LOP group ($p < 0.001$). The EOP group had a Significantly higher mean systolic ($p< 0.005$) and diastolic blood pressure ($p <0.026$) on admission Compared to the LOP group. There were no statistically significant differences between the groups with respect to maternal age and previous preeclamptic pregnancy

Table 3: Distribution of cases according to maternal complication.

Maternal complication	EOP-group	LOP-group
Abruption	2(3.33%)	2(3.33%)
Pulmonary oedema	4(6.67%)	1(1.67)
Acute renal failure	1(1.67%)	0(0%)
DIC	1(1.67%)	0(0%)
PPH	7(11.67%)	2(3.33%)
Total	15(25%)	5(8.33%)

P value 0.712 (ns)

Maternal complication was higher in EOP group (25%) than LOP group (8.33%) but they were not statistically significant.

Ni Y et al (2016)[12] in their study found that there were no statistically significant differences between EOP and LOP groups in comparison to the incidence of Abruption,Pulmonary oedema,Acute renal failure,DIC ,PPH ($P > 0.05$). Kucukgoz U et al (2013)[3] conducted a study in which maternal complications due to pre-eclampsia, such as abruption of the placenta, ARF and pulmonary edema were not sufficient to show differences between the groups. W´ojtowicz A et al (2019)[13] studied that maternal complication Placental abruption, Pulmonary edema and Renal insufficiency were higher in EOP than in LOP but there were no statistically significant difference. LOP had higher ratio of DIC but it was not statistically significant.

Table 4: Distribution of patients according to birth outcome

Birth Outcome	EOP group		LOP group		p-value
	No.	%	No.	%	
NICU Admission	24	40.00	16	26.67	0.175 (ns)
APGAR score at 1 min <7	29	48.33	12	20.00	0.002 (s)
APGAR score at 5 min <7	20	33.33	3	5.00	0.001 (s)
Still birth (SB)	8	13.33	1	1.67	0.038 (s)

Birth weight (gm)	1679 ± 404		2677 ± 569		0.00 (s)
SGA	20	33.33	9	15.00	0.033 (s)
Neonatal Mortality	6	10.00	2	3.33	0.272 (ns)

Low APGAR score at 1 min (p-value = 0.002), 5 min (p-value = 0.001) and still birth (p-value = 0.038) were significantly higher in EOP group as compared to LOP group. Birth weight was significantly higher in LOP group than EOP group (p-value=0.00). NICU admission (40.00%), SGA (33.33%) and neonatal mortality (10.00%) were also higher in EOP group than LOP group.

Kucukgoz U et al (2013)[3] study conducted in which low APGAR score (APGAR score at 5 min <7) (p-value<0.001), admission to NICU (p-value<0.001) and birth weight (p-value < 0.001) were statistically different in between the groups. There was no significant difference in stillbirth (p-value = 0.767). Ni Y et al (2016)[12] study had a significantly higher incidence rate of neonatal intensive care unit admission (p = 0.001), low-birth weight infants (p = 0.001) in the EOP group than in the LOP group. Veerbeek JH et al (2015)[14] studied that the birth weight and small for gestational age offspring were significantly different in women who had early-onset pre-eclampsia when compared with women with late-onset pre-eclampsia. Lisonkova S et al (2013)[15] in there study found that the incidence of NICU admission (p<0.01) and SGA (p<0.01), were significantly elevated among the early onset group than the late onset group.

Conclusion

Early onset preeclampsia(EOP) is a distinct and more severe clinical entity with significantly higher rates of fetal and neonatal morbidity and mortality as compared to the late onset preeclampsia(LOP). Therefore, early recognition and timely intervention can improve the maternal and fetal outcome.

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