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Original Research Article

To Study the Risk Factors Associated with Early Onset versus Late Onset Preeclampsia and Its Fetomaternal Outcome

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ABSTRACT

Objectives: a) To identify the different risk factors in early onset and late onset Preeclampsia. b) To compare the Fetomaternal outcomes in both the groups.
Study design: This was a one year cross-sectional study conducted in the Department of Obstetrics and Gynaecology at Gauhati Medical College and Hospital. 200 mothers with Preeclampsia were taken and 100 were grouped into Early onset preeclampsia (EO-PE) (<34 weeks of gestation) and another 100 into Late onset preeclampsia (LO-PE) (≥34 weeks of gestation). Data about maternal risk factors, maternal complications, foetal and neonatal outcome were analysed and statistical significance determined.
Results: Primiparity, increasing BMI, family history of preeclampsia and male sex of the foetus were found to be important risk factors in development of EO-PE. All the maternal complications like eclampsia, sepsis, systemic disorders, ICU admissions and maternal deaths were higher in EO-PE as compared to LO-PE. Greater number of patients with EO-PE progressed to develop severe preeclampsia. The rate of neonatal complications like abnormal umbilical artery Doppler, low birth weight, reduced APGAR score was higher in EO-PE. Incidence of NICU admissions and neonatal/perinatal deaths was also noted to be higher in EO-PE.
Conclusion: Classification of preeclampsia into early and late onset has both etiological and prognostic value. Early detection, close monitoring, timely intervention by the obstetrician and good neonatal care by the paediatrician is the key for successful outcome in both early onset and late onset preeclampsia.

Keywords: Early onset preeclampsia, Late onset Preeclampsia, Maternal, neonatal outcome, risk factors and outcome.

INTRODUCTION

Hypertensive disorders of pregnancy are an important cause of maternal morbidity and mortality. It is reported to be the second most common cause of maternal death worldwide. Globally, incidence of hypertensive disorders in pregnancy is about 5-10%. Data collected from the National Eclampsia Registry (NER) of India shows the incidence of hypertensive disorders in pregnancy as 10.08%. [1] The prevalence of Preeclampsia in Assam was found out to be 57.4%. [2]

Preeclampsia is characterized by elevated blood pressure and proteinuria after 20 weeks of gestation and upto 6 weeks postpartum, and/or associated organ involvement. [3,4] It is unique to human pregnancy, and is characterized by abnormal vascular response to placentation associated with increased systemic vascular resistance, enhanced platelet aggregation, activation of coagulation system and endothelial dysfunction. [5] Although, the exact pathogenesis of preeclampsia still remains to be unrevealed and is most likely multifactorial, it is increasingly clear that

pathological processes at the interface of the fetal and maternal circulation leading to generalized endothelial cell dysfunction contribute to the spectrum of the disease. [6] Recently, investigators have begun to classify preeclampsia based on the period of gestation at which first onset of the disease occurred. Early onset preeclampsia (EO-PE) is that which develops before 34 weeks of gestation and Late onset preeclampsia (LO-PE) is that which develops at or after 34 weeks of gestation. The two subtypes have similar clinical presentation but studies indicate that they are associated with different predisposing factors, heritability, biochemical markers and different maternal, foetal and neonatal outcome. [1,7]

Early onset preeclampsia (EO-PE) has been identified to be a placental disease and Late onset preeclampsia (LO-PE) as a maternal disease. EO-PE has familial predisposition suggestive of genetic factors and high recurrence risk. It is typically associated with placental dysfunction, reduction in placental volume, intrauterine growth restriction, abnormal uterine and umbilical artery Doppler studies, low birth weight, multiorgan dysfunction, perinatal death and adverse maternal and neonatal outcomes. LO-PE arises due to metabolic risk factors of the mother such as obesity, chronic hypertension and diabetes. It being typically a maternal disease is more often associated with normal placenta, larger placental volume, normal fetal growth, normal uterine and umbilical artery Doppler studies, normal birth weight and more favourable maternal and neonatal outcomes. [8,9] For preeclampsia, the complications often quoted are eclampsia, abruption placentae, renal failure and DIC. [10,11] Foetal complications are foetal hypoxia leading to intrauterine growth restriction and death. Neonatal morbidity includes prematurity, low birth weight and asphyxia injury necessitating increased need of NICU admissions. [12,13]

Early onset preeclampsia in particular confers a higher risk of maternal and foetal complications. Early delivery of the foetus is the only definitive treatment for this condition, but this early termination is fraught with the risk of poor neonatal outcome. [14,15] To counter this, expectant management is a strategy employed by Obstetricians to improve perinatal outcome, however this may lead to increased maternal complications. [10,11]

Objectives:

1) To identify the different risk factors in early onset and late onset preeclampsia.
2) To compare the fetomaternal outcomes in both the groups.

MATERIALS AND METHODS

Setting

It was a Cross-sectional study conducted in the Department of Obstetrics and Gynaecology, Gauhati Medical College and Hospital, Guwahati for a period of 1 year from July 2017 to June 2018. 200 antenatal patients with preeclampsia were included in the study, out of which 100 had Early onset preeclampsia and another 100 had Late onset preeclampsia.

Inclusion criteria

All pregnant women ≥20 weeks of gestation with blood pressure ≥ 140/90 mm of Hg along with proteinuria.

Exclusion criteria

1) Pregnant women with essential hypertension or hypertension present before 20 weeks of gestation.
2) Patients with pre-existing renal disease, diabetes mellitus, liver disease and other medical disorders.

Data of the patients who were admitted with preeclampsia were collected in a proforma from time to time and were followed upto delivery and discharge. All the antenatal patients were subjected to clinical and obstetrical examination, laboratory investigations and ultrasound examination along with Doppler study of the umbilical artery. The patients were divided into Early onset and Late onset preeclampsia and were matched according to their characteristics.

Statistical analysis

Statistical analysis was done using Chi square test and p values were taken. A p value of <0.05 was considered significant.

RESULTS AND OBSERVATIONS

Table 1: Age Distribution

AGE GROUP	NUMBER OF EO-PE	PERCENTAGE (%)	NUMBER OF LO-PE	PERCENTAGE
15-19	4	4%	12	12%
20-24	13	13%	35	35%
25-29	51	51%	43	43%
30-35	32	32%	10	10%

Patients with both type of Preeclampsia presented more in the 25-39 years age group, although the difference between the two groups was not statistically significant (p<0.05).

Table 2: Parity Distribution

PARITY	EO-PE	PERCENTAGE (%)	LO-PE	PERCENTAGE (%)
PRIMIGRAVIDA	94	94%	75	75%
MULTIGRAVIDA	6	6%	25	25%
TOTAL	100	100%	100	100%

Early and late onset preeclampsia was found to be manifested more in Primigravida mothers as compared to multigravida, which was found to be statistically significant (p<0.05).

Table 3: BMI Distribution

BMI (kg/m^2)	EO-PE	PERCENTAGE (%)	LO-PE	PERCENTAGE (%)
< 18.5	7	7%	10	10%
18.5 – 24.9	66	66%	88	88%
25 – 29.9	14	14%	2	2%
> 29.9	13	13%	0	0

Higher BMI (> 24.9) was associated with higher incidence of EO-PE than LO-PE, which was found to be statistically significant (p<0.05).

Table 4: Relation of other Risk factors

RISK FACTORS	EO - PE	PERCENTAGE (%)	LO - PE	PERCENTAGE (%)	P VALUE
FAMILY H/O PREECLAMPSIA	26	26%	11	11%	0.0101
CHRONIC HYPERTENSION	30	30%	0	0	0.0001
H/O PREECLAMPSIA IN PREVIOUS PREGNANCIES	6	6%	6	6%	1
OTHER CO-EXISTING MEDICAL DISORDERS	28	28%	16	16%	0.0597

The incidence of family h/o preeclampsia, Presence of chronic hypertension and other co – existing medical disorders was higher in Early onset preeclampsia as compared to Late onset preeclampsia. The incidence of preeclampsia in previous pregnancies was equal in both the groups. Presence of chronic hypertension in present pregnancy was found to be associated solely with Early onset preeclampsia and was found to be statistically significant (p<0.05).

Table 5: Severity of the disease

	EO-PE	PERCENTAGE (%)	LO-PE	PERCENTAGE (%)
MILD PREECLAMPSIA (<160/110 mm Hg)	26	26%	57	57%
SEVERE PREECLAMPSIA (≥160/110 mm Hg)	74	74%	43	43%

The incidence of severe preeclampsia is higher in early onset preeclampsia than late onset preeclampsia, which was found to be statistically significant (p<0.005).

Table 6: Maternal outcomes

	EO-PE	PERCENTAGE (%)	LO-PE	PERCENTAGE (%)	P VALUE
ECLAMPSIA	20	20%	8	8%	0.0237
SEPSIS	14	14%	1	1%	0.0006
SYSTEMIC DISORDERS	24	24%	6	6%	0.0006
OTHER COMPLICATIONS	16	16%	4	4%	0.0081
ICU ADMISSIONS	9	9%	1	1%	0.0185
MATERNAL DEATH	3	3%	0	0%	0.2462
UNEVENTFUL	46	46%	80	80%	0.0001

There was higher incidence of complications like eclampsia (20%), sepsis (14%), systemic disorders (24%), other complications (16%), ICU admissions (9%) and maternal deaths (3%) in Early onset Preeclampsia, which was statistically significant ($p<0.05$).

Table 7: Distribution of Doppler findings

DOPPLER FINDINGS	EO - PE	PERCENTAGE (%)	LO - PE	PERCENTAGE (%)
NORMAL	72	72%	83	83%
ABNORMAL	28	28%	17	17%

The incidence of abnormal Umbilical artery Doppler findings on ultrasound was found to be higher in EO – PE than LO – PE. It was found to be not statistically significant ($p<0.05$).

Table 8: Condition at birth

CONDITION AT BIRTH	EO-PE	PERCENTAGE (%)	LO-PE	PERCENTAGE (%)
LIVE	74	74%	98	98%
STILLBORN	18	18%	2	2%
MACERATED STILLBORN	8	8%	0	0

Most of the pregnancies in EO-PE and LO-PE resulted in live births though the incidence was higher in LO-PE, which was statistically significant ($p<0.05$). The incidence of stillbirth was higher (18% vs 2%) in EO-PE than LO-PE with no cases of macerated stillbirth reported in LO-PE.

Table 9: Differences in birthweight

BIRTHWEIGHT (kg)	EO-PE	PERCENTAGE (%)	LO-PE	PERCENTAGE (%)
> 3.5	0	0	1	1%
2.5 – 3.5	2	2%	74	74%
1.5 - < 2.5	43	43%	25	25%
1 - < 1.5	38	38%	0	0
< 1	17	17%	0	0

A majority of babies born to mothers with Preeclampsia (both early and late onset) were low birth weight (1.5 - < 2.5 kg). Very low birth weight babies (1 - < 1.5 kg) were seen only in mothers who presented with EO – PE.

Table 10: Variations in sex of the baby

SEX OF THE BABY	EO-PE	PERCENTAGE (%)	LO-PE	PERCENTAGE (%)
FEMALE	48	48%	46	46%
MALE	52	52%	54	54%

The incidences of male and female babies were almost equal in both EO-PE as well as in LO-PE ($p<0.05$).

Table 11: Other neonatal complications

COMPLICATIONS	EO-PE	PERCENTAGE (%)	LO-PE	PERCENTAGE (%)	P VALUE
MECONIUM STAINING OF AMNIOTIC FLUID	10	10%	35	35%	0.0001
APGAR SCORE < 7 AT 5 MINUTES	23	23%	11	11%	0.0373
NICU ADMISSIONS	57	57%	47	47%	0.0886
PERINATAL/NEONATAL DEATHS	42	42%	5	5%	0.0001

Except meconium staining of amniotic fluid, almost all other neonatal complications had a higher incidence in EO-PE than LO-PE respectively like APGAR score less than 7, NICU admissions and Neonatal/Perinatal deaths. The p value was 0.3015, which was not statistically significant between the two groups.

DISCUSSION

In the present study, age of the patients ranged from 18-37 years. The highest numbers of patients were in the age group 25-29 years in both EO-PE and LO - PE (51% and 34% respectively), followed by 30-35 years in EO-PE (32%) and 20-24 years in LO-PE (35%) respectively. This was followed by 20-24 years (13%) and 15 - 19(4%) in EO-PE as compared to 30-35 years (12%) and 15-19 years (10%) in LO-PE respectively. Though preeclampsia is described in extremes of age groups, there is no such trend seen in our study. Jeong E J et al (2009) and Nagajan Bhadarka et al (2016)

found no significant differences in maternal age between EO-PE and LO-PE. [16,17]

The incidence of Preeclampsia was found to be higher in Primigravida (n = 169) than in Multigravida (n = 31) in our study. It applied to both EO-PE and LO-PE. Raymond D et al (2011) and Lisonkova et al (2013) observed that primiparity increases the risk of EO-PE. [9,18]

Majority of the patients of both forms of Preeclampsia had normal BMI (n = 154). While there were no obese patients (BMI > 30) in LO-PE group, the number was as high as 13% in the EO-PE group. Rozanna Fang et al (2009) observed that pre - pregnancy and pregnancy obesity was associated with higher risk of Preeclampsia; though there was no such difference between EO-PE and LO-PE, [19] which was similar to our findings.

Although not statistically significant, 26% of EO-PE patients had positive family history of Preeclampsia as compared to 11% in LO-PE group, which was similar to the findings of Jayashree et al (2018) who observed that family history of Preeclampsia was an important risk factor for development of EO-PE. [20]

Only 6% of patients gave history of suffering from Preeclampsia in their previous pregnancies in both EO-PE and LO-PE. This was similar to the conclusions of Jeong E J et al (2009) who found no significant differences in EO-PE and LO-PE with regards to presence of family history of Preeclampsia. [19]

28% of patients with EO-PE and 16% of patients with LO-PE had other co-existing medical disorders in our study. Raymond D et al (2011), Lisonkova et al (2013) and L Markin et al (2017) observed that diabetes mellitus was associated with increased incidence of LO-PE. [9,21]

Most of the patients with EO-PE had or developed severe disease (≥ 160/110 mm Hg) as compared to LO-PE (74% vs 43%). This was similar to the observations made by Vinitha Wills et al (2014) who found that severe preeclampsia was more in patients of EO-PE than LO-PE. [22]

In our study, the incidences of all the maternal complications were found to be higher in EO-PE than in LO-PE, which was statistically significant: Eclampsia (20% vs 8%), Sepsis (14% vs 1%), systemic disorders (24% vs 6%) and other complications like PPH, abruptio placentae etc (16% vs 4%). The number of ICU admissions (9%) and mortality (3%) was also high in EO-PE. Umran Kucukgoz Gulec et al (2013) and Aziz A et al (2016) concluded that both maternal morbidity and mortality was higher in EO-PE. [23,24]

Overall in our study, the incidence of neonatal morbidity and mortality was higher in EO-PE than LO-PE. Although not statistically significant, 28% of the foetuses had abnormal Doppler findings in the EO-PE group as compared to only 17% in the LO-PE group. The incidence of fresh stillbirth (18% vs 2%) and IUFD (Macerated stillbirth) (8% vs 0%) was also high in EO-PE than LO-PE. The birth weight was observed to be better in the LO-PE group as compared to the EO-PE group most probably due to foeto placental blood flow wasn't compromised early in this group and pregnancy can be continued for longer duration. Birth weight of most babies was between 1.5 – 2.5 kg in the EO-PE group (43%) and between 2.5 – 3.5 kg in the LO-PE group (74%). There were no VLBW and ELBW babies in the LO-PE group. Although the total number of male foetuses was higher (106%) than female foetuses (94%) in our study, we didn't find any such statistically significant differences between EO-PE and LO-PE. Again, amongst the other neonatal complications except for meconium staining of amniotic fluid which was found to happen more in LO-PE than EO-PE (35% vs 10%), rest all other complications had a higher incidence in EO-PE; 23% of foetuses had APGAR score < 7 at birth in EO-PE as compared to 11% in LO-PE. Almost 60% of the babies born to mothers with EO-PE required NICU admissions. The perinatal/neonatal death rate was 42% in EO-PE as compared to only 5% amongst LO-PE babies. Jeong E J et al

(2009) reported higher rates of intrauterine fetal death; low APGAR score and perinatal death in EO-PE and Lisonkova et al (2013) found that EO-PE is associated with high risk of fetal death and neonatal morbidity. **[19,21]**

CONCLUSION

Hypertensive disorders of pregnancy have become a challenging problem. Nowadays, in the society, people wish to have less number of children but with best possible quality in the future development of the growing children. The classification of Preeclampsia into Early onset and Late onset has both etiological and prognostic importance. Association of various risk factors with both EO-PE and LO-PE has been demonstrated in the study. Hence, both primordial and primary prevention has an important role to play in decreasing the incidence and prevalence of the disease. The need for regular antenatal checkups should be stressed upon so that gestational hypertension can be detected at an early stage before it progresses to preeclampsia and so that timely intervention can be made and thus avoiding an unfavourable outcome. Preeclampsia without severe disease can be tried with conservative management to improve the neonatal outcome. However as the severity of the disease increases, the rate of maternal and foetal complications worsens necessitating termination of pregnancy. Finally, we conclude that early detection; monitoring and timely intervention by the obstetrician and good neonatal care by the paediatrician is the key for successful outcome in both forms of preeclampsia.

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