

A COMPARATIVE STUDY OF PERINATAL OUTCOME IN WOMEN WITH RECURRENT PRE-ECLAMPSIA TO WOMEN WITH PRE-ECLAMPSIA WHO WERE NORMOTENSIVE DURING THEIR PREVIOUS PREGNANCIES

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ABSTRACT

BACKGROUND AND OBJECTIVE

Pre-eclampsia is a systemic syndrome that occurs in 3-5% of the pregnant women and is the leading cause of maternal/neonatal morbidity and mortality. We designed a study to compare perinatal outcome in women with recurrent pre-eclampsia to women with women with pre-eclampsia who were normotensive during their previous pregnancies.

MATERIALS AND METHODS

This study was conducted in Dept. of Obstetrics and Gynaecology, Institute of Maternal and Child Health, Government Medical College, Kozhikode for a period of 1 year from March 2013 to February 2014. We conducted this study in multiparous women who developed pre-eclampsia in index pregnancy (n=110). Among these, women who had pre-eclampsia in previous pregnancies (n=55) were compared to those who remained normotensive during their prior pregnancies (n=55). Maternal and foetal variables were compared. Multivariate logistic analyses were performed to examine the impact of pre-eclampsia on foetal outcome, preterm delivery, IUGR, still births adjusted for confounding variables.

RESULTS

No statistical significant difference was observed between the 2 groups in terms of age, gravida, parity. Women who experienced recurrent pre-eclampsia were at elevated risk for early onset of pre-eclampsia, deranged laboratory investigations (Hepatic and Renal parameters, Coagulation Profile), higher chances of maternal complications, foetal mortality and morbidity (Statistically significant $P < 0.05$). Foetal loss was higher in women with recurrent pre-eclampsia (14.5%) than in women with pre-eclampsia who had normotensive pregnancy history (1.8%).

CONCLUSION

Women with recurrent pre-eclampsia had a higher rate of perinatal loss compared to women with pre-eclampsia who were normotensive in their prior pregnancies.

KEYWORDS

Pre-eclampsia, Proteinuria, Intrauterine Growth Restriction.

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INTRODUCTION: Pre-eclampsia (PE) is an idiopathic multisystem disorder specific to pregnancy puerperium.¹ Despite the considerable morbidity and mortality, the cause of PE has remained enigmatic.² Complications of hypertension are the third leading cause of pregnancy-related deaths and associated with increased risks of placental abruption, acute renal failure, cerebrovascular and cardiovascular complications, disseminated intravascular coagulation, and maternal death. Consequently, early diagnosis of pre-eclampsia and close observation are imperative.³⁻⁴ Recurrence of PE has been shown to affect 13-18% of subsequent pregnancies.⁵⁻⁹ Isolated PE in the second pregnancy was about 2%.¹⁰

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Risk factors for recurrent PE include family history of PE/HTN, Hypertensive disorders in pregnancy, Overweight, Gestational length at the onset of HTN.¹⁰ Various authors studied regarding the perinatal outcome in recurrent PE and in women with isolated PE with previous normotensive pregnancies and had conflicting results. Mbah et al noted that pre-eclampsia in the first pregnancy was associated with significantly increased risk of recurrent PE, reduced foetal growth, stillbirth and placental abruption in the second pregnancy.¹¹⁻¹³ Mendilcioglu et al¹³ also had similar findings. Chen et al¹⁴ had noted no statistically significant difference in maternal-foetal outcomes such as gestational age at delivery and maternal serum biochemical levels.¹⁴

The various mechanisms have been implicated for the poor outcome in recurrent PE women.¹⁴ Based on these observations, we designed a cohort study consisting of 2 groups: Group A with Isolated PE (Who has PE in this pregnancy, normotensive in previous pregnancy) and Group B with recurrent PE. Perinatal outcomes between both the groups were compared.

AIM OF THE STUDY: The aim of the study is to compare perinatal outcome in women with recurrent pre-eclampsia to women with pre-eclampsia who were normotensive during their previous pregnancies.

STUDY DESIGN: It was a cohort case study conducted in Institute of Maternal and Child Health.

MATERIALS AND METHODS:

1. All multigravida patients (with gestation age >20 weeks) were evaluated and prior history of pre-eclampsia/eclampsia were documented.
2. Patients were included in the study as per Inclusion and Exclusion Criteria.
3. Written Informed Consent was taken for the study.
4. Patients were evaluated and categorised into pre-eclampsia and severe eclampsia (As per ISSHP definition).
5. Treatment initiated according to the guidelines.
6. Periodic checkup with BP was done.
7. Radiological, Urine and blood investigation, USG was done.
8. Patients were followed up.
9. Intrapartum monitoring was done.
10. Neonate evaluated and Birth weight/APGAR scores were documented.
11. Postpartum monitoring done for 6 weeks.

Study Setting: Patients getting admitted in Institute of Maternal and Child Health.

Study Period: 1 Yr. (March 2013 to Feb 2014).

Sample Size: 110 (55 each).

Inclusion Criteria: Multigravida with gestational age > 20 weeks.

Exclusion Criteria:

- Postpartum eclampsia.
- Foetal weight less than 1000 g.
- Gross Congenital Anomalies.
- Diabetes Mellitus.
- Chronic Medical Diseases.

Ethical Consideration: Patients were informed that they were a part of the study and consent was obtained from them. Confidentiality of the patients' identity was maintained.

Statistical Analysis: The Statistical software SPSS 16 (SPSS Version 16, SPSS, Inc.) was used for the analysis of the data and Microsoft Word and Excel have been used to generate graphs, tables, etc.

RESULTS: This study was carried out on a total number of 110 patients, 55 in each group: Group A - Women with pre-eclampsia who were normal in previous pregnancy. (Isolated pre-eclampsia).

Group B- Women with recurrent pre-eclampsia.

	Group A Isolated	Group B Recurrent	P value
Age (mean)	27.5	28.8	0.1
Booked case	41.8%	54.5%	0.01
Referred early	18.2%	30.9%	
Referred late	40%	14.5%	
Onset of PE			
<28 weeks	1.8%	7.3%	0.001
28-32 weeks	5.5%	50.9%	
>32 weeks	92.7%	41.8%	
SBP			
140-150	58.2%	40%	0.038
150-160	38.2%	60%	
>160	3.6%	0	
DBP			
90-100	60%	40%	0.011
100-110	34.5%	60%	
>110	5.5%	0	
Thrombocytopenia <1.5 L	14.5%	20%	0.04
Abnormal coagulation status	0	12.7%	0.001
Abnormal LFT	1.8%	43.6%	0.0001
Abnormal RFT	12.7%	49.1%	0.0001
Interval between onset of PE to delivery			
< 4 weeks	96.4%	50.9%	0.0001
4-8 weeks	3.6%	47.3%	
>8 weeks	0	1.8%	

Table 1: Maternal Characteristics in Both Groups

Baseline characteristics of each group is given in Table 1. Among the study population, majority belong to age group 20-35 yrs. In regard to gravidity and parity, there was no significant difference between two groups. Most of the subjects of study population were booked cases. Among referred cases, patients of group A were referred late to our institute. Impending symptoms were seen more among group B. 13 patients in group B had severe pre-eclampsia in previous pregnancies.

In this study group, majority of patients had late onset pre-eclampsia >34 weeks. All the patients were on anti-hypertensives in both groups. In this study, patients with systolic BP of 140-150 were 32 among group A, 22 among group B; SBP of 150-160 were 21 in group A, 33 in group B; SBP >160 were 2 in group A, none in group B. 33 patients of group A, 22 of group B had DBP 90-100 mmHg. 19 patients in group A, 33 in group B had DBP 100-110. Only 3 in group A had DBP >110 mmHg. Majority of patients had no thrombocytopenia. 8 patients in group A, 11 in group B belong to class 1 thrombocytopenia. In this study, only group B patients had abnormal coagulation profile. Group B patients had statistically significant abnormal LFT and RFT. In group A, 11(20%) had spontaneous vaginal delivery, 38

(69.1%) had induced vaginal delivery, 6 (10.9%) underwent LSCS.

In group B, 19 (34.5%) had spontaneous vaginal delivery, 23 (41.8%) had induced vaginal delivery, 13 (23.6%) underwent LSCS. In this study, majority of patients' interval between onset of pre-eclampsia to delivery is <4 weeks. Maternal complications were more seen in group B.

	Group A Isolated PE	Group B Recurrent PE	P value
Preterm foetus			0.006
28 weeks	1.8%	0	
28-34 weeks	5.5%	27.3%	
>34 weeks	92.7%	72.7%	
Birth weight (mean±SD)	2.68±0.36	2.32±0.3	0.0001
IUGR	29.1%	67.3%	0.0001
Low APGAR	18.1%	36.3%	0.023
Neonatal death	1.8%	14.5%	0.015
Still birth	3.6%	9%	0.3

Table 2: Perinatal outcome in Each Group

The Birth weight of the child between Group A and Group B was statistically significant (P value - 0.0001). In this study, birth weight <2.5 kg was found in 19 patients in group A, 40 in group B. Birth weight between 2.5 kg to 3.5 kg was in 34 patients in group A, 14 in group B. Weight >3.5 kg was found in 2 patients in group A. IUGR babies between Group A and Group B was statistically significant (P value - 0.0001). In our study, 16 in group A and 37 patients in group B had IUGR, APGAR Scores between Group A and Group B were statistically significant (P value-0.023).

Neonatal death was noted more in Group B (14.5%) and was statistically significant (p value-0.015). Still births between Group A and Group B were statistically not significant (P value - 0.3). Postpartum stay for more than 4 weeks was seen in two patients in group A, both of them were for baby sake. Post-delivery BP status between group A and group B was statistically not significant (p value - 0.19).

DISCUSSION: We conducted this study in Government Medical College, Calicut for a period of 1 Yr. from March 2013 to Feb 2014. 110 patients were enrolled in the study (55 in each group). For women without pre-eclampsia in the first pregnancy, the risk of pre-eclampsia in the second pregnancy increased with increasing time interval between deliveries, whereas for women with pre-eclampsia in the first pregnancy the risk tended to decrease with increasing time interval between deliveries.¹⁵ The incidence rate of pre-eclampsia in the second pregnancy was 2.0%. Our study focuses on the perinatal outcome between the 2 groups. The age, gravidity and parity was matched within the 2 groups. Most of the women who had previous normotensive pregnancy probably had no complications in this pregnancy, so they were referred late to our institute. The women who

had PE in their previous pregnancy were more cautious and most of these cases were booked.

They had regular ANC visits. The previous normotensive women had epigastric pain as their major symptoms whereas those with previous eclampsia had wide array of symptoms. The possible cause for this is not known. Onset of labour was <32 weeks in 58.2% of women with recurrent PE whereas most of them who had previous normotensive pregnancy had onset of labour >32 weeks (94.5%). Mbah et al had 45% onset of labour <32 weeks in recurrent PE and 33% in isolated PE in whites; in blacks 50.3% in recurrent PE and 41.7% in isolated PE; and in Hispanics 46.7% in recurrent PE and 39% in isolated PE. Mendilcioglu et al¹³ showed onset of labour <32 weeks in recurrent PE was 19% and with isolated PE was 27.9%. Nir et al had 5.7% of onset of labour <34 weeks in recurrent PE.

Our study had more onset of labour <32 weeks in recurrent PE and less onset of labour <32 weeks in isolated pregnancy. So with such variation of results from 5.7% (<34 weeks) to 50.3% we conclude similar to Mbah et al that ethnicity plays a factor in preterm delivery regardless to previous PE status. Mean Systolic and Diastolic BP was slightly higher in women with recurrent pre-eclampsia. Some women in the isolated pre-eclampsia had peaked with systolic BP>160 mmHg and Diastolic BP >110 mmHg and such high BP was not found in recurrent hypertensive group. This difference may be due to more frequent antenatal checkups and adequate control of the BP in the recurrent pre-eclamptic group. Thrombocytopenia was more in the recurrent pre-eclamptic group (20%) as compared to 14% in isolated pre-eclampsia. It was statistically significant in our study. Medilcioglu noted no significant difference between the two.

Proteinuria was >3+ in 20% of the recurrent pre-eclampsia group whereas it was 7.3% in isolated pre-eclampsia group. Brown et al noted that recurrence rate of proteinuric pre-eclampsia was higher in the women who had proteinuric pre-eclampsia in their first pregnancy. As we do not have the data of previous pregnancies, we conclude that this variation may be due to proteinuric pre-eclampsia in their previous pregnancies.

Coagulation profile was abnormal in 12.7% of the women with recurrent pre-eclampsia and there was no abnormality in isolated pre-eclampsia group. Abnormal LFT (43.6%) and RFT (49.1%) were seen mainly in the recurrent pre-eclampsia group. The reason for this may be patients with recurrent pre-eclampsia had chronic hypertension which has led to superimposed renal dysfunction. Higher rate of proteinuria also suggests patient with recurrent pre-eclampsia have renal dysfunction. The USG findings were abnormal in 72.7% of the patients with recurrent pre-eclampsia and in 27.3% of patients with isolated pre-eclampsia. IUGR was noted at 67.3% of the women with recurrent eclampsia as opposed to 29.1% in isolated group. Low birth weight was seen in 72.7% in recurrent PE group and 34.5% in isolated PE group. Both were statistically significant. LSCS was more in women with recurrent pre-eclampsia. (23.6%).

Mean Gestational age was less than 34 weeks in 27.3% of the women with recurrent pre-eclampsia as compared to isolated pre-eclampsia group (7.3%). 96.4% of the isolated pre-eclamptic women had pre-eclampsia <4 weeks whereas only 50.9% of recurrent pre-eclamptic women had pre-eclampsia <4 weeks. Neonatal death was more in recurrent PE (14.5%) as compared with isolated PE group (1.8%) According to Habli et al.,¹⁶ NICU admission was seen in 25.6% in babies in women with recurrent PE. Postpartum stay for the isolated pre-eclampsia patients had wide range from <2 weeks to >4 weeks, whereas recurrent pre-eclampsia patients were discharged by 4 weeks. The reason for >4 weeks stay for isolated pre-eclampsia group was due to the longer duration of NICU stay for their babies.

At 6 weeks postpartum, BP was normalised in 78.2% of women with isolated pre-eclampsia and in 67.3% of women with recurrent pre-eclampsia.

CONCLUSION: We conclude that Women with recurrent pre-eclampsia have higher rate of poor perinatal outcomes compared to women with pre-eclampsia who were normotensive in their prior pregnancies. Hence it's imperative that we closely monitor these patients and offer timely intervention, so as to improve the perinatal outcome.

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