

A Study of Posterior Reversible Encephalopathy Syndrome (PRES) in Eclampsia and in Severe Preeclampsia Patients with Neurological Symptoms.

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Abstract

Background: PRES is an often underdiagnosed neurological disorder occurring as a complication of eclampsia and severe preeclampsia. It resolves completely in most patients but some may develop residual neurological deficits.

Methods: An institution based prospective observational study done at Medical College, Kolkata in department of Obstetrics and Gynaecology. Study period was 18 months and sample size was 42. **RESULTS:** In our study we found that PRES occurred in 6 out of 11 patients with eclampsia (54 %) and 1 out of 31 patients with severe preeclampsia with neurological symptoms (3. 22%), higher values of serum LDH can be associated with the occurrence of PRES and most recovered fully with one death (2.38 % mortality) and 2 patients developing residual neurological deficit.

Conclusion: PRES has a stonger association with eclampsia than severe preeclampsia, certain biomarkers like LDH may have significant predictive value and prompt management of hypertensive disorders of pregnancy along with prevention of progression of preeclampsia as well as eclampsia may be key in preventing the development and fatal consequences of PRES.

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Introduction

Hypertensive disorders in pregnancy are one of the most worrisome complications which may lead to severe morbidity and mortality of both mother and child. Gestational hypertension, preeclampsia and chronic hypertension with superimposed preeclampsia are hypertensive disorders that can occur during pregnancy or peripartum. [1] The pathogenesis of preeclampsia is poorly understood, and the exact etiology remains unknown. [2] The posterior reversible encephalopathy syndrome (PRES) is a neurological disorder of subacute onset characterized by varied neurological symptoms, which may include headache, impaired visual acuity or visual field deficits, alteration of sensorium, confusion, seizures, and focal neurological deficits. It is an under diagnosed neurological complication of eclampsia and severe preeclampsia which occurs secondary to failure of cerebral auto regulatory response to acute changes in the blood pressure. [3] PRES is a misnomer as the syndrome can involve or

extend beyond the posterior cerebrum. In most of the patients, it resolves completely, but some can progress to develop permanent neurological defects. [4]

Clinical and radiological features of PRES include headache, encephalopathy, seizures, cortical visual changes, and parieto-occipital white matter edema visualized on neuroimaging modalities.[5] Typical signs of PRES are best detected by T2- weighted and fluid-attenuated inversion recovery (FLAIR), MRI, which is the golden standard. CT scans only reveal 50% of the lesions. [6] MRI is more sensitive displaying hyperintense lesions in T2-weighted or fluid-attenuated inversion recovery (FLAIR) sequences. While the parieto-occipital distribution occurs in about 70% of all patients, a frontal sulcus or watershed pattern is also frequently seen. [7] Magnesium sulfate (MgSO₄) is the first choice for the treatment of PRES: it improves both seizures and

hypertension. [8] The goal of the therapy is to control elevated blood pressure, seizures, minimize vasospasm and risk of secondary infarct or hemorrhage. early recognition of symptoms and immediate diagnosis, can guarantee a good prognosis with a complete resolution of neurological symptoms and cerebral lesions. [9]

Aims and Objectives

a) To determine the incidence of Posterior Reversible Encephalopathy Syndrome (PRES) in eclampsia and in severe preeclampsia patients with neurological symptoms and to study the clinical features and neuroimaging parameters of PRES.

c) To diagnose PRES early and assess response to standard treatment and outcome. To find association between PRES and other variables.

Materials and Methods

It is an institution based prospective observational study conducted in the Department of Obstetrics and Gynecology of Medical College and Hospital, Kolkata from May 2020- November 2021 during which time patients admitted from May 2020 to May 2021 with severe preeclampsia with neurological symptoms and with eclampsia were initially considered for the study. They were followed up till November 2021 at 1 month, 3 months and 6 months after discharge. Of the total 2567 patients admitted 379 patients were diagnosed with gestational hypertensive disorders and among them 50 patients found to have either severe preeclampsia with neurological symptoms or eclampsia. Among 50 above patients, 8 patients were lost to follow-up; thus finally 42 patients were included in this study.

Inclusion Criteria

- Patients with gestational hypertensive disorders who developed clinical symptoms such as headache, visual disturbances, focal neurological deficits, altered consciousness and seizures.
- Patients with severe preeclampsia who developed neurological symptoms and who developed eclampsia of any age group.
- Patients with eclampsia in both antepartum and postpartum period.
- Patients willing to participate in the study.

Exclusion Criteria

- Patients with gestational hypertensive disorders who did not develop preeclampsia or eclampsia.
- Patients with preeclampsia without neurological symptoms.
- Patients with previous history of seizure disorders not related to pregnancy and with alternative diagnoses of symptoms or imaging explained by other structural or metabolic disorders (example- hyponatremia or tumours).

- Patients in whom magnetic resonance imaging was absolutely contraindicated such as those with pacemakers or defibrillators in chest and metallic devices in the eye or aneurysm clips in the brain.
- Patients in whom magnetic resonance imaging was done 7 days after symptom onset.
- Patients who were unwilling to participate in the study or were lost to follow-up.

Clinical symptoms, course of disease, laboratory parameters and radiological findings were documented for all 42 participants with severe preeclampsia and eclampsia included in the study among whom 11 had eclampsia and 31 had severe preeclampsia with neurological symptoms. All underwent detailed general, obstetric and neurological evaluation. Blood pressures were documented at least twice 4-6 hours apart by auscultatory method with a mercury sphygmomanometer and stethoscope in the sitting position after a period of rest with the arm supported at the heart level. Serial blood pressure monitoring was done following institution protocol. Eclampsia was treated with magnesium sulphate as per the Pritchard regimen. If the women continued to have seizures they were given intravenous phenytoin. Intravenous labetalol was given for the control of blood pressure. An expert obstetrician performed delivery of all women of eclampsia on an emergency basis. Socioeconomic status was determined according to the modified Kuppuswamy scale. Basal metabolic index was calculated by dividing the weight of the patient in kilograms by the square of their height in metres. Dipstick test was done for each patient to confirm presence of urine protein. Biochemical parameters of blood were measured in the Biochemistry department of Medical College and Hospital, Kolkata as per protocol. Haemoglobin and platelet values were measured by an automated hematology analyzer. Serum lactate dehydrogenase, liver enzymes (SGOT, SGPT), urea, creatinine, uric acid, coagulation profile (PT, INR, APTT) and C reactive protein values were determined using standard laboratory methods.

Magnetic resonance imaging was performed for the patients within 7 days of onset of symptoms at Medical College and Hospital, Kolkata with a 1.5 Tesla MRI machine (Signa Voyager, GE), free of cost. T1 weighted spin echo, T2 weighted spin echo, fluid attenuated inversion recovery (FLAIR), diffusion weighted imaging (DWI), apparent diffusion coefficient (ADC) and gradient echo sequences (GRE) were done along with magnetic resonance angiography and venography for all patients. Imaging was interpreted by an expert radiologist. MRI Brain was repeated in all patients with suggestive lesions for reversibility.

For statistical analysis, logistic regression was adopted for this study. Both single variable regression and double variable regression models were applied. KS statistic and AUROC were done for each model.

Results

We found that while severe preeclampsia and eclampsia was more common in primi gravidas, the same cannot be said about PRES. The occurrence of severe preeclampsia or eclampsia was found to be more common during the early twenties. Most common ages were from 19- 27. This was also the most common age range of the patients admitted.

PRES was found in 7 out of 42 patients in this study group including both eclampsia and severe eclampsia patients with neurological symptoms i.e. 16.66 % developed PRES. Most significant clinical feature for PRES was the presence of convulsions i.e. PRES was more common in eclamptic patients than those with severe preeclampsia with neurological symptoms. PRES occurred in 6 out of 11 patients with eclampsia (54 %) and 1 out of 31 patients with severe preeclampsia with neurological symptoms (3. 22%), thus implying that timely prevention of progression from severe preeclampsia to eclampsia with antihypertensives, magnesium sulphate and termination of pregnancy can also reduce the incidence of PRES significantly.

Presence of altered mental status can also be associated, however it is not that significant. The most common type of headache observed in this study was of throbbing type followed by gradual type.

Of the biochemical parameters, it was concluded that higher values of serum LDH can be associated with the occurrence of PRES (p value = 0.0540). Mean LDH for PRES patients was 1122 whereas for those without PRES, the mean value was 563 thus implying PRES patients have significantly higher LDH. It was also observed that general tendency of serum SGOT is higher in patients with PRES than those without (p value = 0.04754). Average SGOT value with PRES was 178.286 while in those without was 98.114. Similarly, average serum SGPT values among PRES patients was 131. 429 in comparison to those without PRES which is 73.743 (p value = 0.06). No particular pattern was observed in any other laboratory parameters.

The characteristic MRI finding of bilateral symmetric vasogenic edema was found to be most commonly holohemispheric watershed followed by the parieto- occipital pattern. Most patients with PRES recovered fully with one death (2.38 % mortality) and 2 patients developing residual neurological deficit (4.7%) which consisted of mild visual symptoms.

Tables

Table 1: Gravida with and without PRES

Gravida	Without PRES	With PRES	Total
1	20	3	23
2	7	2	9
3	6	2	8
4	1	0	1
5	1	0	1

Table 2: CL Feature with and without PRES

CL Features	Frequency	Percentage
Headache	22	52.38%
Visual Symptom	19	45.24%
Epigastric/ RUQ Pain	15	35.71%
Nausea/Vomitting	15	35.71%
Pedal edema	15	35.71%
Convulsion	10	23.81%
Altered mental status	6	14.29%

Table 3: Independent variable is LDH

Independent variable is LDH				
	Estimate	Standard Error	Z-value	P-Value
(Intercept)	-2.26368	0.607066736	-3.72889	0.000192
LDH	0.000843	0.000498585	1.690462	0.09094

Table 2: Outcome with and without PRES

Outcome	Without PRES	With PRES	Total
Fully recovered	35	4	39
Residual neurological deficit	0	2	2
Death	0	1	1

Discussion

It was found that while severe preeclampsia and eclampsia was more common in primi gravidas, the same cannot be said about PRES. The occurrence of severe preeclampsia or eclampsia is more common during the early twenties. Most common ages were from 19- 27. This was also the most common age range of the patients admitted. PRES was found in 7 out of 42 patients in this study group including both eclampsia and severe eclampsia patients with neurological symptoms i.e. 16.66 % patients developed PRES.

Most significant clinical feature for PRES was the presence of convulsions i.e. PRES was more common in eclamptic patients than those with severe preeclampsia with neurological symptoms. PRES occurred in 6 out of 11 patients with eclampsia (54 %) and 1 out of 31 patients with severe preeclampsia with neurological symptoms (3. 22%), thus implying that timely prevention of progression from severe preeclampsia to eclampsia with antihypertensives, magnesium sulphate and termination of pregnancy can also reduce the incidence of PRES significantly.

Demirtas et. al. [10] 2005 in their study found that of the 39 patients, 37 (94.9%) had headaches, 14 (35.9%) had visual disorders, 9 (23%) had seizures, and 9 (23%) had depression of consciousness. Cranial MR imaging was normal in 21 patients (53.8%). In the remaining 18 patients, cortical subcortical lesions that were iso-/hypointense on T1-weighted images and hyperintense on T2-weighted images.

Presence of altered mental status can also be associated, however it is not that significant. The most common type of headache observed in this study was of throbbing type followed by gradual type. It was found that PRES is more common in people with higher BMI. But the proportion is the highest for those with low BMI thus making it difficult to conclude.

Of the biochemical parameters, it was concluded that higher values of serum LDH can be associated with the occurrence of PRES (p value = 0.0540). mean LDH for PRES patients was 1122 whereas for those without PRES, the mean value was 563 thus implying PRES patients have significantly higher LDH. It was also observed that general tendency of serum SGOT is higher in patients with PRES than those without (p value = 0.04754). Average SGOT value with PRES was 178.286 while in those without was 98.114. Similarly, average serum SGPT values among PRES patients was 131. 429 in comparison to those without PRES which is 73.743 (p value = 0.06).

Gao et al [11] 2011 in their study of 35 patients with typical clinical symptoms and characteristic MR

imaging findings of PRES and after correlating levels of biochemical parameters with the degree of edema found that serum LDH concentrations between patients with cytotoxic edema and with vasogenic components were not statistically different (NWU test, $U = 93.0$, $Z = 1.818$, $P = 0.069$). Only serum lactate dehydrogenase (LDH) concentration was significantly correlated with the score of brain edema distribution

The characteristic MRI finding of bilateral symmetric vasogenic edema was found to be most commonly holohemispheric watershed followed by the parieto- occipital pattern.

Most patients with PRES recovered fully with one death (2.38 % mortality) and 2 patients developing residual neurological deficit (4.7%).

Thus it was concluded that PRES occurs in eclampsia and severe preeclampsia patients with neurological symptoms and has a stronger association with the former. MR imaging is an essential modality for the diagnosis of PRES. MR imaging showing bilateral symmetrical vasogenic edema characteristic of PRES most commonly of the holohemispheric watershed pattern but may involve other areas of the brain as well. Rise in certain biochemical parameters such as serum LDH and liver enzymes such as SGOT and SGPT may have significant association with PRES and may act as predictors of the same. Most patient have a full recovery but PRES may lead to death or residual neurological deficit as well as preterm births and thus prompt management of hypertensive disorders of pregnancy along with prevention of progression of preeclampsia as well as eclampsia may be key in preventing the development and fatal consequences of PRES.

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