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Original Research Article

Posterior reversible encephalopathy syndrome in preeclampsia

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ABSTRACT

Background: Posterior reversible encephalopathy is a clinico-radiological syndrome marked by headache, altered mental status, seizures, visual disturbances, and extensive white-matter changes, also known as hyper perfusion encephalopathy, brain capillary leak syndrome, and hypertensive encephalopathy. This syndrome was a possible consequence of several medical conditions but especially in pregnancy it is associated with pre-eclampsia and eclampsia. Objective of this study was to know the incidence and analyze the clinical features, biochemical, and radiological abnormalities in posterior reversible encephalopathy syndrome (PRES) as a complication of preeclampsia.
Methods: This was a one-year cross-sectional analytical study conducted at NRI general hospital, Chinakakani, Guntur of patients with the diagnosis of PRES. Data was obtained from medical records and analyzed them in terms of mean for continuous variables and percentages for categorical data.
Results: Total no of patients diagnosed as PRES were 16 out of 127 patients of preeclampsia. Among them, 14 presented with eclampsia, and two presented with severe preeclampsia and imminent symptoms of eclampsia. Headache was the most common symptom (100%). PRES occurred at a peak SBP of ≥160 mmHg in 75% cases and peak DBP of ≥110 mmHg in 50% cases. Serum lactate dehydrogenase (LDH) level was ≥600 in 56.25% and serum uric acid level ≥6 in 50% of patients of PRES. The drug of choice was magnesium sulfate.
Conclusions: Neuroimaging abnormality is a definitive component in the diagnosis of PRES. These cerebral abnormalities are vital components in the pathogenesis of eclampsia. Considerable number of patients of preeclampsia might develop PRES even without eclampsia, with mild elevation in BP, serum LDH, and serum uric acid levels.

Keywords: Eclampsia, Posterior reversible encephalopathy syndrome, Pre-eclampsia, Serum lactate dehydrogenase, Serum uric acid

INTRODUCTION

Preeclampsia is a pregnancy-specific hypertensive disorder with multiorgan involvement. It is defined as BP ≥140/90 mm Hg with proteinuria ≥300 mg in a 24-hour urine sample or protein /creatinine ratio ≥0.3 or dip stick reading of 1+ persistently.

(or)

In the absence of proteinuria

New-onset hypertension with the newer onset of any of the following:

- Thrombocytopenia with platelet count <1,00,000/µl
- Renal insufficiency with serum creatinine >1.1 mg/dl or doubling of baseline in the absence of renal disease

- Liver involvement with Serum transaminase levels twice normal
- Pulmonary edema
- Cerebral symptoms like headache, visual disturbances, convulsions

Occurring after 20 weeks period of gestation in a previously normotensive patient.[1]

Worldwide, 5-10% of all pregnancies are complicated by hypertension that contributes significantly to maternal morbidity and mortality.[2] 0.5% of mild Pre-eclampsia patients and 2-3% of severe pre-eclampsia patients might progress to eclampsia. In developed countries, the incidence of eclampsia ranges from 1 in 2000 to 3000 deliveries, whereas in developing countries, the rate is around 1 in 100 to 1 in 1700 births.[3-6]

On neuroimaging in patients of eclampsia, the underlying central nervous system pathology showed subcortical edema involving the posterior lobes predominantly. This was first described in 1996 by Hinchey et al, as posterior reversible encephalopathy, a clinico-radiological syndrome which was marked by headache, altered mental status, seizures, visual disturbances, and extensive white-matter changes suggestive of posterior cerebral edema and was given the name reversible posterior leukoencephalopathy syndrome.[7] It is also known as hyper perfusion encephalopathy, brain capillary leak syndrome, and hypertensive encephalopathy. This syndrome was a possible consequence of several medical conditions apart from pre-eclampsia and eclampsia such as hypertensive encephalopathy, hemolytic uremic syndrome, acute or chronic renal diseases, use of cytotoxic and immunosuppressant drugs, blood transfusion and electrolyte disturbances.[8]

This clinical syndrome is increasingly recognized, commonly because of the improvement and availability of brain imaging. One of the distinctive features of PRES is the reversibility of the clinical and radiological abnormalities after appropriate treatment and removal of the precipitating factor.

METHODS

It was a cross-sectional analytical study done at NRI medical college and general hospital, Chinakakani, Guntur, for a period of one year from 1st October 2018, to 30th September 2019. All patients diagnosed with clinical and radiological features of PRES were taken. Their demographic, clinical features, laboratory investigations, radiological abnormalities, and treatment given were analyzed by collecting the data from the medical records. Institutional ethical committee acceptance was taken before the start of the study.

Inclusion criteria

- Women >20 weeks period of gestation and <6 weeks postpartum admitted to labor room with a confirmed diagnosis of preeclampsia, eclampsia, and radio imaging showing PRES, were included in the study.

Exclusion criteria

- Non pregnant women, women with <20 weeks period of gestation or >6 weeks postpartum, without a diagnosis of preeclampsia or eclampsia and with any other co-morbidities like diabetes mellitus, renal disease, liver disorder, epilepsy was excluded.

Statistical analysis

The data of patients with the diagnosis of PRES were taken for the study. Their demographic, clinical characteristics, peak SBP, peak DBP, biochemical, radio imaging reports, and treatment given were collected and analyzed the data in terms of mean for continuous variables and percentages for categorical data are calculated.

RESULTS

Total no of deliveries during the study period were 1863. Among them, 127 were diagnosed as pre-eclampsia, accounting for 6.8%. Out of 127 pre-eclampsia patients, 59 were mild pre-eclampsia, and 68 were severe pre-eclampsia accounting for 46.45% and 53.54%, respectively.

Total no of eclampsia patients were 18, with an overall incidence of eclampsia being 0.96%. No of cases diagnosed as PRES were 16 (Table 1), with an overall incidence of 0.85%. Among 16 patients, 14 presented with eclampsia (28.5% of antepartum eclampsia and 71.5% of postpartum eclampsia), and two patients presented with severe preeclampsia with imminent symptoms.

Among 16 patients of PRES, four were booked with hospital, and 12 patients were booked elsewhere and referred to us because of elevated BP readings or eclampsia or imminent symptoms. All patients had undergone MRI study at the institute.

Out of 16 patients 13 were primigravida / para (81.25%). The mean age of these individuals was 22.3 years. All patients who were diagnosed as PRES presented with headache making it the most common presenting symptom, vomiting occurred in (50%), visual disturbances like blurring of vision (37.5%), drowsiness (25%), epigastric pain (18.75%), and reversible blindness occurred in (12.5%) individuals.

PRES and eclamptic seizures occurred at an SBP of ≥160 mmHg in 12 of 16 individuals and DBP of ≥110 in 8 out of 16. Fundoscopy showed grade 1 hypertensive

retinopathy changes in 5 (31.25%), papilledema in 1 patient.

Table 1: Demographic and clinical features of 16 patients.

No.	Age	Period of gestation	POG at the time of diagnosis of pres	Eclampsia	Clinical feature	Peak SBP (mmHg)	Peak DBP (mmHg)	Fundoscopy
1.	23	37+2 weeks	P1L1, POD-4	PPE	Headache, blindness blurring of vision	170	90	Papilledema
2.	20	34+5 weeks	Primi with twins	APE	Headache	200	100	Normal
3.	21	39 weeks	P2L2, PND-5	PPE	Headache, blurring of vision	180	100	GR 1 HTNR
4.	21	25 weeks	A1, PAD-1	no eclampsia	Headache, visual disturbance	150	90	Normal
5.	20	38+2 weeks	P1L1, PND-5	PPE	Headache, blindness Blurring of vision	170	110	Normal
6.	19	37 +6 weeks	Primi	APE	Headache, epigastric pain, vomiting, blurring of vision	170	110	Normal
7.	26	25+4 weeks	Primi	APE	Headache, epigastric pain, vomiting	170	110	Gr 1 HTNR
8.	24	39+3 weeks	P1L1, POD -5	PPE	Headache	140	80	Normal
9.	20	40 weeks	P1L1, POD-6	PPE	Headache, drowsiness, Blurring of vision	160	100	Normal
10.	22	31+3 weeks	G2A1	APE	Headache, epigastric pain, vomiting	140	110	Normal
11.	21	39 weeks	P1L1A1 POD -8	PPE	Headache, vomiting	140	100	Gr 1 HTNR
12.	20	39+1 weeks	P1L1, POD -6	PPE	Headache, vomiting, drowsiness	180	110	Normal
13.	19	28+5 weeks	P1L1, PND-5	PPE	Headache, vomiting	170	110	Normal
14.	25	33 weeks	P1D1, PND-1	PPE	Headache, vomiting, drowsiness	190	120	Normal
15.	31	26 weeks	A1, PAD-1	no eclampsia	Headache, vomiting, drowsiness	190	130	Gr 1 HTNR
16.	25	32 weeks	P1L2, POD-0	PPE	Headache	170	100	Gr 1 HTNR

POG: period of gestation, PRES: posterior reversible encephalopathy syndrome, APE: antepartum eclampsia, PPE: postpartum eclampsia, HTNR: hypertensive retinopathy, SBP: systolic blood pressure, DBP: diastolic blood pressure.

Table 2: Biochemical abnormalities of the patients of PRES.

No.	Hb%	Platelet count	Serum creatinine	LDH	Serum uric acid	AST (SGOT)	ALT (SGPT)	Urine albumin
1.	10.9	3	0.7	650	5.2	40	25	1+
2.	10.5	3.3	0.8	480	6.2	43	16	1+
3.	11.6	4.7	0.5	560	5.4	45	18	2+
4.	7.3	2	1.6 *	604	10.4	76	22	2+
5.	9.6	2.6	0.7	874	8.4	47	37	3+
6.	10	2.1	0.9	451	3.7	21	24	1+
7.	9.4	2.1	0.8	529	7.3	115	126	2+
8.	12.5	2.1	0.6	659	2.3	17	25	1+
9.	10.9	2.6	0.6	520	5.6	15	11	2+
10.	5.7	0.9	0.6 **	4460	9.1	838	276	3+

No.	Hb%	Platelet count	Serum creatinine	LDH	Serum uric acid	AST (SGOT)	ALT (SGPT)	Urine albumin
11.	11.3	4.3	0.5	781	5	29	24	1+
12.	10.2	4.1	0.9	360	8.4	20	12	1+
13.	9.2	2.9	0.9	600	7.8	91	66	4+
14.	12.7	1.6	0.6	701	4.4	26	23	3+
15.	15.3	1.7	0.7	1335	7.8	63	26	4+
16.	10.2	2.5	0.8	408	5.5	22	10	4+

*Sr Ceatinine, ** HELLP Syndrome. LDH: lactate dehydrogenase, AST: Aspartate aminotransferase, SGOT: serum glutamic oxaloacetic transaminase, ALT: alanine transaminase, SGPT: serum glutamic pyruvic transaminase.

Table 3: Radiological findings, treatment modality, and mode of termination in the patients of PRES.

Site of lesion	Treatment modality				Mode of termination
	$MgSo_4$	Anti-HTN	Anti-epileptic	Mannitol	
b/l parieto occipital and capsuloganglionic area	Given	T. Labetalol	Levetiracetam Clobazam	Given	LSCS
b/l temporal, frontal, occipital, parietal	Given	T. Labetalol	Levetiracetam	Given	Primary emergency LSCS
b/l parieto occipital	Given	Stamlodipine	Levetiracetam		NVD
b/l occipital lobes up to subcortical white matter	Given	Stamlodipine			2nd trimester induced abortion
b/l occipital, lt posterior parietal	Given	T. Labetalol, Nifedipine, Stamlodipine	Levetiracetam		NVD
b/l frontal, occipital, parietal	Given	T. Labetalol, Nifedipine, Stamlodipine	Levetiracetam Fentanyl		Primary emergency LSCS
b/l temporal, frontal, occipital,parietal, lt thalamus	Given	T. Labetalol, Nifedipine, Stamlodipine	Levetiracetam	Given	2nd trimester induced abortion
b/l occipital, parietal, lt temporal, frontal,cerebellar	Given	Stamlodipine Nifedipine.			LSCS
b/l parieto occipital	Given	Labetalol	Levetiracetam	Given	LSCS (thick MSL)
b/l parieto occipital	Given		Levetiracetam		Primary emergency LSCS
b/l parieto occipital and cerebellar hemispheres	Given	Labetalol Stamlodipine			LSCS
b/l posterior parietal and occipital lobes and lt frontal lobe	Given	Nifedipine.	Levetiracetam Clobazam	Given	LSCS
b/l frontal,temporo-parieto-occipital lobes ,peri ventricular white matter, b/l lentiform nuclei,b/lthalami	Given	Labetalol, Nifedipine	levetiracetam Clobazam		labour preterm
b/l parietal	Given	Labetalol Stamlodipine	Levetiracetam	Given	3rd trimister IUD
b/l fronto parietal,occipital and rt temporal lobe	Given	Labetalol, Clindipine, Stamlodipine	Levetiracetam	Given	2nd trimister induced abortion
b/l parietal and occipital	Given	Labetalol Stamlodipine	Levetiracetam		primary preterm emergency LSCS

Nine of 16 patients of PRES showing Serum LDH Level ≥600 accounting to (56.25%) (Table 2). Among these nine individuals with serum LDH >600, severe BP recordings with SBP of ≥160 or DBP of ≥110 were noted

in 7 individuals (77.7%). Eight out of 16 showing serum uric acid level ≥6 (50%) among these eight individuals SBP was ≥160 or DBP was ≥110 in 7 individuals (87.5%). Liver enzymes were elevated in 4 Individuals (25%), taking twice the level of normal SGOT and SGPT as baseline. Urine albumin was >1+ in 10 individuals (62.5%). One individual showed features suggestive of HELLP syndrome with elevated liver enzymes, low platelet count, and severe anemia. Sr. Creatinine was ≥1.1 in one individual.

MRI showed edema mainly involving the posterior cerebral regions (Table 3). Other regions of the brain involved were thalamus, capsuloganglionic area, frontal lobes, pons, and cerebellar hemispheres. Magnesium sulfate was given to all the 16 patients by Pritchard's regimen. Along with magnesium sulfate, levetiracetam, and clobazam were required to treat seizures in 13 patients. Injection Mannitol was administered in 7 cases who did not respond to magnesium sulfate alone and who had extreme irritability and visual disturbances. Antihypertensives like Inj/Tab labetalol, Tab stamlodipine, or Tab nifedipine were given in required doses based on the severity.

Mode of delivery was vaginal in 25%, LSCS in 56.25% for different obstetric indications.

There was no residual morbidity and maternal mortality in the present study until the time of discharge.

DISCUSSION

Wagner et al, proposed that PRES and eclampsia are pathophysiologically related.[9] Eclamptic patients may have seizure onset at lower blood pressures than patients with hypertensive encephalopathy. The two most accepted theories in the pathogenesis of PRES are vasogenic and cytotoxic theory. Vasogenic edema occurs due to sudden elevation of SBP >150 mmHg, which affects the intrinsic myogenic vasoconstriction. This leads to hyperperfusion and edema.[10] Cytotoxic edema is due to a sudden rise in BP, leading to vasospasm resulting in hypoperfusion, hypoxia, and ischemia, which leads to the development of cytotoxic edema and endothelial cell damage with or without actual cerebral infarction.[11]

In this study, the demographic, clinical features, biochemical, radiological abnormalities, and treatment modalities opted for the cases of PRES were analyzed.

All patients were less than 30 years of age except one. Most of them were primigravida /para presented antenatally or postnatally. Only 3 patients (3/16) presented at less than 28 weeks period of gestation and all others are in the 3rd trimester. Among these 3 patients, 2 patients did not have eclampsia. They presented with headache, visual disturbances, and vomiting with elevated BP has undergone MRI and diagnosed as PRES.

Among 16 patients of PRES, 14 presented with eclampsia, and 2 patients presented with severe preeclampsia with imminent symptoms. Out of 14 eclampsia patients, 4 had antepartum eclampsia, and 10 patients had postpartum eclampsia. 14 out of 18 patients of eclampsia (77.7%) were diagnosed to have PRES in comparison to Brewer et al, study on 47 eclamptic patients which revealed PRES in 46 cases (97.8%), and it was suggested that PRES is a vital component in the pathogenesis of eclampsia.[12]

An overall incidence of eclampsia being (0.96%), in comparison to the study done by Nobis et al, the incidence of eclampsia in India is about 1.5 %.[13]

In this study headache was the most common presenting symptom (100%) followed by vomitings (50%), visual disturbance like blurring of vision (37.5%), drowsiness (25%), epigastric pain (18.75%), and reversible blindness occurred in (12.5%) individuals when compared to study by Brewer et al, (47 patients) noted that headache was the most common presenting symptoms in 87.2% of the patients, altered mental status occurred in (51.1%), involvement of vision in (34%), nausea and vomitings in (19.1%) of patients.[12]

PRES and eclamptic seizures occurred at an SBP of ≥160 mmHg in 12 of 16 (75%) individuals and DBP of ≥110 in 08 out of 16 (50%). Fundoscopy showed grade 1 hypertensive retinopathy changes in 5 (31.25%), papilledema in 1 patient.

Study showed elevated serum LDH in 56.25% and uric acid levels in 50% patients of PRES. LDH is an intracellular enzyme responsible for the interconversion of lactate and pyruvate in the cells. LDH levels are more inside the cells than in plasma. Uric acid, which is an end product of purine metabolism, was filtered through glomeruli, and most of it is completely reabsorbed in proximal convoluted tubules. Endothelial dysfunction leads to elevated levels of LDH and uric acid indicative of the cellular damage and dysfunction; thus, they can be regarded as early biochemical markers to identify the occurrence of the complications of preeclampsia and reflects the severity of the disease.[14,15]

Posterior circulation is commonly involved in PRES; this was similar to WS Bartynski's study.[11] The parieto occipital region is most commonly involved (100%), similar to a study by Mckinney et al, showing involvement of the parieto occipital region in 98.7%.[16]

$MgSo_4$, which controls the eclamptic seizures, was also thought to reduce the cerebral perfusion pressure. So, it has been used not only to control but also to prevent seizures.[9] In this study, Inj $MgSo_4$ was used to control and avoid eclamptic convulsions and in selected cases with extreme irritability anti-edema agent like mannitol was used which was very similar to study by Suman

Sardesai et al, which concluded that Inj $MgSO_4$ was the drug of choice.[17]

CONCLUSION

Neuroimaging abnormality is a core component in the diagnosis of PRES, which indicate cytotoxic or vasogenic edema in the cerebral vasculature. In some patients, even with mild elevation of BP, there may be symptoms of PRES with or without eclampsia. Elevated serum LDH and serum uric acid, which indicate cellular damage, also acts as early biochemical markers for the prediction of severity of preeclampsia, leading to PRES.

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REFERENCES

1. ACOG; Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol. 2013;122(5):1122-31.
2. Cunningham FG, Leveno KJ, Bloom SL, Dashe SJ, Hofman BL, Casey BM, et al. Williams Obstetric 25th ed. New York NY: McGraw Hill Medical Publishing Division, Chapter 40, Hypertensive disorders in pregnancy; 2018:710-754.
3. Andersgaard AB, Herbst A, Johansen M, Ivarsson A, Ingemarsson I, Langhoff-Roos J, et al. Eclampsia in Scandinavia: incidence, substandard care, and potentially preventable cases. Acta Obstet Gynecol Scand. 2006;85(8):929-36.
4. Ventura SJ, Martin JA, Curtin SC, Mathews TJ, Park MM. Births: final data for 1998. Natl Vital Stat Rep. 2000;48(3):1-100.
5. Misra R, Donald's I. Practical Obstetrics problems.7th edition, Greater Noida; Wolter Kluwer India Pvt. Ltd. Chapter 8: Hypertensive Disorders; 2014:42-175.
6. Chua S, Arulkumaran S, Eclampsia- no room for complacency. Singapore Med J. 1995;36(5):470-1.
7. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, et al. A reversible posterior leukoencephalopathy syndrome. N Engl J Med. 1996;334(8):494-500.
8. Stott VL, Hurrell MA, Anderson TJ. Reversible posterior leukoencephalopathy syndrome: a misnomer reviewed. Int Med J. 2005;35(2):83-90.
9. Wagner SJ, Acquah LA, Lindell EP, Craici IM, Wingo MT, Rose CH, et al. Posterior reversible encephalopathy syndrome and eclampsia: Pressing the case for more aggressive blood pressure control. Mayo Clin Proc. 2011;86:851-6.
10. Bartynski WS. Posterior reversible encephalopathy syndrome-part 2: controversies surrounding pathophysiology of vasogenic edema Am J Neuroradiol. 2008;29(6):1043-9.
11. Bartynski WS. Posterior reversible encephalopathy syndrome- part 1: fundamental imaging and clinical features. Am J Neuroradiol. 2008;29(6):1036-42.
12. Brewer J, Owens MY, Wallace K, Reeves AA, Morris R, Khan M, et al. Posterior reversible encephalopathy syndrome in 46 out of 47 patients with eclampsia. Am J Obstet Gynecol. 2013;208:468.e1-6.
13. Nobis PN, Hajong A. Eclampsia in India through the decades. Obstet Gynaecol India. 2016;66(Suppl 1):172-6.
14. Joseph L, George M, Alex A. A review on the estimation of serum LDH and uric acid in hypertensive versus normal pregnant women and its correlation with maternal outcome in a tertiary care hospital. Int J Ther Appli. 2016;32:35-7.
15. Gao B. Serum LDH as an early marker of posterior reversible encephalopathy syndrome. Anaesth Intens Care. 2012;40:902-3.
16. McKinney AM, Short J, Truwit CL, McKinney ZJ, Kozak OS, SantaCruz KS, et al. Posterior reversible encephalopathy syndrome: incidence of atypical regions of involve-ment and imaging findings. AJR Am J Roentgenol. 2007;189:904-12.
17. Sardesai S, Dabade R, Deshmukh S, Patil P, Pawar S, Patil A, et al. Posterior reversible encephalopathy syndrome (PRES): evolving the mystery of eclampsia. J Obstet Gynecol India. 2019;69:334.

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