

Eclampsia Preeclampsia; Clinical and Neurological Correlates

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Background: Eclampsia is defined as seizures which cannot be attributed to other causes in a woman with preeclampsia. Severe preeclampsia may be complicated by HELLP syndrome (hemolysis, elevated liver enzyme, low platelets). Magnetic resonance imaging (MRI) findings of the head have been reported to be abnormal in up to 90% of women imaged. Abnormal findings include an increased signal at the gray-white matter junction on T2-weighted images, as well as cortical edema and hemorrhage. The syndrome of posterior reversible encephalopathy (PRES), indicative of central vasogenic edema, has been increasingly recognized as a component of eclampsia.

Aims: To study cranial MR imaging with clinical correlation in eclampsia and severe preeclampsia

Materials And Methods: 20 pregnant (after 20 week of gestation) patients each of severe preeclampsia and eclampsia were taken into study, their course of pregnancy studied and an MRI scan done at admission after stabilization. Statistical comparison of MRI finding was done and various clinical and laboratory parameters by unpaired t test and chi-square test.

Results: There was a greater incidence of headache, seizures, neurological disturbances and visual disorder in patients with positive MRI findings as compared to patients with no MRI findings. The difference was statistically significant (p values 0.0085, 0.0001, 0.0001, 0.0001 respectively). Most common symptom in both the MRI positive and MRI negative group was headache suggesting it as a premonitory symptom for eclampsia. There was a statistically significant difference in the mean BP of the two groups (p value < 0.0001)

Occipital lobe was involved in 100% of the MRI positive patients suggesting its role in visual disturbance in the MRI positive group.

Conclusion: Patients suffering from severe preeclampsia and having positive cerebral findings on MRI scan have a greater chance of developing seizures as compared to the patients diagnosed as severe preeclampsia and having negative findings on MRI scan. This is suggestive of PRES as an antecedent to the eclamptic seizure as opposed to the result of eclamptic seizure. This group of patients have the maximum potential to benefit from aggressive therapy to control the elevated blood pressure.

Keywords: severe preeclampsia, eclampsia, PRES, seizures, neurological disturbances, MRI

I. Introduction

Preeclampsia, by definition, is the new onset of hypertension (BP \geq 140/90) and either proteinuria or end-organ dysfunction or both after 20 weeks of gestation in a woman who was previously normotensive. Eclampsia is currently defined in the obstetrical literature as the occurrence of unexplained seizure during pregnancy in a woman with preeclampsia.^{1,2} The incidence of eclampsia in developed countries range from 1 in 2000 to 1 in 3448 pregnancies which is much lower than in developing countries like India. The incidence of eclampsia in India has been quoted as 1.56%.³ Abnormal magnetic resonance imaging (MRI) findings of the head have been reported in up to 90% of women imaged. These include an increased signal at the gray-white matter junction on T2-weighted images, as well as cortical edema and hemorrhage. The syndrome of posterior reversible encephalopathy (PRES), indicative of central vasogenic edema, has been increasingly found as a component of eclampsia.⁴ The most common abnormality on neuroimaging in PRES was edema involving the white matter, especially in the parietal and occipital lobes. Vasogenic edema was reported to be seen in the parietal or occipital regions in 92% of patients, but other brain regions were also involved in patients with PRES, such as the temporal lobes, brain stem, cerebellum, basal ganglia, and frontal lobes.^{5,6} Preferential posterior circulation distribution has been suggested to be due to the decreased sympathetic innervation of the posterior circulation.⁷ Failure of the protective cerebro-vascular auto-regulatory mechanism in situations of high blood pressure or circulating toxins leads to vasodilatation and leakage of fluid into the interstitial tissue causing vasogenic edema. Patients with brain edema in MRI also had evidence of more severe systemic symptoms than those who had normal MR imaging findings. As compared with patients without brain edema, these patients had significantly increased uric acid and creatinine levels, which implied renal dysfunction.⁸

Seizures were more frequent in patients with brain edema than in those with normal findings. This most likely reflects the fluid in the subcortical and cortical tissues which had irritative effect. It has been suggested that radiologic findings in patients with eclampsia are probably due to seizure edema⁹.

II. Materials And Methods

After admission, laboratory investigations were done and recorded. All pregnant ladies who were admitted for indication of severe preeclampsia or hypertensive crisis with or without neurological signs were first stabilized and sent to MRI centre for MRI(1.5T magnetic resonance imaging system was used). The examination protocol consisted of T1 weighted spin echo (axial and sagittal), T2 weighted spin echo (axial sagittal and coaxial) sequences ,Fluid attenuated inversion recovery (FLAIR) imaging with injection of intravenous contrast.All the data required along with the patient’s signs and symptoms were recorded in the profoma designed for this study.All statistical analyses were performed with the SPSS 18.0 program for Windows.Student’s unpaired T test and chi-square test were used for statistical evaluation and p<0.05 was accepted to be statistically significant. Data dependent upon verbal explanations were depicted as frequency and %. Data dependent upon laboratory parameters were depicted as mean ±SD.

III. Observation Tables And Results

In this prospective study, a total of 40 eclampsia and severe preeclampsia patients underwent cranial MRI.Following the MRI scan patients were divided into MRI finding positive and MRI finding negative groups.

Group MRI finding positive:Patients diagnosed with eclampsia/severe preeclampsia who had abnormal findings in their cranial MRI scan(n=17)

Group MRI finding negative:Patients diagnosed with eclampsia/severe preeclampsia who had normal cranial MRI scan(n=23)

Table -1. Comparison of MRI finding in severe preeclampsia and eclampsia

	Severe Preclampsia (n=20)	Eclampsia(n=20)	p- value
MRI positive	2(10%)	15(75%)	< 0.0001
MRI negative	18(90%)	5(25%)	

Statistical significant (p<0.05)using Chi-square tests

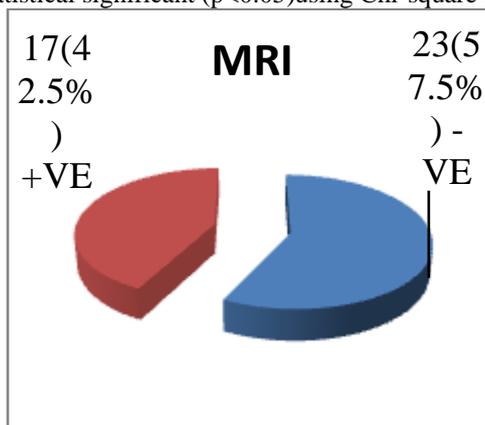


Figure 1.Distribution of number of patients in the two groups of study.

Table 2: Comparison of Biochemical data and mean blood pressure in patients with no MRI findings and MRI findings

	MRI findings Negative (N=23)			MRI findings Positive (N=17)			P value
	Minimum	Maximum	Mean±SD	Minimum	Maximum	Mean±SD	
Mean BP (mm Hg)	113.3	133.3	126.2±5.346	133.3	146.7	140.2±4.326	<0.0001*
Hb	4.50	12.80	9.29±1.557	8.0	11.6	9.224±1.141	0.8802
WBC	4200	22500	11378±3648	4000	24300	9753±5268	0.2557
Platelets	145000	450000	234565±72443	145000	380000	214765±67901	0.3858
AST (IU/L)	20	50.2	34.10±8.186	32	76	45.47±11.57	0.008*
ALT (IU/L)	22	58	31.38±8.810	31	63	42.71±8.260	0.0002*
Uric acid(mg/dl)	2	3.90	2.357±0.4531	2.40	6.20	4.853±0.9664	<0.0001*

Urea(mg/dl)	14.04	48	32.78±7.659	34	58	44.53±7.229	<0.0001*
S. Albumin(g/dl)	2.2	4.2	3.183±0.6506	2	4	2.824±0.7207	0.1075
Creatinine (mg/dl)	0.40	1.80	1.039±0.3665	0.9	2.20	1.771±0.3236	<0.0001*
PT	13	18.69	14.94±1.908	13	18.4	15.20±1.748	0.6594
aPTT	20	52.44	30.02±9.895	20	30.8	25.92±3.532	0.1121

*Statistically significant (p<0.05) using student unpaired t Test (spss17)

23 (57.5%) out of 40 patients had normal cranial MRI while 17(42.5%) had cortical and subcortical lesions in brain. Cortical lesions that were iso-/hypointense on T1-weighted images and hyperintense on T2-weighted images

were detected. When the mean BP and lab data were compared between the patients with and without MRI finding, there was a statistically significant difference in mean BP, S.AST and S.ALT, S.uric acid, B.Urea and S.creatinine (p value <0.0001, 0.008, 0.0002, <0.0001, <0.0001 and <0.0001 respectively). When coagulation studies PT and aPTT were compared among patients with or without MRI findings, the difference was not found to be statistically significant (p value 0.6594 and 0.1121 respectively).

Table 3. Clinical findings in patients with and without MRI findings and their statistical comparison

	MRI Finding (N=17)	No MRI Findings (N=23)	P value
Headache	16	13	0.0085*
Seizures	15	5	<0.0001*
Mental status changes	13	2	<0.0001*
Visual Disorder	10	6	<0.0001*

Statistical significant (p<0.05) using Chi-square tests

On comparing the patients with pathological MRI finding and no MRI finding, we found that there was a statistically significant difference in view of headache, seizures, visual disturbance and mental status changes (p value 0.0085, <0.0001, <0.0001 and <0.0001 respectively). On comparing the mode of delivery among eclampsia patients, we found that 17(85%) had vaginal delivery while 3(15%) landed up into caesarean section. In preeclampsia patients, we found that 15(75%) had a vaginal delivery while 5(25%) landed up into caesarean section. As has already been quoted that nulliparity is one of the prime risk factors contributing to eclampsia and preeclampsia, 26(65%) out of 40 were nulliparous.

Table 4- Clinical findings and distribution of cranial lesions in patients with MR imaging findings

Patient no	Distribution of MRI finding								Clinical finding
	occipital	frontal	Parietal	Temporal	Basal ganglia	Cerebellum	Thalamus	Brain stem	
1.	+1	+1	+1	0	0	0	0	0	HA, VD, S, DC
2	+1	0	0	0	0	0	0	0	HA, S, DC, VD
3	+1	0	+1	+1	0	0	0	0	HA, S, DC, VD
4	+1	+1	+2	0	0	0	0	0	HA, S, DC, VD
5	+1	+1	+1	0	0	0	0	0	HA, S, DC, VD
6	+1	+1	+1	0	0	0	0	0	HA, S, DC, VD
7	+1	+1	+1	0	0	0	0	0	HA, S, DC, VD
8	+1	0	0	0	0	0	0	0	HA, S, DC, VD
9	+1	+1	+1	0	0	0	0	0	HA, S, DC, VD
10	+1	+1	0	0	0	0	0	0	HA, S
11	+2	0	+2	0	+2	0	0	0	HA, S, DC, VD
12	+1	0	+1	0	0	0	0	0	S, VD, DC
13	+1	+1	+1	0	0	0	0	0	HA, S, DC, VD
14	+1	+1	0	0	0	0	0	0	HA, S, DC, VD
15	+1	+1	0	0	0	0	0	0	HA, S, DC, VD
16	+1	0	0	+1	0	0	0	0	HA, VD, DC
17	0	0	0	0	+2	0	0	0	HA, DC, VD

HA: headache, S: seizure, DC: depression of consciousness, VD: visual disorder
 +1-lesions iso/ hyperintense on T1 and hypointense on T2, +2-infarct/haemorrhage

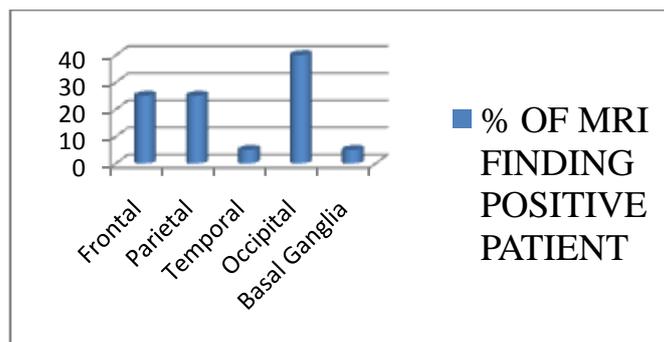


Figure 2. Distribution of cranial lesions in MRI finding positive group.

In MRI finding positive patients, occipital cortex was involved in 100% patients, parietal cortex in 58.82% patients, frontal cortex in 58.82% and temporal cortex in only 11.77% patients. Basal ganglia had infarct in 11.77% MRI positive patients.

IV. Discussion

On MR imaging, eclampsia patients demonstrate hyperintense lesions on T2-weighted images while iso- to hypointense lesions are found on T1-weighted images. The most common findings on MRI were located in the area of the posterior cerebral circulation and were associated with visual disturbances. Rarely Basal ganglia and subcortical white matter lesions were found and were associated with mental status changes. Most of the MR imaging lesions in patients with eclampsia are reversible.¹⁰

In our study, we also found that cortical MRI lesions in eclampsia were hyperintense on T2 weighted images while iso or hypointense on T1 weighted images. Haemorrhage was found in two of the eclamptic patients in our study involving the posterior parietal cortex in both patients while basal ganglia and temporal cortex in one of the patients.

Vasogenic edema is most commonly present in the parietal or occipital regions (98%), but other locations were also common. The frontal lobes (68%), inferior temporal lobes (40%), and cerebellar hemispheres (30%) were affected often. The basal ganglia (14%), brain stem (13%), and deep white matter (18%) including the splenium (10%) were also involved though less commonly than the other locations mentioned above.¹¹

There is strict similarity with the pathological findings characterizing hypertensive encephalopathy which suggests that hydrostatic edema is caused by a focal impairment in cerebral autoregulation leading to vasodilation and fluid extravasation. Posterior circulation areas are predominantly involved because they have lesser degree of adrenergic innervation supporting circulatory autoregulation mechanisms.¹²

In our study, we found that among the eclampsia patients having abnormal MRI, the occipital cortex was involved in 100% patients, parietal cortex in 66.67% patients, frontal cortex in 66.67% and temporal cortex in only 6.67% patients. The subcortical region (basal ganglia) had minute haemorrhages in 1 out of 20 (5%) of the pre eclamptic patient while none of the eclamptic patients had any lesions in the subcortex. Occipital lobe was involved in 100% of the eclampsia patients with positive MRI findings. Hence posterior circulation areas are inadvertently involved in eclampsia patients.

The laboratory evidence in preeclampsia/eclampsia suggests that endothelial injury is often present with platelet consumption (thrombocytopenia) and evidence of red cell fragmentation (schistocyte formation, increase in lactate dehydrogenase [LDH]). Hypertension in preeclampsia is related to systemic vasoconstriction with accompanying increased capillary permeability, reduced intravascular volume and hemoconcentration. Renal dysfunction with proteinuria and hypomagnesemia occur; systemic edema develops due to a combination of altered endothelial function and reduced oncotic pressure. Hepatic ischemia may lead to liver dysfunction and, when severe, hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome develops. Abnormal liver function test results were found to be associated with an increased risk for adverse maternal outcomes. Levels of AST, ALT, and LDH were found to be modestly predictive. The adverse maternal outcome included maternal mortality and any of the following maternal complications: hepatic dysfunction; seizures of eclampsia; posterior reversible encephalopathy syndrome; retinal detachment or cortical blindness, Glasgow coma score < 13; stroke; transient ischemic attack; reversible neurologic deficit; need for positive inotropic support; myocardial ischemia or infarction; acute renal insufficiency; acute renal failure; dialysis; pulmonary edema; SpO₂ < 90%; intubation (other than solely for Caesarean section); transfusion of any blood product; thrombocytopenia (< 1,00,000).¹³

In our study, we also found that in patients with positive MRI findings, AST and ALT levels were deranged and the difference between AST and ALT levels of patients with and without positive MRI findings was found to be statistically significant (p value 0.008 and 0.0002 respectively).

Serum creatinine level >1.0 mg/dL, uric acid level >7.8 mg/dL can be used to predict the patient at high risk for significant maternal morbidity.¹⁴

In our study, on comparing the patients with and without positive MRI findings, the uric acid levels and serum creatinine levels were higher among those with MRI findings and the difference was statistically significant (p value <0.0001, <0.0001). Cortical blindness is manifested in 1–15% of patients with severe preeclampsia and eclampsia.¹⁵ Acute cortical blindness is one of the most alarming presentations of preeclampsia and is often found to be reversible. It is defined as blindness found in association with normal pupillary function and fundoscopy.¹⁶

In our study, we found that visual blindness manifested in 47.5% of the total eclampsia and severe preeclampsia patients. The blindness found in our study was associated with normal fundoscopy and pupillary function and was reversible within 7 days of termination of pregnancy.

V. Conclusion

As we have observed patients suffering from severe preeclampsia and having positive cerebral findings on MRI scan have a greater chance of developing seizures as compared to the patients diagnosed as severe preeclampsia and having negative findings on MRI scan. This is suggestive of PRES as an antecedent to the eclamptic seizure as opposed to the result of eclamptic seizure. This group of patients have the maximum potential to benefit from aggressive therapy to control the elevated blood pressure. This correlates very well with the other lab parameters and the imminent symptoms and signs of preeclampsia. So MRI should be included in initial workup of patient of severe preeclamptic toxemia along with the other necessary investigations. However, employing MRI for screening is not cost effective and large scale randomized control trials are needed to further confirm the role of MRI in severe preeclampsia.

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