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ORIGINAL ARTICLE

Correlation of Clinical and Neuroimaging Findings affecting Management in Postpartum Eclampsia: A Prospective Study

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ABSTRACT

Objectives: To correlate clinical and radiologic findings, to determine whether brain tomography affects management and routinely indicated in uncomplicated postpartum eclampsia and to differentiate it from other potentially treatable conditions.

Methodology: This was a prospective hospital-based study of 28 postpartum eclamptics with atypical or complicated course. Neuroimaging was done after stabilizing them with standardized eclampsia regimen. The relationship between maternal demographic, clinical and neuroimaging data with the cause for postpartum seizures was statistically analyzed with Yate's Chi-square test and Odds ratio with 95% confidence interval.

Results: The eclampsia incidence was 3.64% (326/8944 deliveries). Noneclamptic organic cause for seizures was more in late postpartum eclamptics. Among ten early postpartum eclamptics, 80% had normal neuroimaging, one cerebral edema and one neurocysticercosis. Among 18 late postpartum eclamptics, four had normal neuroimaging, one falcian calcification, one cerebral hypoxia, eight (28.6%) cortical venous thrombosis, three granuloma and one gliosis.

Conclusion: Despite many abnormalities seen on imaging studies, some are incidental and transient, without chronic neurologic sequelae. Thus, expensive neuroimaging has limited role in uncomplicated cases with typical clinical course and prompt response to standard therapy. Thus, neuroimaging is indicated in atypical and fatal cases where specific therapy may be required.

Keywords: Postpartum eclampsia, Neuroimaging, CVT, Eclampsia.

INTRODUCTION

Hypertensive disorders remain among the most significant unsolved problems in obstetrics. They form a deadly triad with hemorrhage and infection contributing to high fetomaternal morbidity and mortality. These contribute to 13% of maternal deaths in India[1] and 10 to 20% globally (maternal and neonatal directed assessment of technology). Preeclampsia, a complex multisystem disorder characterized by triad of newly onset labile hypertension and proteinuria after 20 weeks of gestation. Eclampsia, the dramatic and life-threatening complication of preeclampsia, characterized by convulsion or coma not attributable to any organic neurological disease.[2] Eclampsia and other neurologic manifestations, like headache, hyper-reflexia, visual symptoms, somnolence are due to cerebral circulatory dysregulation.[2]

"Delivery is the ultimate cure of eclampsia" is a traditional belief but it does occur in the postpartum period too. Thus, the cause for postpartum eclampsia especially late is viewed with skepticism.[3] In late postpartum eclampsia seizures could occur from 48 hours of delivery up to four weeks.[3-5] Its incidence is increasing in western countries with decreasing incidence of antepartum eclampsia.[6] Its presentation differs from that of antepartum eclampsia, as it may occur without antecedent premonitory symptoms or preeclampsia. But appearance and recognition of premonitory symptoms could lower maternal morbidity and mortality by early detection. However, delayed onset and atypical presentation lead to misdiagnosis.[4,6] Thus, only high index of suspicion and close follow-up in the postpartum period help in early detection. Eclampsia contributes to one-third maternal mortality in developing countries where resources for patient investigation and management are limited. So awareness of this condition could prevent unnecessary expensive investigation.[7]

The late postpartum eclampsia needs to be differentiated from other catastrophic but potentially treatable conditions, like cortical venous thrombosis (CVT), tuberculoma, brain tumor neurocysticercosis, meningitis, encephalitis, brain abscess and cerebral malaria by early evaluation.[3,4] Computed tomography (CT) and MRI of brain have revolutionized visualization of lesions in eclampsia and other organic conditions. CT is a rapid initial imaging tool preferred to MRI in some conditions, like hemorrhage and space occupying lesions and complementary to MRI in others.

This study was done to correlate clinical and neuroimaging findings, to determine whether CT of brain affected management and whether it was routinely indicated in otherwise uncomplicated postpartum eclampsia to differentiate it from other potentially treatable conditions.

MATERIALS AND METHODS

This was a hospital-based study done during June 2003 to June 2005. Prospective ascertainment of postpartum eclamptic women with atypical or complicated features, like-late onset postpartum eclampsia, more than five episodes of convulsions, recurrence of convulsions after standard therapy, mean arterial pressure (MAP) < 105 mm Hg, prolonged altered sensorium, visual symptoms and neurologic deficits, like facial palsy/ hemiparesis, were done.

Eclamptic women were stabilized with standardized regimen that included fluid restriction, use of magnesium sulphate as anticonvulsant and antihypertensives. Depending on clinical situation specific laboratory investigations and neuroimaging were done. After initial plain CT, contrast-enhanced CT was done where indicated. Maternal demographic, clinical, laboratory and neuroimaging data; fetomaternal outcome and associated morbidities, were collected and analyzed.

Statistical analysis was accomplished using Yate's correted chi-square test with one degree freedom for testing differences in proportion assuming significance at probability < 0.05. As more than 20% of expected frequencies were less than five, Yate's correction was employed to improve accuracy. Odds ratio and its 95% confidence interval was constructed.

Ethical clearance was obtained from institutional ethical committee.

RESULTS

During the study period, 326 eclamptic women were managed among 8,944 deliveries. Thus, the incidence of eclampsia was 3.64 per 100 deliveries. There were 91women with postpartum eclampsia, out of which 28 women needed prompt neuroimaging due to severe symptoms and signs.

Demographic, obstetric, clinical and laboratory data are summarized in Table 1. Mean maternal age was 23.89 years (range 18-30 years). Of 28 eclamptic women 67% (19) were from rural areas, 71% (20) were unbooked and 40% (11) were multipara. There was history of preeclampsia in previous pregnancy in 9% (1) of multiparous women. Five women were diagnosed to have preeclampsia before onset of seizures (four in antepartum and one in postpartum period). None of them had past history of seizure disorder or neurologic diseases. 14.3% (4) had delivered in the hospital; 82% (23) had seizures following term delivery, one following evacuation of molar pregnancy at four months and remaining following preterm delivery. Three (10.7%) women were delivered by cesarean section for obstetric reasons and one had induced delivery. 50% (14) of them had normal MAP. Evidence of renal dysfunction with significantly increased uric acid was seen in 10.7 % (3) of women.

Noneclamptic organic cause for seizures was more common in 21 to 25 years age group, urban women, unbooked, multipara, following term delivery, with normal MAP, without peripheral edema and with mild to moderate proteinuria but none of them were statistically significant (Table 1).

Mean day of seizures after delivery was 5.43 days (6 hours to 20 days). 64.3% (18) had late postpartum eclampsia. Presence of atleast one premonitory symptom was more common in late postpartum eclampsia (OR = 1.5, p = 1). More than one premonitory symptom was present in 22.2% (4) in late postpartum eclampsia compared to 10% (1) in early (OR = 2.57, p = 0.7680) (Table 2). Headache was most common premonitory

Table 1 Relationship between maternal demographic, clinical, laboratory findings with cause of postpartum convulsions

Factors		O	%	E	%	T	%	OR	CI	p-value
1. Age	< 20 years	—	—	4	26.7	4	14.2	—	—	—
	21-25 years	10	76.9	6	40	6	57.1	2.77	—	—
	26-30 years	3	23.1	5	33.3	8	28.6	1	0.48-16.03	0.4691[b]
2. Residence	Rural	8	61.5	11	73.3	19	67.9	1	—	—
	Urban	5	38.5	4	26.7	9	32.1	1.71	0.35-8.51	0.7942[b]
3. Booking status	Booked	2	15.3	6	40	8	28.6	1	—	—
	Unbooked	6	84.6	9	60	20	71.4	3.67	0.59-22.78	0.3085[b]
4. Parity	Primi, nulli	7	53.8	10	66.7	17	60.7	1.71	0.37-7.92	0.7602[b]
	multipara	6	46.2	5	33.3	11	39.2	1	—	—
5. Period of gestation	Term	11	84.6	12	80	23	82.1	1.375	—	—
	Preterm	2	15.3	3	20	5	17.9	1	0.19-9.83	0.8602[b]
6. Premonitory symptoms	Present	10	76.9	11	73.3	21	75	1.21	0.22-6.80	0.8265[b]
	Absent	3	23	4	26.7	7	25	1	—	—
7. Number of convulsions	< 5	6	46.2	7	46.7	13	46.4	1	—	—
	6-10	7	53.8	8	53.3	15	53.6	1.020	0.23-4.53	0.7247[b]
8. Edema	Present	9	69.2	8	53.3	17	60.7	1.988	0.42-9.32	0.6375[b]
	Absent	4	30.7	7	46.7	11	39.2	—	—	—
9. MAP	≤ 105	7	53.8	7	46.7	14	50	1.33	—	—
	>105	6	46.2	8	53.3	14	50	1	0.03-5.91	1[b]
10. Proteinuria	Present	10	76.9	9	60	19	67.9	2.22	0.43-11.60	0.5820[b]
	Absent	3	23	6	40	9	32.1	1	—	—
11. Uric acid	High	—		3	20	3	10.7	0	—	0.2739[b]
	Normal	13	100	12	80	25	89.3	—	—	—

O: Noneclamptic organic lesions; E: Eclampsia; T: Total; OR: Odds ratio; CI: Confidence interval
p-value: Level of significance; [b]: Not significant; MAP: Mean arterial pressure in mm Hg

symptom (n = 20, 71 %). 14.3% (4) had visual symptoms ranging from blurring of vision to blindness. Two out of these four women had normal CT and two had CVT of superior sagittal sinus (SSS) (Table 3). 7.14% (2) of women had recurrent convulsions after standard therapy. Neurological evaluation revealed hyper-reflexia and flexor plantar in all except three (10.7%) women who revealed unilateral hemiparesis and extensor plantar. Two of them had unilateral upper motor neuron facial palsy. Prolonged altered sensorium in the form of drowsiness, confusion and irritability was present in 17% (5) of them. Fundoscopy showed bilateral mild retinal edema in 25% (1/4) of women with visual symptoms and normal in others.

Noneclamptic organic cause of seizures was more common in women with recurrent convulsions (OR = 1.17, p = 0.5281), with prolonged altered sensorium (OR = 6.22, p = 0.2435), with visual symptoms (OR = 1.18, p = 0.6985) and in those with focal deficits (p = 0.1749) (Table 3).

Average time to scan to seizure was 3.4 days (1st-6th day after convulsion). 80% with early postpartum eclampsia had normal study, one had focal cerebral edema in parietal and occipital lobes (Fig. 1) attributed to eclampsia perse whereas in the other it was explicable by unexpected unrelated finding: neurocysticercosis (Fig. 2) that is speculated atleast to contribute to seizures. Four (22.22%) women with late postpartum eclampsia had normal study, one had falcine calcification (Fig. 3), one cerebral hypoxia (Fig. 4), eight (28.6%) CVT (Figs 5 and 6), three granuloma and one gliosis (Table 4).

One woman with cerebral infarct due to CVT died. Family denied autopsy, thus exact cause of death could not be ascertained. Others had complete neurological recovery by discharge.

DISCUSSION

The pathophysiology of eclampsia, the enigmatic pregnancy complication, is explained by two polarized theories.[8] The first called 'overregulation', intense cerebral vasospasm due to explosive increase in blood pressure results in microischemic damage to blood-brain barrier leading to cytotoxic edema. The second called 'breakthrough', loss of autoregulation with resultant dilation leading to subsequent vasogenic edema. Both theories may be operative in some eclamptics. Endothelial damage, abnormal placentation, imbalance between vasodilatory and vasoconstrictive prostaglandins[3] are some

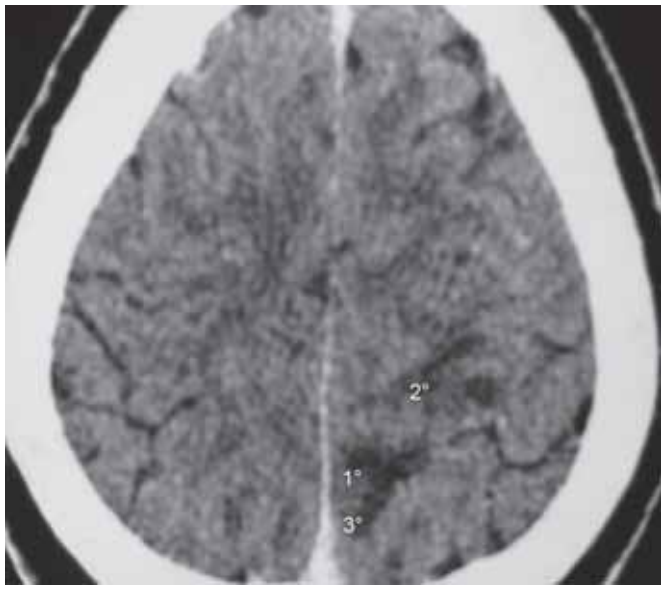

Fig. 1: Focal hypodensities in left parietal and occipital lobe-cerebral edema

Table 2 Antecedent preeclampsia in early and late postpartum eclampsia

Factors		*Early*	*%*	*Late*	*%*	*T*	*%*	*OR*	*CI*	*p-value*
1. History of preeclampsia	Present	4		1		5		11.33	1.05-122.5	0.0775[b]
	Absent	6		17		23				
2. Premonitory symptoms	1	9		14		23		2.57	0.25-26.85	0.7680[b]
	>1	1		4		5				

[b]: Not significant

Table 3 Relationship between neurologic manifestations and cause of postpartum convulsions

Factors		*O*	*%*	*E*	*%*	*T*	*%*	*OR*	*CI*	*p-value*
1. TOC	Early < 48	1	7.7	9	60	10	35.7	1	–	–
	Late > 48	12	92.3	6	40	18	64.3	18	1.83-177.2	0.0129[a]
2. NOC	≤ 5	6	46.2	7	46.7	13	46.4	1	–	–
	> 5	7	53.8	8	53.3	15	53.6	1.020	0.23-4.53	0.7247[b]
3. ROC	Present	1	7.7	1	6.67	2	7.14	1.17	0.07-20.72	0.5281[b]
	Absent	12	92.3	14	93.3	26	92.8	1	–	–
4. Focal deficits	Present	3	23.1	–	–	3	10.7	1	–	0.1749[b]
	Absent	10	76.9	15	100	25	89.3	–	–	–
5. PAS	Present	4	30.8	1	6.7	5	17.9	6.22	0.59-64.97	0.2435[b]
	Absent	9	69.2	14	93.3	23	82.1	–	–	–
6. Visual symptoms	Present	2	15.4	2	13.3	4	14.3	1.18	0.14-9.827	0.6985[b]
	Absent	11	84.6	13	86.7	24	85.7	1	–	–

TOC: Timing of convulsion; NOC: Number of convulsions; ROC: Recurrence of convulsions after standard therapy; PAS: Prolonged altered sensorium; CI: Confidence interval; [a]: Statistically significant; [b]: Statistically not significant.

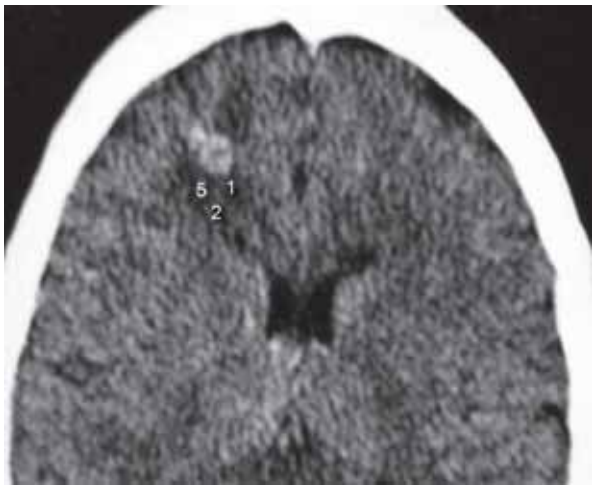

Fig. 2: Neurocysticercosis ring enhancing lesion with eccentric enhancing focus in right frontal lobe

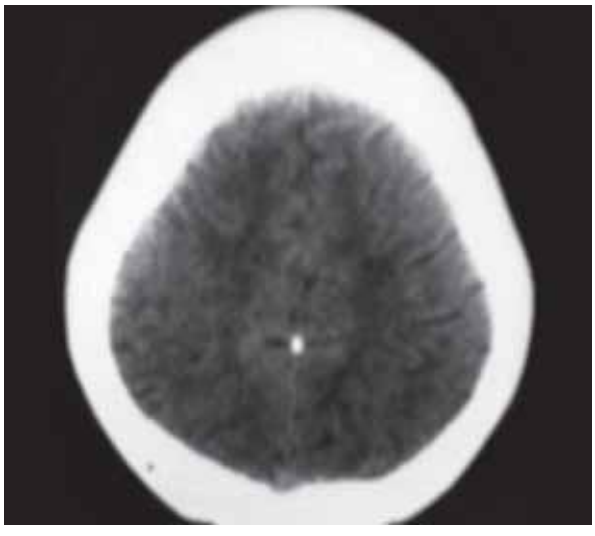

Fig. 3: Focal nodular calcification of falx cerebri

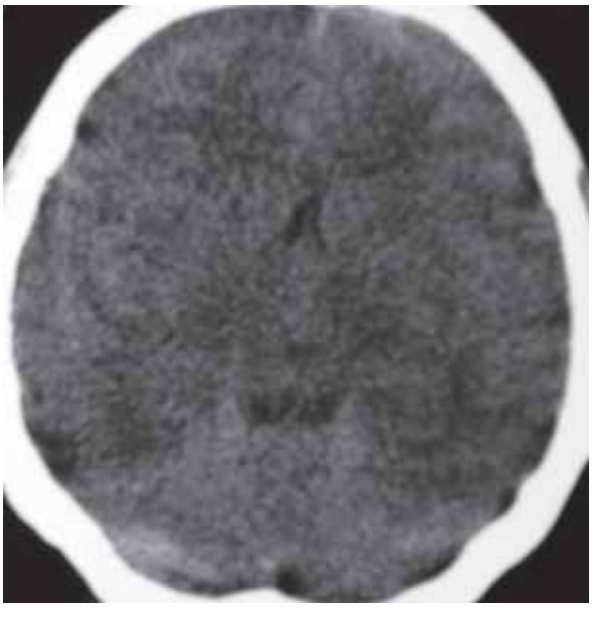

Fig. 4: Effacement of sylvian fissure and basal cisterns with loss of differentiation between grey and white matter suggestive of cerebral hypoxia

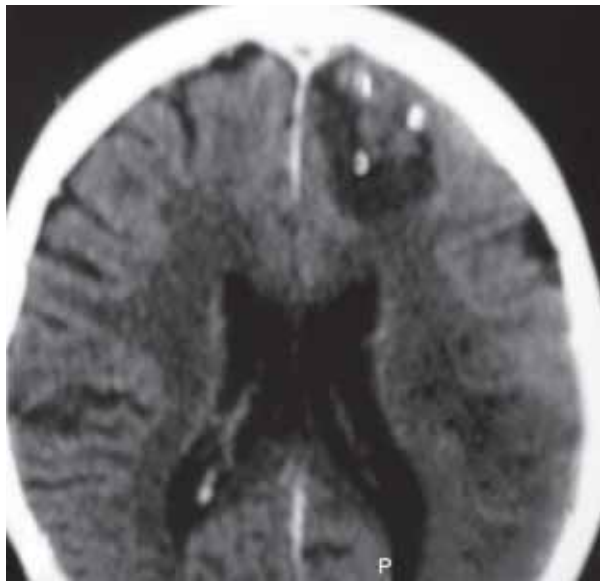

Fig. 5: CVT with hemorrhagic venous infarct in left frontal lobe

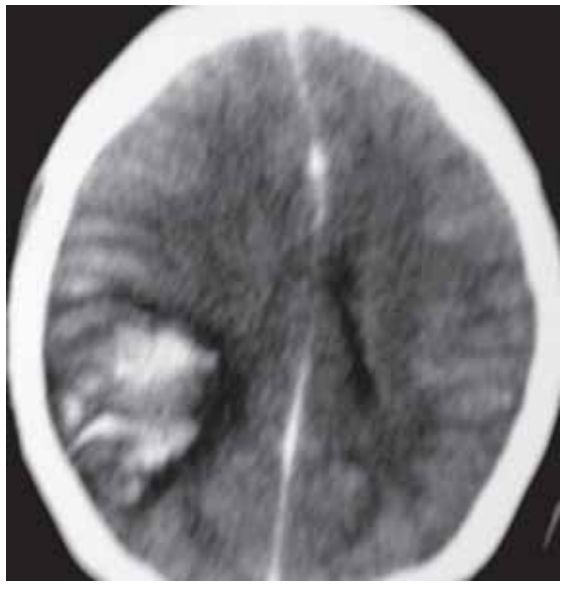

Fig. 6: CVT with hemorrhagic infarct of right parietal lobe

proposed triggers for vasospasm. Predilection of symptoms and neuroimaging findings in posterior circulation explained by more anterior sympathetic innervation.

The eclampsia incidence of 3.64% in this study was comparable to 3.7% by Chakravarthy[2] and higher than 0.11% by Cunningham[8] and 3/1000 by Sibai.[3] 28% of them had postpartum eclampsia compared to 25% reported by Sibai.[3] About 18% of all eclampsia and 64% of postpartum eclampsia was late postpartum eclampsia, comparable to 25% and 79.3% respectively by Chames,[9] 18.5% and 56 % by Lubarsky.[5] Only 5.8 % (1/18) of late postpartum eclampstics had to preeclampsia before seizure onset compared to 21.7% (5/23) as reported by Chames[9] and 56% by Lubarsky.[5]

Convulsions usually occur after one or more premonitory symptoms or accompany emergence of overt preeclampsia in women receiving regular obstetric care. Yet eclampsia can strike

Table 4 Neuroimaging findings (CT brain) in early and late postpartum convulsions

CT of brain findings	*Early <48 hours*	*Late >48 hours*	*Total*	*N*	*%*
Eclampsia					
Normal study	8	4			
Cerebral edema in BP and RO	1			15	53.6
Cerebral hypoxia		1			
Cerebral calcification in Falx		1			
Cortical venous thrombosis				13	
Superior sagittal (SS)		3			
SS + HI LF		1			
SS+ HI BF		1	8		
Transverse sinus (TS)		1			
TS + HI RP		1			
TS+ HI LTP		1			
Granuloma					46.4
LF-calcified		1			
RF-neurocysticercosis	1		4		
RP-calcified		1			
RP- with perilesional edema (tuberculoma)		1			
Gliosis – LT		1	1		
Total (%)	10 (35.7)	18 (64.3)		28	100

F: Frontal; P: Parietal; T: Temporal; O: Occipital; B: Bilateral; R: Right; L: Left; HI: Hemorrhagic infarct

Table 5 Maternal complications/Associated comorbidities and fetal outcome

Complications	*Number*
Severe anemia	4 (14.2%)
Pyrexia	2 (7.14%)
Respiratory infection	4 (14.2%)
Urinary tract infection	1 (3.6%)
Blindness	1 (3.6%)
Hydatidiform mole	1 (3.6%)
Facial palsy	2 (7.14%)
Hemiparesis	3 (10.7%)
Pulmonary edema	1 (3.6%)
Pleural effusion	1 (3.6%)
Maternal death	1 (3.6%)
IUGR	1 (3.6%)
Intrauterine death	1 (3.6%)
Stillbirth	4 (14.2%)
Early neonatal death	1 (3.6%)

without anticipatory symptoms. There could be absolutely no premonitory symptom or increased blood pressure until just before or after convulsions as in some women in this study (see Table 1). Sibai noted 19 to 32% of such eclamptic women. But physicians should be aware of sudden surge in blood pressure, headache, hyper-reflexia, mental status and visual changes and thoroughly evaluate such postpartum women. 75% had atleast one premonitory symptom in this study compared to 91% by Chames.[9] Headache was the most common premonitory symptom present in 71% in this study compared to 83% by Lubarsky,[5] 87% by Chames.[9] 17.9% had more than one premonitory symptom which was less than 52% by Chames.[9] There was normal CT finding in two women with visual symptoms, which might be due to delayed scan on fourth day of seizure. Incidence of Pulmonary edema and maternal death was 3.5% each in this study comparable to 5.9% and 4.2% by Matthys (Table 5).[10]

In most instances brain CT in eclamptics might be normal due to temporal relationship of scan to seizure. Postpartum seizures in women with normal CT were due to eclampsia. Most common lesions detected on CT in eclampsia are focal areas of cerebral edema in subcortical white matter of parietal and occipital areas [3] as seen in one case in this study (Fig. 1). Neuroimaging within a short time after seizure in eclamptics may yield more abnormalities, presumably due to transient nature of lesions. CT revealed falcian nodular calcification which was considered to be physiological. Seizures in women with falcian cerebral calcification and features of cerebral hypoxia on CT were considered to be due to eclampsia. In this study, 46.4% (13) of women had other noneclamptic organic causes for postpartum seizures compared to 12.9% (8/62) by Lubarsky [5], 33% by Santos (2/6).[4]

CVT incidence is one in 250. Sepsis, preeclampsia, puerperium, dehydration, hyperviscosity are risk factors. Most commonly CVT occurs in SSS and transverse sinus (TS). They present with hypertension, severe progressively worsening headache, altered sensorium, recurrent convulsions and focal deficits. It could be treated with anticonvulsants, anticoagulants and steroids. In this study, 28.6% (8) of postpartum seizures were due to CVT, five of them in SSS and three in TS. Women with tuberculoma present with seizures/focal deficits and could be seen as ring enhancing lesions on CT. They being uncommon and could be treated with antitubercular drugs. Seizures were due to parenchymal neurocysticercosis in one woman. The characteristic neuroimaging ring enhancing lesion with eccentric enhancing focus was diagnostic whereas negative serology did not exclude it. Treatment was done by anticonvulsants and anthelmenthic. This finding was similar to a case report by Grondin et al.[11]

Inspite of absence of any recognizable cause for postpartum seizures by medical, neurological, laboratory and imaging findings, another possibility could be spontaneous postpartum cerebral angiopathy because of overlap of features between this and the late postpartum eclampsia.[4]

This study had some limitations. CT scan could be done in only 28 of 91 postpartum eclamptic women during 2-year period due to limited access. In some women, CT could not be done on same day of seizure due to scheduling problems. Follow-up scan to look for resolving lesions could not be done because of uneventful clinical course in some and cost constraints in others. MRI was not done as the facility was not available.

During the study period, 14% of maternal mortality was due to eclampsia. Delivery did not eliminate risk of eclampsia. Therefore, any postpartum convulsion should be treated as eclampsia with magnesium sulphate and blood pressure needs to be optimized to 140/90 mm Hg till other neurological cause for seizures is excluded.[3] Postpartum eclampsia is associated with significant morbidity and mortality, so efforts should be made to prevent its occurrence by continuous monitoring and evaluating of prodromal symptoms and patient's education at discharge. It can also occur without warning or any ante/intra/postpartum complication. So once seizures occur, prompt obstetric and neurological evaluation and neuroimaging where indicated should exclude other potentially treatable conditions that could be responsible for convulsions.[3]

Studies have shown that focal hypodense lesions in posterior occipital and parietal areas are the most common findings on CT and there is no difference in their incidence in eclamptics and hypertensives,[12] so it cannot be accepted as common cause for convulsions. They are also seen in women with uneventful recovery on routine eclamptic management. In this study, management was affected by imaging findings in cases of CVT, tuberculoma and neurocysticercosis. But even some cases of CVT without severe neurologic manifestations had rapid uneventful recovery with routine measures despite ominous findings and none of them required emergency intervention on the basis of radiologic findings. So whether therapeutic measures in cases with typical clinical course have salutary effect is conjectural and on the other hand in some cases imaging findings might lead to mismanagement. If cerebral edema is seen on tomography mannitol is recommended, vasogenic edema improves but cytotoxic edema worsens. Despite high incidence of abnormalities seen on imaging studies, some are incidental (calcification) and transient (focal areas of edema) findings that do not have long-term neurologic sequelae. Because of cost constraints, especially in developing countries where resources for investigations and management are limited, there is limited role for expensive investigations, like imaging evaluation in uncomplicated cases (without focal deficits or prolonged coma) with typical clinical course and prompt response to standard therapy.

The nature of anatomic lesions causing cerebral manifestations in preeclampsia remains unanswered. So neuroimaging should not be indicated only to know pathophysiology of postpartum eclampsia. It could be indicated in atypical and potentially fatal cases where specific therapy might be required. On the horizon development of better modalities, like diffusion weighted MRI, MR angiography, single photon emission tomography, transcranial Doppler and larger studies using them with proper timing of scan and serial imaging might throw more light on natural history of cerebral manifestations in the research setting for such grave complications in pregnancy.

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