

A STUDY OF THE VARIED AETIOLOGY AND CLINICAL PRESENTATION OF NEW ONSET SEIZURES IN POSTPARTUM PERIOD

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ABSTRACT

BACKGROUND

Seizures in the postpartum period are the major cause of mortality and morbidity. A variety of neurological disorders causing seizures may be encountered during pregnancy and puerperium. These disorders may be unrelated to pregnancy (e.g. Meningitis) or peculiar to pregnancy (e.g. Eclampsia) or. Pregnancy may affect the course of the pre-existing neurological disorders such as epilepsy. So, keeping in mind the varied aetiology of postpartum seizures and its response to appropriate treatment, our study has been conducted to find out the most common causes in our setup to guide the optimal therapy.

AIM OF THE STUDY

To study the varied aetiology and clinical presentation of new onset seizures in the postpartum period over a period of two years.

MATERIALS AND METHODS

50 patients who developed first episode of seizures in postpartum period (that is after delivery to 6 weeks) admitted to Osmania General Hospital on random selection. All women complaining of new onset seizure with in postpartum period up to 6 weeks. All those women who are known epileptics and who had seizures in the antenatal period were excluded from the study. The selected patients were studied in detail with history and physical examination.

RESULTS

Different causes for first episode of seizures in postpartum period are enlisted here. Cavernous sinus thrombosis in 17 patients, late postpartum eclampsia accounted for 13 patients, intracranial haemorrhage in 6 patients, ischaemic stroke in 5 patients, posterior reversible encephalopathy syndrome in 4 patients, CNS infections in 6 patients, glioma in 1 patient, viral hepatitis in one patient, idiopathic in 3 patients.

CONCLUSIONS

Cavernous sinus thrombosis and late postpartum eclampsia constitute the major aetiology of first onset of seizures occurring in the postpartum period.

KEYWORDS

New Onset Seizures, Postpartum Seizures.

HOW TO CITE THIS ARTICLE: Sudarsi RK, Ratikrinda A. A study of the varied aetiology and clinical presentation of new onset seizures in postpartum period. J. Evid. Based Med. Healthc. 2016; 3(68), 3710-3714. DOI: 10.18410/jebmh/2016/795

INTRODUCTION: Seizures are defined as "Abnormal electrical activity associated with certain behavioural and neurological effects." Seizures can also occur in the normal nervous system when its metabolic environment is disturbed. It has been estimated that seizure disorder affects nearly 1.1 million women of child bearing age in the United States.⁽¹⁾ Approximately 1% of pregnant women suffer seizures, and the initial seizure can present in the antepartum, intrapartum or postpartum period.⁽²⁾ The most common cause of seizures during pregnancy and postpartum period is pre-existing epilepsy, followed by eclampsia as the second most common cause.

Epilepsy has been defined as recurrent seizures resulting from congenital or acquired factors, affecting approximately 0.6% of the population.^(1,3) Seizures in the postpartum period are major cause of mortality and morbidity. A variety of neurological disorders causing seizures may be encountered during pregnancy and puerperium. These disorders may be unrelated to pregnancy (e.g. Meningitis) or peculiar to pregnancy (e.g. Eclampsia). Pregnancy may affect the course of pre-existing neurological disorders such as epilepsy. Seizures may also occur in metabolic encephalopathies secondary to hypoxia-ischaemia, hypoglycaemia, hepatic failure, azotaemia, and hyperglycaemia.

So, keeping in mind the varied aetiology of postpartum seizures and its response to appropriate treatment, our study has been conducted to find out the common causes in our setup to guide optimal therapy.

Financial or Other, Competing Interest: None.
Submission 04-07-2016, Peer Review 17-07-2016,
Acceptance 24-07-2016, Published 25-08-2016.
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DOI: 10.18410/jebmh/2016/795

AIM OF THE STUDY: To study the varied aetiology and clinical presentation of new onset seizures in the postpartum period over a period of two years.

METHODS: A prospective study in which 50 patients from medical wards with seizures in postpartum period up to 6 weeks admitted into OGH were included. The patients were taken from the medical wards of the hospital based on random selection.

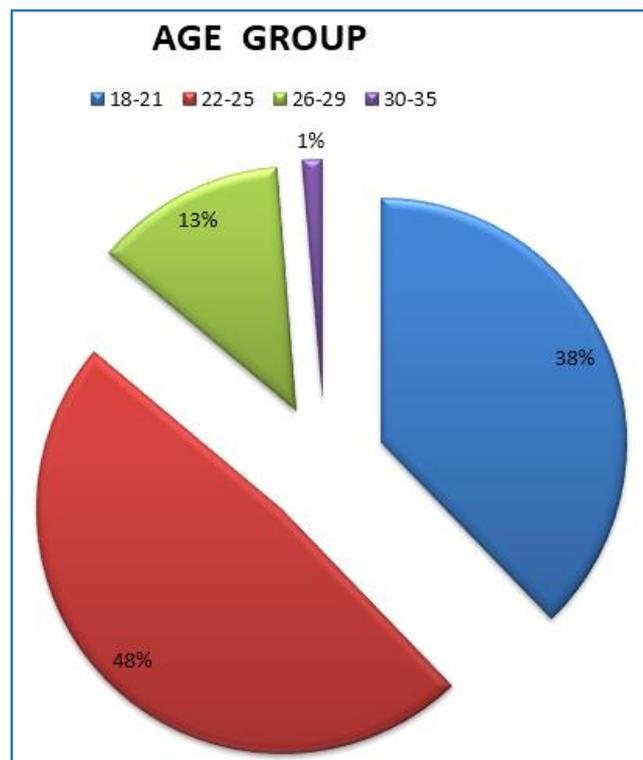
Inclusion Criteria: All women complaining of new onset seizure within postpartum period up to 6 weeks.

Exclusion Criteria: All those women who are known epileptics and who had seizures in the antenatal period were excluded from the study. The selected patients were studied in detail with history and physical examination.

OBSERVATIONS & RESULTS: We included 50 women with seizures in the postpartum period due to different neurological disorders who came to Osmania General Hospital and the data is analysed as follows. Age group studied is 18-35 yrs., out of them maximum of patients are falling within the age group of 22-25 yrs.

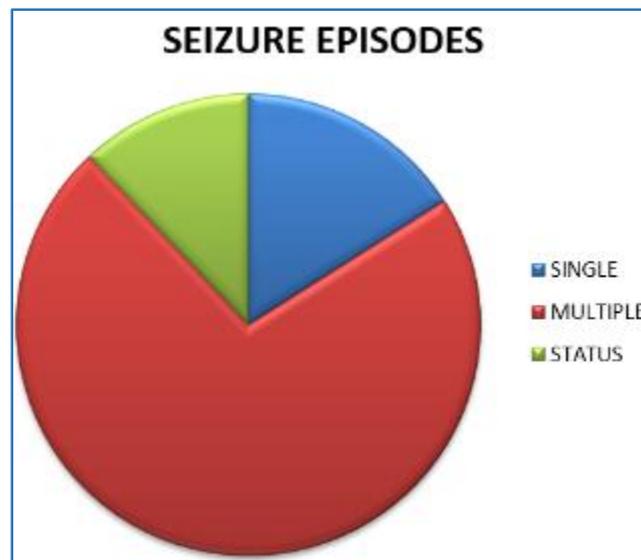
Age Group	No. of Patients	Percentage
18-21	18	36
22-25	23	46
26-29	6	12
30-35	3	6

Table 1: Demographic Data



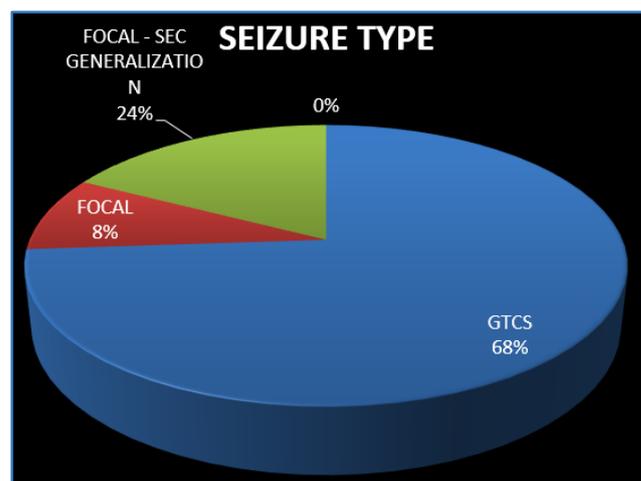
	Number	Percentage
Single Episode	8	16
Multiple Episode	36	72
Status Epilepticus	6	12

Table 2: Number of Seizure Episodes



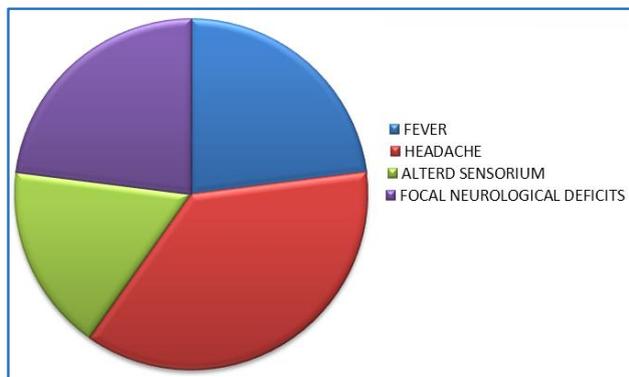
	Number	Percentage
GTCS	34	68
FOCAL	4	8
FOCAL - Secondary Generalisation	12	24

Table 3: Type of Seizure



Symptoms	No. of Patients	Percentage
Fever	20	40
Headache	32	64
Altered Sensorium	15	30
Focal Neurological Deficits	20	40

Table 4: Presenting Symptoms



Etiology	No. of Patients	Percentage
Cavernous Sinus Thrombosis	17	34
Late Postpartum Eclampsia	13	26
Intracranial Haemorrhage	6	12
PRES	4	8
Ischaemic Stroke	5	10
Cerebral Malaria	3	6
TB Meningitis	2	4
TB Granuloma	1	2
CNS Glioma	1	2
Idiopathic	3	6
Acute Viral Hepatitis	1	2

Table 5: Aetiology

Six patients were observed to have more than one aetiological factor.

RESULTS:

Late Postpartum Eclampsia: Accounted for thirteen patients. They presented between 3rd to 21st day postpartum. Nine of them had history of preeclampsia. All the classical symptoms of preeclampsia like oedema, proteinuria and hypertension were not observed in other 4 patients. It is observed that these patients had symptoms of cerebral oedema like visual disturbances and headache even when blood pressure remains normal. Three patients of postpartum eclampsia were found to have CSVT and three more patients were associated with ICH. All the patients with eclampsia were treated with MgSO₄ and antihypertensives, remained stable and had no further convulsions. They had an uneventful recovery. One patient with preeclampsia developed HELLP syndrome and DIC and expired on day 4 of admission.

Posterior Reversible Encephalopathy Syndrome: In a study carried out by Hinchey et al, most of their patients (n=11/15) had focal or generalised seizures.⁽⁴⁾ Visual abnormalities were present in 10 patients; consisted of cortical blindness, homonymous hemianopia and blurred vision. FND's were uncommon.

In our patients (Four), we did not find any FND. Visual abnormalities (Blurring of vision in one, Cortical blindness in another) were found in 2 patients. All of them had generalised seizures. All the patients presented with blood pressure ranging from 140/90 to 170/100 for the first time during onset of seizures. None of them had proteinuria or any other stigmata of preeclampsia. All the four patients reported here had white matter abnormalities on imaging consistent with RPLES.

Cavernous Sinus Thrombosis: Is the most common cause of seizures in our study. Total number of patients were 17. Most of them presented between 10-21st postpartum day. Ten patients showed venous sinus thrombosis. Seven patients had haemorrhagic infarcts in the venous territory. Three of them had associated history of eclampsia. One patient was positive for antinuclear antibody, hyperhomocystinaemia in one patient, two patients have found to have protein C deficiency. Pyrexia as noted in 15-60% of cases does not necessarily imply infection and is probably caused by an aseptic thrombosis. Pyrexia is seen in 50% of our cases.

Papilledema: The incidence of papilledema is variable and depends on the aetiology, rate and site of venous thrombosis. It is less common in puerperal cerebral venous thrombosis with acute presentation of headache, seizures, focal neurological deficits and altered sensorium. The incidence among Indian patients varies from 7.4-55 %. Papilledema is seen in 21.5% of patients in our study.

Ischaemic Stroke: Five patients presented with arterial infarctions, one had rheumatic mitral stenosis with atrial fibrillation. She was not under regular penicillin prophylaxis. She presented on the 9th postpartum day with left hemiplegia and left facial nerve palsy along with seizures and was found to have an infarct in the right capsule ganglionic region. The second patient presented in the 3rd postpartum day with right focal seizures and her CT-brain showed small infarct in the middle cerebral artery territory. Her 2D-Echo was suggestive of peripartum cardiomyopathy with severe LV dysfunction (Ejection fraction-24%) with apical clot 2-3 cm². Her coagulative and connective tissue profile was normal.

Two patients presented on 10th postpartum day-one had aphasia, left hemiparesis with left third nerve palsy; the other presented with bilateral cerebellar signs, more on the left side. The former was found to have multiple infarcts in the internal capsule, basal ganglia, midbrain and cerebellum, while the latter had bilateral cerebellar infarcts on neuroimaging. Both these patients were diagnosed as anti-phospholipid antibody syndrome with positive lupus anticoagulant and anti-cardiolipin antibodies. The fifth patient presented on the 4th postpartum day with GTC Seizures and left hemiplegia with CT brain showing infarct over the temporoparietal region. No specific underlying cause was found. All were treated with aspirin and anticoagulants and had mild residual neurological deficits.

Intracranial Haemorrhage: Out of the six patients with ICH, eclampsia was seen in three of them. Haemorrhage is the result of severe hypertension, although coagulation disorders associated with eclampsia may also play a role. Persistent neurological deficit was seen in two of them. One patient had history of chronic hypertension not under regular treatment. One patient has been diagnosed to have lupus vasculitis. No underlying cause has been found in one patient.

CNS Infections: Out of the six patients with CNS infections, there were 2 cases of tuberculous meningitis who presented with fever, headache, seizures, altered sensorium and focal neurological defects. One of them was found to be co-infected with HIV along with Cryptococcal meningitis with hydrocephalus. She expired after 4th day of admission, the other patient improved with ATT. One patient had tuberculoma in the parietal region, she presented with headache and 2 episodes of right focal seizures. Her seizures were controlled with antiepileptic drugs, one patient presented with fever, altered sensorium and status epilepticus. Meningeal signs were positive and CT imaging showed diffuse cerebral oedema with hyperdensities over bilateral temporal regions. CSF analysis suggestive of viral aetiology. Her seizures were hardly controlled on antiepileptics and she expired after 3 days.

There are two patients diagnosed to have cerebral malaria. One of them have been documented to have hypoglycaemic seizures, she improved on treatment, and the other patient had concomitant acute renal failure with thrombocytopenia and bleeding manifestation. Her seizures were not controlled on antiepileptics. She went into DIC after 2 days and expired. One patient of hepatic encephalopathy presented in the postpartum period (7th day), with fever, altered sensorium, jaundice, seizures and oliguria. Her Glasgow Coma Score was 7, LFT, coagulation profile, RFT and electrolytes were deranged. She had fever right from the antepartum period and had a still birth which was followed by seizures and altered sensorium. She recovered completely after treatment. One patient of CNS meningioma presented on the 6th day postpartum with 3 episodes of left focal seizures and were controlled with antiepileptics. She has been referred to neurosurgery department.

DISCUSSION: In the present study, 50 females who had seizures of new onset in the postpartum period (up to 6 wks.) with no h/o epilepsy are included. Each case was studied in detail with regard to clinical presentation and aetiology of seizure. Most of the patients are within the age group of 22-25 yrs. (23 of 50 patients). The most common cause of new onset seizure in the postpartum in our study is as follows-CSVT in 17 patients (34%), LPPE in 13 patients (26%), ICH in 6 patients (12%), PRES in 4 patients (8%), ischaemic stroke in 5 patients (10%) and the rest by the CNS infections (21%) which are incidental to the pregnancy, in the decreasing order. Eclampsia when associated with ICH has poor prognosis and associated with persistent neurological deficits.

In our study, among 3 of the ICH patients with eclampsia, 2 of them expired and one patient had residual neurological deficit. All patients with postpartum eclampsia except the one with HELLP syndrome and DIC (Expired), improved with complete neurological recovery. In a review by Douglas and Redman of the UK in the BMJ 1994;⁽⁵⁾ 309:1395-1400 found that in over 300 cases of eclampsia, 12% occurred more than 48 hrs. and 2% more 7 days postpartum. 90%-suffered from headache and visual disturbances prior to seizures and no classical preeclamptic signs are present in over 50% of the cases.

In our study, out of thirteen patients of LPPE, nine of them had h/o preeclampsia.

- Most common symptom is headache (90%).
- 60% (4 patients) experienced visual symptoms prior to the seizure activity.
- Only 9 of the patients had symptoms of preeclampsia.

As cited by Hinchey et al in their study of RPLES. N Engl J Med 334: 494-500,⁽⁴⁾ all 4 patients of RPLES recovered completely with antihypertensives and antiepileptics. The incidence rates for ischaemic strokes associated with pregnancy or puerperium vary in literature from five to 210 per 100,000 deliveries. The incidence of arterial thrombosis in most studies varied between 8 and 64% of the total cases (10% in our study). Residual paralysis as seen in this study, is a common sequelae of ischaemic arterial occlusion.^{(6),(7)} in the study by Sharshar et al i.e. Incidence and causes of strokes associated with pregnancy and puerperium. A Study in public hospitals of Ile de France. Stroke 1995; 26:930-6 concluded that 47% of non-Hg pregnancy related strokes occurred in the context of toxemia. Here in our study 2 out of 6 patients with ischaemic stroke had associated eclampsia.

Intracranial haemorrhage constituted from 2 to 7% of the total cases of neurological disorders in most studies ⁽⁸⁾ (12% in our study). As cited by Stern BJ⁽⁹⁾. in Neurol Clin 2004; 22:821-40 approximately half of the patients who survive a pregnancy related stroke are left with a residual neurological deficit. In our study out of 28 patients, (Including ICH, CSVT, Ischaemic stroke) of pregnancy related stroke, 11 patients had residual paralysis and three of them expired. As cited by Sharshar T, Lamy C, Mar J. in a study in public hospitals of Ile de France. Stroke 1995; 26: 930-6, mortality from pregnancy related stroke typically results from ICH or malignant HTN.⁽¹⁰⁾ Maternal deaths from ischaemic events are uncommon, and when they do occur, usually result from secondary haemorrhage. According to the data from the Nationwide Inpatient Sample by James A, Bushnell CD, Jamison M, et al in Obstet Gynecol. 2005; 106:509-16⁽¹¹⁾ reported an estimated overall case fatality rate for pregnancy related stroke of 4.1%. As expected, this is significantly lower than the CFR of 24% of all strokes 113. But is also lower than the reported mortality of 4.5-24% of all-cause strokes, in young adults. The case fatality rate for pregnancy related stroke in our patients is 10.6 %. i.e. three out of twenty eight patients.

TBM usually presents with classical manifestations during pregnancy, commonly between the 5th and 7th month or in the postpartum period. Most patients improve with treatment.⁽¹²⁾ as in our study. The sole patient with a CNS tumour (Meningioma) presented in the postpartum period, which is relatively rare. Usually there is an increase in the size of the tumour during pregnancy due to hormonal changes and amelioration of symptoms in the postpartum period.⁽¹³⁾ HE in pregnancy and puerperium may be related to a wide variety of acute and chronic liver diseases, out of which Hepatitis E virus infection is an important cause in India.⁽¹⁴⁾ Acute fatty liver of pregnancy (AFLP) generally presents after the 30th week of pregnancy. Fulminant viral hepatitis (FVH) leading to hepatic encephalopathy may be seen in any trimester or after puerperium. Our patient presented with jaundice and altered sensorium of less than 10 days' duration, in accordance with the definition of fulminant hepatic failure.⁽¹⁴⁾ Leucocytosis can be observed in HE due to AFLP, FVH or complicating infection.⁽¹⁴⁾ and is seen in our case also.

Cerebral venous thrombosis has an exceptionally high incidence in India, attributable to a combination of dehydration, infection; and the traditional fat rich diet fed to postpartum women causing a hypercoagulable state. The risk of peripartum CVT increases with hypertension, advancing maternal age, caesarean delivery, associated infections and excess vomiting during pregnancy. The rate of death from all-cause CVT is 2-10%, although mortality is significantly less for pregnancy-associated CVT. When maternal deaths occur, they usually result from secondary intracranial haemorrhage, although one analysis reported the most common cause of death to be transtentorial herniation.

CONCLUSIONS OF THE STUDY:

1. CSVT and LPPE constitute the major aetiology of seizures in the postpartum period.
2. Although delivery is usually the ultimate measure in the management of patient with preeclampsia, it does not eliminate the possibility of LPPE in the puerperal period.
3. The occurrence of LPPE without typical preeclampsia emphasises the need to be aware of the possibility of this diagnosis even in a pregnant patient with no hypertension and proteinuria, when headache and visual changes develop during the postpartum period.
4. Convulsions in the puerperium should be treated as eclampsia until proven otherwise.
5. The mortality is higher in patients with neurological disorders unrelated or incidental to the pregnancy state (CNS infections) than patient with disorders which are more prevalent during pregnancy like CSVT, LPPE.

6. Mortality from pregnancy related stroke mostly results from secondary haemorrhage.
7. About half of the patients with pregnancy related stroke (Ischaemia, ICH) had residual neurological deficits.

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