

TO STUDY THE COMMON ETIOLOGIES ASSOCIATED WITH SEIZURE DURING PERIPARTUM PERIOD

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Abstract

Background: Most seizures occur during pregnancy in women who already have epilepsy. In patients with new-onset seizure during the peripartum period, significant morbidity and mortality can be avoided by thorough examination and investigations to identify the specific cause to initiate appropriate treatment. Still, in developing countries like India, there is a significant burden of peripartum mortality with seizure being one of the important causes that encourage the present study. **Materials and Methods:** In the present Observational cross-sectional study, a total of 50 patients with seizures according to the definition given by ilesa and who had POG 9th month to 1 month postpartum were included. A detailed clinic-radiological examination along with biochemical investigations were done and analysed. **Result:** More than one-third of patients were <25 years (44%) followed by 25-30 (38%) and >30 (18%) years. EEG was abnormal in 11.1% of patients. ECL was in 14% of patients. Press aetiology was in 10% of patients. Unknown aetiology was among 52% of patients. The association of aetiology with time. Only ECL was significantly ($p=0.01$) associated with time. **Conclusion:** Most common aetiology in the antepartum period was Eclampsia, whereas, in the postpartum period, it is PRES. In primigravida, the most common aetiology was also PRES while it is CVT among multigravida.

INTRODUCTION

The occurrence of seizures in the peripartum period is a rare but particularly challenging situation. Seizures in the peripartum period could result from three conditions: first and most frequent is the exacerbation of a known pre-existing seizure disorder, mainly epilepsy. A therapeutic evaluation is needed; second is the new onset of seizures due to a non-pregnancy-related problem. An accurate diagnosis and a specific treatment are required; the third is the range of pregnancy-related conditions. Seizure is defined as a paroxysmal event due to abnormal excessive or synchronous neuronal activity in the brain.^[1]

Most seizures during pregnancy occur in women who already have epilepsy. During pregnancy, most women will continue their previous level of seizure control, although 15-30% may experience an increase in seizures. Pregnancy-induced changes in antiepileptic drug pharmacokinetics are a major factor affecting changes in seizure control during pregnancy, although compliance is also a significant factor. Status epilepticus occurs in only 1-2% of pregnancies, and, if treated appropriately and aggressively, carries a fairly low risk of morbidity

and mortality. Structural and metabolic changes may precipitate new-onset seizures during pregnancy. The structural causes include intracranial haemorrhage of multiple types, cerebral venous sinus thrombosis, and ischemic stroke. Metabolic causes include hyperemesis gravidarum; acute hepatitis (due to fatty liver of pregnancy or viral hepatitis); metabolic diseases, such as acute intermittent porphyria; infections, such as malaria; and eclampsia.^[2]

In pregnant WWE, the cause for any increase in seizures is not clearly understood and is likely to be multifactorial. Pregnancy is associated with a number of physiological, endocrine and psychological changes, any or all of which might contribute to lowering the seizure threshold. Physiological changes during pregnancy alter the pharmacokinetics of AEDs, which may result in lower levels and seizure deterioration in WWE. It was also found that women with focal onset epilepsy or those undergoing polytherapy experienced increased seizure frequency during pregnancy. During & immediately after labour, there is also a relatively increased risk of seizures(post-partum).^[3]

Women who have catamenial epilepsy (CE) have been shown to have better seizure control, during pregnancy than those who do not have CE. Hence, information regarding CE should be considered while taking management decisions & counselling pregnant women. Women with epilepsy (WWE) have been shown to have peculiar issues regarding management. The burden of epilepsy is not well defined in women in low- & middle-income countries, considering that a large proportion is of childbearing age. This is different in high-income countries where there is a growing concern for WWE with regards to marriage, fertility, pregnancy & childbirth, teratogenicity, menopause & contraception⁴. Most women with epilepsy will not experience an increase in seizure frequency, and in 96% of pregnancies, they will deliver a healthy child. However, some women (between 14 and 32 per 100) will experience an increase in seizure frequency, which can be harmful to the mother or fetus.⁴

Convulsion during the third trimester of pregnancy and 48 hours postpartum period is considered Eclampsia until proven otherwise. Although other causes should be sought for, there may be overlap, which makes the condition difficult to diagnose and treat.⁵ Eclampsia, PRES, CVT, HELLP syndrome etc. are identified as essential disorders in pregnancy, resulting in seizures and thus contributing to mortality.

There is significant morbidity and mortality in patients with new onset seizure during the peripartum period, which can be avoided by thorough examination and investigations to identify the specific cause to initiate appropriate treatment. Still, in developing countries like India, there is a significant burden of peripartum mortality with seizure being one of the important causes that encourage the present study.⁶

MATERIALS AND METHODS

Study on etiological assessment of seizure disorder in the peripartum period was conducted in B.R.D. Medical College, Gorakhpur. Total 50 subjects of aged 18-45 yrs were enrolled who followed the inclusion criteria and with POG 9th month to 1-month postpartum from patients presenting to Obs. and Gynecology department and Medicine emergency ward during the study period of December 2017-December 2018. However, subjects with a known seizure disorder and on any antiepileptic drugs were excluded. Ethical Approval (.....) was taken, and informed consent

was taken from the attendant, and detailed history and investigations were made to find the aetiology of the event. All data were collected using a structured pro forma and analyzed in detail.

A detailed clinical history and examination were obtained according to predesign questionnaire. Samples for Complete blood count, renal and liver function test, viral markers, urine examination, blood sugar, and serum electrolytes were collected and analysed. Radiological assessment such as CT Head, MRI with epilepsy protocol, and MRV was done in selected patients. CSF examinations were done if needed.

Statistical Analysis

The results are presented in frequencies, percentages and mean±SD. The Chi-square test was used to assess the associations. The p-value<0.05 was considered significant. All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

RESULTS

The present study was conducted in the Department of Medicine, B.R.D. Medical College, Gorakhpur to study the aetiology of seizures during the peripartum period. A total of 50 patients were included in the study. The distribution of patients according to age. More than one-third of patients were <25 years (44%) followed by 25-30 (38%) and >30 (18%) years. More than half of the patients had primigravida (56%) [Table 1]. Abnormal Sodium and calcium were in 8% and 6% of patients, respectively. Sugar was high in 10% of patients. PRES was in 10% of patients, and CVT was in 8% of patients [Table 2, Figure 1]. EEG was abnormal in 11.1% patients. UMERIC and hepatic failure was nil among all the patients [Figure 2].

As per CSF findings, UA (un applicable) was in 90% of patients. Tubercular and viral were in 2% and 4% of patients [Table 3]. ECL was in 14% of patients. Press aetiology was in 10% patients. Unknown aetiology was among 52% of patients. ANC <2 was among more than half of the patients (66%). CVT was in all the patients of age 25-30 years. ECL was in 14.3% of patients of age <25 years. ECL was in 57.1% of patients of primigravida. Gliosis and infarct were in all the patients of primigravida. Primigravida was in 25% at antepartum, which became 75% in post-partum. However, the association was insignificant (p>0.05) [Figure 3]. Only ECL was significantly (p=0.01) associated with time [Table 4].

Table 1: Demographical distribution of patients.

Age in years	No. (n=50)	%
<25	22	44.0
25-30	19	38.0
>30	9	18.0
Mean±SD	26.52±6.02	
Gravida		

Primigravida	28	56.0
Multigravida	22	44.0

Table 2: Distribution of patients according to biochemical parameters

Biochemical parameters	No. (n=50)	%
Sodium		
High	4	8.0
Normal	46	92.0
Calcium		
High	3	6.0
Normal	47	94.0
Sugar		
High	5	10.0
Normal	45	90.0

Table 3: Distribution of patients according to CSF findings

EE findings	No. (n=50)	%
Tubercular	1	2.0
UA	45	90.0
Viral	2	4.0
Normal	2	4.0

Table 4: Association of etiology with time.

Etiology	No. patients of Time	Ante partum		Post-partum		pvalue ¹
		No.	%	No.	%	
Unknown	26	4	15.4	22	84.6	0.24
ECL	7	4	57.1	3	42.9	0.01*
PRES	5	0	0.0	5	100.0	0.21
CVT	4	0	0.0	4	100.0	0.26
NCC	3	2	66.7	1	33.3	0.05
Metabolic encephalopathy	2	0	0.0	2	100.0	0.44
Infarct	1	0	0.0	1	100.0	0.59
Gliososis	1	0	0.0	1	100.0	0.59
Tubercular	1	1	100.0	0	0.0	0.06

¹Chi-square test, *Significant

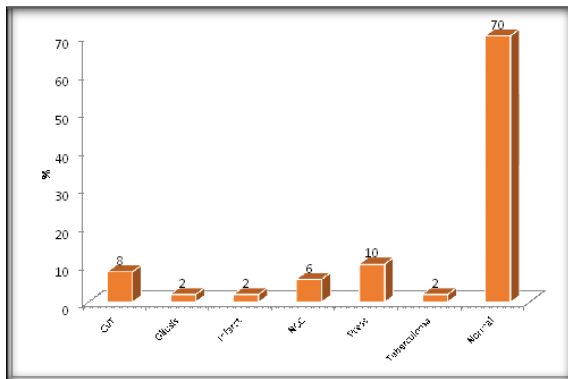


Figure 1: Distribution of patients according to radiography of brain findings

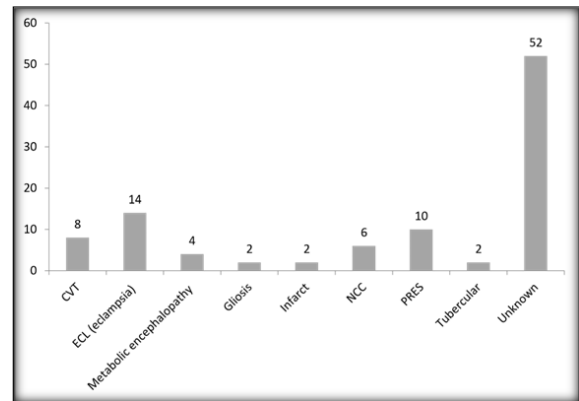


Figure 3: Distribution of patients according to Etiology

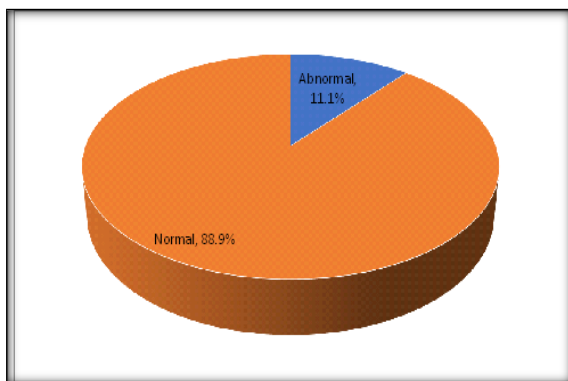


Figure 2: Distribution of patients according to EEG findings

DISCUSSION

We studied 50 patients who presented to the emergency medicine ward or obstetric ward in B.R.D. Medical college fulfilling the inclusion criteria. In the various studies, the seizure was identified as the most common neurological disorder during pregnancy and puerperium.^[7,8,9,10]

Our study found that most patients (44%) who suffered an event of seizure during the peripartum period were within 25 yrs of age. Mean age of the studied population was 26.5 yrs. Subha L et al,^[8] Thatikonda et al,^[10] and Bharathi et al,^[11] also observed occurrence of seizures was most common

within 25 yrs of age. This may be because most of the patients in this age group were primigravida, who is known to be more prone to seizures due to eclampsia per se.

In our study, we found that 56% of patients were primigravida, which was similar to observations of Bharathi et al,^[11] Shobha et al,^[12] and Manish et al,^[13] found primigravida women had a higher risk of seizure.

We found that 22% (11 out of 50) of patients with seizures were in the antepartum period and 39(78%) were postpartum, although we did not study the exact gestation period among them. This may be because patients who presented to us in the antepartum period with seizure were due to status epilepticus not controlled at another health centre and thus referred to us, making the duration of the antepartum period in our study be short. Most of the patients enrolled in our study were admitted here in obstetrics department, thus posing selection bias in our study.

In those who were in antepartum period most common aetiology was eclampsia 36% (4 out of 11) followed by NCC(18%).In 36% of the patients, cause could not be identified. It is a known fact that eclampsia is more common in the antepartum period,^[8,14,15] which could be the reason of our finding. Raghuraman et al,^[16] also observed the same in their study.

Nigro et al,^[17] found hyponatraemia as an important cause of the seizure, although those patients' observed serum sodium level was <125meq/l. We found 4 patients with hyponatraemia (ranging from 123meq/l-131 meq/l) although 2 were diagnosed with eclampsia,1 had CVT, and 1 had PRES. This suggests that hyponatraemia among these patients could be an incidental finding or could be acted as an associated risk factor to precipitate seizure. Our study did not identify other metabolic causes of seizures like hypoglycaemia, hepatic failure, azotaemia, hypercalcaemia, etc.

Radiological assessment was done according to Recommendations for neuroimaging of patients with epilepsy.^[17] We found 70% of the patients had normal study, PRES in 10%, CVT in 8%, NCC in 6% and Tuberculoma, Infarct and Gliosis in 2% of patients. Thus, PRES was the most common radiological finding in our study. Subhashree et al,^[18] in their study, observed CVT being the most common radiological finding among patients with recent-onset neurological symptoms.

Similarly, in relevant cases, only CSF examination and EEG were done. CSF analysis done in 5 patients showed 2 having viral aetiology and 1 to be tubercular. EEG was informative in 4 of the patients out of 26 patients screened, showing abnormal epileptic discharges.

In our study we found eclampsia 14% (7/50), Cerebrovascular disorder 20% (PRES 10%, CVT 8%, infarct 2%), NCC 6% (3/50), Metabolic encephalopathy 4% (2/50) and tuberculoma, gliosis being 2% each as the cause of seizure. We did not

find the exact aetiology in 52% of the patients. Thus eclampsia is the most common cause identified. This finding was comparable to studies done by Firdushi et al Thatikonda et al studied patients presenting with neurological disorders including seizures during pregnancy and 6 weeks postpartum and observed 35% of the patient having the cerebrovascular disorder, with PRES being the most common entity followed by CVT. There is an increased risk of cerebrovascular complications during pregnancy.^[19,20,21,22,23,24,25]

With PRES, there is a loss of autoregulatory capacity, BBB disruption, and subsequent vasogenic oedema around cerebral arteries and arterioles, which predisposes for the occurrence of seizure during peripartum period.^[20] Ravindra et al,^[21] found PRES as an increasingly recognized cause of seizures in their study. They also found that it is related to eclampsia which may be the reason for such findings.

In our study eclampsia was present in 14% of the patient and was the most common recognizable cause of the seizure. This was found in accordance with the study by Begum et al,^[22] Pandey et al,^[23] and Ravindra et al.^[21] Eclamptic seizures can occur antepartum, intrapartum or postpartum. Postpartum eclampsia is not as rare a condition as once thought.^[24]

In our study, we found 57% of eclamptic patients to be antepartum, which is comparable to study by Shobha et al,^[12] In our study Eclamptic patients in antepartum as well as postpartum were >25 yrs of age which is contrary to study by Neelam Rajput et al, Pradeep MR et al.^[24] and Choudhary et al,^[25] who observed younger age having more odds to have eclampsia irrespective of the period of gestation. This may be due to the small number of subjects included in our study.

ANC is a cost-effective measure.^[15,26] In our study majority of patients (66%) had <2 ANC, which may be the predisposing factor for the occurrence of seizures as morbidities like HTN, which is a proven risk factor for eclampsia and PRES, could have been missed. In our study, the most common aetiology of seizure among primigravida was PRES, followed by Eclampsia. However, in the study by Shobha et al,^[12] Eclampsia was found to be more common among primigravida. However, both are Hypertensive disorders observed in pregnancy, and their spectrum is overlapping, thus explaining our observation.^[27,28]

Pregnancy and puerperium are common causes of transient prothrombotic states. Further use of OCP increases the risk of thrombosis. In our study, the most common aetiology among multigravida was CVT. CVT 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.³⁸ A study by Darji et al,^[27] reported the same. In our study, out of 50 subjects, we cannot find any aetiology of seizure among 26 subjects (52%). This

variation may be attributed to the facilities available at the centre for neurological care or the number of cases referred from a gynaecological centre. We did not find any radiological abnormalities; however, better diagnostic evaluation such as MRI and PET cannot be done in these patients.

CONCLUSION

To conclude, many different neurological conditions may be encountered during pregnancy. Epilepsy and eclampsia emerge as the predominant neurological disorders during pregnancy and puerperium with a substantial contribution by cerebrovascular diseases and metabolic encephalopathies, Gliosis and infections such as NCC and Tuberculoma. Most of the patients who presented with seizures were in less than 25 years of age. The mean age of studied population is 26.52years. Most common aetiology in the antepartum period was Eclampsia, whereas, in the postpartum period, it is PRES. In primigravida, the most common etiology was also PRES, while it is CVT among multigravida.

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