



## Clinico-etiological profile of new onset seizures in children admitted at a tertiary referral hospital

Authors

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### Abstract

**Background:** Seizure is one of the commonest neurological disorder and also a common cause of hospitalization in adolescence with significant morbidity and mortality.

**Materials & Methods:** This was a prospective study conducted in Pediatrics department, RMCH, Bareilly, UP among the admitted patients from 1<sup>st</sup> Nov 2018-31<sup>st</sup> Oct 2019 among 3months to 15year age group. Age, sex, type of seizure, associated complaints, clinical examination, laboratory investigations, neuroimaging, EEG findings were interpreted and clinic-etiological profile was made.

**Results:** Incidence of new onset seizures was common in older children with male predominance and GTCS being the most common type of seizure followed by focal seizures. Fever was the most common associated symptom. Most commonly CNS infection followed by seizure disorder, intracranial space occupying lesions predominantly NCC, febrile seizures, metabolic disorders were the etiologies found.

**Conclusion:** CSF analysis, EEG, Neuroimaging plays an important role in evaluating the seizure etiology and thorough history and clinical evaluation is very important before undergoing investigations. clinico-etiological profile of seizures can help in better understanding of the disease and help in better management. Larger sample size and long term follow up is required for the better understanding of the etiologies of seizures in context of a developing country.

### Background

Seizure is one of the commonest pediatric neurological disorder and also a common cause of hospitalization in childhood with significant morbidity as well as mortality<sup>1</sup>.

Seizure is termed as a transient occurrence of signs and symptoms caused due to the abnormal excessive neuronal activity in the brain. And when the seizures are associated with motor component they are also called as convulsions. Two or more repeated unprovoked seizures occurring more than a day apart are termed as epilepsy<sup>1,2</sup>. Both seizure and epilepsy refer to a removal of the patient from reality<sup>3</sup>.

Four to ten percent of children suffer from seizure at least once in the initial 16 years of their life. Seizures not only accounts for 1% of total emergency visits but also accounts for 2% of visits of emergency department in a children's hospital<sup>1,2,3,4</sup>.

Studies which were done on epidemiology conclude that around 150,000 children will suffer from a new onset unprovoked seizure each year, and 30,000 of them will develop epilepsy. Epilepsy incidence in children and adolescents is almost same across the world, which is 50 to 100 per 1 lakh person years and the incidence of epilepsy is highest in the first year of life<sup>5</sup>.

Many studies regarding seizures around the world conclude that febrile seizures are the commonest type of seizures seen in the children and also the reason for majority of seizures in children less than 5 years<sup>6,7</sup>.

Understanding the seizure clinical presentation and etiology is necessary not only to control an acute attack but also for epilepsy control in long term. Seizures cause high morbidity and mortality in children and also impose mental, physical, and economical burden on parents<sup>2</sup>.

There are various possible etiologies of a new onset seizure in children which include traumatic head injury, central nervous system infections, metabolic disorders and neuro developmental causes<sup>7</sup>. CNS infections are one of the primary causes of seizures in children, and also an acquired cause for epilepsy in the developing countries. Seizures which are acute are commonly associated with viral encephalitis, meningitis, and neurocysticercosis and are associated with increased morbidity and mortality, which includes epilepsy<sup>1</sup>. In India, tuberculous is a common cause of seizures<sup>8</sup>. Gastroenteritis can also cause acute symptomatic seizures<sup>9</sup>.

Neurocysticercosis is endemic in countries where hygiene and sanitation are poor. Partial seizure in pediatric population must be considered as an important indicator of the disease and is highly suggestive.<sup>8,10</sup> In Asia, Japanese encephalitis is one of the most significant viral encephalitis which causes significant neurological sequelae and also mortality in children<sup>11</sup>.

It is the etiology of seizure which is the most significant risk factor for increased mortality in patients with new onset seizures<sup>12</sup>. In patients with remote symptomatic etiology, the mortality is significant<sup>13</sup>.

For patients who present with a first attack of seizure it is a challenge to the physician to decide the investigations. Lumbar puncture is required in all children with meningeal signs and it is accepted universally<sup>7</sup>, acute neuroimaging is advised in all patients who are admitted to pediatric intensive care unit and should be taken

into consideration in patients with predisposing conditions causing intracranial abnormalities and in patients less than 33 months old with focal seizures<sup>14,15</sup>.

The International League against Epilepsy (ILAE) 2017 presented a revised operational classification of seizure types. There are now 3 major groups of seizures namely generalized onset, focal onset, and unknown onset<sup>17</sup>.

Febrile seizures are defined as seizures that occur among age of 6 and 60 months with a temperature of 100.4°F or higher, that are not the result of central nervous system infection or any metabolic imbalance, and that occur in the absence of a history of prior afebrile seizures<sup>18</sup>.

Most studies had done so far have focused on epilepsy and clinical seizure types. In this prospective study, we therefore propose to analyse and assess the incidence of various etiologies, clinical spectrum of new onset pediatric seizures in a tertiary care hospital.

### Materials & Methods

This was a prospective study conducted in Pediatrics department, RMCH, Bareilly, UP among the admitted patients with new onset seizures from 1<sup>st</sup> Nov 2018-31<sup>st</sup> Oct 2019 among 3 months to 15 years age group. Known cases of epilepsy/epileptic syndromes, children with neuro developmental delay /regression and children with seizure onset after hospitalization were excluded from the study. A Written Consent was taken from the parents and only those patients included who were willing to participate.

Detailed history of each patient admitted with seizures in pediatric ward/ pediatric ICU including age, sex, type of seizure, associated symptoms and family history of seizure or epilepsy, neurodevelopmental history were taken in the prescribed proforma and clinical examination was done. Seizure type was classified according to ILAE 2017 classification. Etiologies of seizures were analysed based on clinical presentation, relevant investigations including TLC, DLC,

Serum electrolytes (Sodium, Potassium, calcium), Random Blood sugar were done.

Cerebrospinal fluid (CSF) analysis was done by Manual Cell Counting with Neubauer Chamber. ADA (Adenosine Deaminase), micro protein and sugar using chemical analyzer, smear examination with ZN (Ziehl-Neelsen) staining for detecting Acid Fast Bacilli, Gram’s staining for bacteria, Culture and sensitivity using MacConkey agar and Blood agar. Reference values for analysis of the various laboratory investigations were taken from a standard pediatric text book<sup>18,19</sup>. MRI (Magnetic Resonance Imaging) Brain, CT (Computed Tomography) Brain was done and interpretation of the neuroimaging and reporting was done by designated radiologist. EEG (Electroencephalography) was done, interpretation

and reporting of the EEG was done by the neurologist. Final diagnosis was made using clinical examination and investigations. If no etiology could be determined and other investigations apart from EEG were normal, then those patients were diagnosed as seizure disorder. Data was filled in a predesigned proforma. The data was entered on a Microsoft Excel spreadsheet and imported into Statistical Package for Social Sciences (SPSS) version 23 for statistical analysis. Qualitative data was presented in frequency and percentage. Chi-square test was performed to find association between different variables. A P-value less than 0.05 were considered statistically significant and A P-value less than 0.001 was considered statistically highly significant.

**Results**

**Table 1-** Incidence of seizure according to age group and gender

Age Group	Number	Percentage (%)	Male	Female	Total
3 months-5 years	38	30.2	24	14	38
6-10 years	37	29.4	18	19	37
11-15 years	51	40.5	27	24	51
<b>Total</b>	<b>126</b>	<b>100.0</b>	<b>69</b>	<b>57</b>	<b>126</b>

In our study maximum 51 (40.5%) patients were in age group of 11-15 years followed by 38 (30.2%) in age group 3 months-5 years and 37

(29.4%) in age group of 6-10 years. Majority were male (n=69, 54.8%) and 57 (45.2%) were female patients.

**Table 2-** Incidence of type of seizure according to age group

Seizure Type	3m-5yrs	6-10yrs	11-15yrs	Total	P value
General Tonic Clonic	27	27	22	76	0.014
Tonic	7	0	6	13	
Myoclonic	1	0	4	5	
Focal Onset Aware	0	1	2	3	
Focal Onset Impaired	3	8	14	25	
Unclassified	0	1	3	4	
<b>Total</b>	<b>38</b>	<b>37</b>	<b>51</b>	<b>126</b>	

General Tonic-Clonic was the most common type of seizure in our study in 76 (60.3%) of patients followed by focal onset impaired in 25 (19.8%), there were 13(10.3%) cases of tonic, 5 (4.0%) of

myoclonic, 3 (2.4%) of focal onset impaired awareness and 4 (3.2%) were unclassified. There was significant difference in between age group of patients and type of seizure of patients (p=0.014).

**Table 3** Associated Symptoms Distribution

	3m-5yrs	6yrs-10yrs	11yrs-15yrs	Total
Fever	35	22	23	80
Headache	7	21	29	57
Vomiting	16	9	13	38

There was significant difference in between age group of patients and having fever and fever was the predominant associated complaint ( $p < 0.001$ ). Out of 126 patients Cerebro spinal fluid (CSF) analysis was done in 57 (45.23%) patients, in which 18 (31.6%) had normal CSF analysis and 39 (68.4%) had abnormal. EEG was done in 35 (27.8%) patients in which 6 (17.1%) had normal EEG and 29 (82.9%) had abnormal EEG. Neuro

imaging was done in 79 (61.9%) patients in which 35 (44.3%) had normal neuro imaging and majority of the patients ( $n=44$ , 55.7%) had abnormal neuro imaging. Only 6 (4.8%) required other investigations out of which 1 had Abnormal Liver function test and coagulation profile, 3 cases were dengue IgM +, and 2 had Plasmodium vivax in blood.

**Table 4** Incidence of different etiologies of seizures according to age group.

Diagnosis	3m-5yrs	6-10yrs	11-15yrs	Total	P value
Central Nervous System(CNS)Infections	16	13	16	45	<0.001
Febrile Seizures	13	0	0	13	
Seizure Disorder	1	10	18	29	
Intracranial Space Occupying Lesions (ICSOL)	1	12	16	29	
Metabolic Disorders	4	1	0	5	
Others	3	1	1	5	
Total	38	37	51	126	

CNS Infection was the most common diagnosis in 45 (35.7%) out of 126 patients followed by seizure disorder in 29 (23.0%), ICSOL in 29 (23.0%), febrile seizures were found in 13 (10.3%) of patients, metabolic disorders and other diagnoses were found in 5 (4.0%). There was significant difference in between age group of patients and diagnosis ( $p < 0.001$ ).

Pyogenic meningitis was most the common CNS infection in 18 (40.0%) patients followed by viral meningoencephalitis in 14 (31.1%) of patients, tubercular meningitis in 11 (24.4%) of patients and cerebral malaria was found in 2 (4.4%) of patients.

Simple febrile seizures were found in 10 (76.9%) of patient and complex febrile seizures were found in 3 (23.1%) of patients out of 13 patients. Overall, febrile seizures were found in only of patient of age group 3 months – 5 yrs.

Among ICSOL, maximum cases were Neurocysticercosis in 25 (86.2%), Malignancy in 2 (6.9%) and 1 (3.4%) of both Tuberculoma and Tuberos sclerosis.

Among metabolic disorders, 2 (40%) had hyponatremia with hypokalemia.1 (20%) had hyponatremia, 1 (20%) had hyponatremia with hypoglycemia and 1 (20%) had hepatic

encephalopathy. All the metabolic disorders were seen in age group less than 5 years.

Among other diagnoses, 3 (60%) had Head Trauma,1 (20%) had Vein of Galen malformation and 1 (20%) had Rasmussen Encephalitis.

### Discussion

In our study out of 126 patients, the highest incidence ( $n=51$ , 40.5%) of new onset seizures was seen in the 11-15year age group followed by 3 months to 5year age group ( $n=38$ , 30.2%) and in 6 to 10year age group ( $n=37$ , 29.4%).

This incidence was similar to a study by Chaudhary N et al<sup>16</sup>, where majority (47%) of the patients were in the age group more than 10 years. However, in other studies namely Adhikari S et al, Singh RD et al and Chen CY et al<sup>7</sup>, the incidence was majorly seen in less than 5 years of age. Adhikari S et al<sup>1</sup> and Singh RD et al<sup>2</sup> opined that the incidence of seizures decreases with increasing age, however, in our study no such correlation was found.

In our study predominant were males (M) ( $n=69$ , 54.8%) than females (F) ( $n=57$ , 45.2%), M: F ratio being 1.21:1. The same predominance was seen in other studies by Adhikari S et al<sup>1</sup>, Singh RD et al<sup>2</sup>, Chun-yuchen et al<sup>7</sup> and Chaudhary N et al<sup>16</sup>.

General tonic clonic (GTCS) type of seizure (n=76, 60.3%) was more common, followed by focal onset seizures (n=28, 22.2%). Similar observation was found by Adhikari S et al<sup>1</sup>, where GTCS were seen in 69.9% of patients and focal onset seizures in 19.8%. Another study by Singh RD et al<sup>2</sup>, also found higher incidence of GTCS with 71% of the patients and 25% had focal onset type of seizures. Chen CY et al<sup>7</sup> in their study found that 71.2% of the children had GTCS. This was corroborated in a study by Chaudhary N et al<sup>16</sup> who found 82.1% of the patients had GTCS and focal onset seizures in 17.9% which was similar to our study.

While GTCS type of seizure was distributed in all the age groups, focal onset seizures were predominantly seen in the 11-15-year age group (16 out of 28 patients), which was statistically significant unlike in a study by Chaudhary N et al<sup>16</sup> who did not find any statistical significance between the age groups and the seizure semiology. Fever was the major associated symptom with seizures and was present in 80 patients (63.5%) out of 126 in our study and similar observation was seen in a study by Singh RD et al<sup>2</sup>. Presence of fever with seizures was more common in age group less than 5 years (n=35, 43.7%). This observation was correlating to other studies by Adhikari S et al<sup>1</sup>, Singh RD et al<sup>2</sup>, Chun-yuchen et al<sup>7</sup>.

Out of 126 patients, lumbar puncture was performed and CSF evaluation was done in 57 patients as per indication. The CSF findings found to be abnormal in 18 (31.6%) and 39 (68.4%) patients had normal CSF findings. This correlation was similar to Adhikari et al<sup>1</sup> study which reported that 25.9% of the patients had abnormal CSF findings. EEG was performed in 35 (27.8%) patients out of which 6 (17.1%) had normal EEG and 29 (82.9%) had abnormal EEG. This observation was similar to the study by Adhikari S et al<sup>1</sup>. Neuroimaging was done in 79 cases and 35 (44.3%) had normal neuro imaging and 44 (55.7%) neuro imaging was abnormal which correlates to Chaudhary N et al<sup>16</sup>, where 56.5%

had abnormal imaging. Other studies, Sharma S et al<sup>15</sup> had only 8% of abnormal neuroimaging in patients with new onset seizures.

CNS infection was the most common cause of new onset seizures and was found in 45 (35.7%) out of 126 patients. Similar etiological incidence was seen in Singh RD et al study<sup>2</sup>, where CNS infection was seen 31%. CNS infection was distributed in all age groups in our study. However, in the study by Adhikari S et al<sup>1</sup>, incidence of CNS infection was more in patients less than 5 year age group, this difference could be because the majority of the study group were in the age group less than 5 years in their study. Among the CNS infections, pyogenic meningitis was the predominant (40%) cause followed by viral meningoencephalitis which was seen in 31.1% of patients in our study. However, in a study by Singh RD et al<sup>2</sup> viral meningoencephalitis (48%) was more common than pyogenic meningitis (23.5%).

Intracranial space occupying lesions (ICSOL) were seen in 29 (23.0%) out of 126 patients in our study. Similar etiological incidence was seen in Singh RD et al study<sup>2</sup> where, ICSOL were seen in 21%. In our study majority (n=16, 55.2%) of the ICSOL were seen in 11-15 year age group which was similar to Singh RD et al<sup>2</sup>. NCC was the major cause of ICSOL (n=25, 86.2%) which was similar to Singh RD et al study<sup>2</sup> (n=55, 78.6%).

Seizure disorder was seen in 29 (23.0%) out of 126 patients in our study. Similar observation was seen in a study by Singh RD et al<sup>2</sup> where, seizure disorder was present in 21%. In our study majority (n=18, 62%) were in the age group of 11-15 years, which was similar to Singh RD et al<sup>2</sup>.

Febrile seizures were found in only 13 (10.3%) of patients in our study. However, in a study by Chen et al<sup>7</sup> febrile seizures (62.1%) were the major etiology of the new onset seizure. In their study 93.7% of the study group were less than 6 years. Febrile seizures are most common in this age group and could be the reason for higher incidence. Among febrile seizures (n=13) in our study, simple febrile seizures (n=10, 76.9%) were

predominant rather than complex febrile seizures (n=3, 23.1%) which was correlating with Singh RD et al<sup>2</sup> study where they were 70.6% and 29.4% respectively.

Metabolic disorders were seen in 5 (4.0%) out of 126 patients in our study, among them 2 cases of Hyponatremia, Hypokalemia, 1 case each of Hyponatremia, Hyponatremia, Hypoglycemia. All these cases were seen in age group less than 5 years of age, which was similar to Singh RD et al study<sup>2</sup> and there was 1 case of Hepatic Encephalopathy in the present study.

Other diagnoses were found in 5 (4.0%) in our study. Out of 5 cases of other diagnosis, 3 cases of Head Trauma, 1 case each of Vein of Galen Malformation and Rasmussen encephalitis which was correlating to Singh RD et al<sup>2</sup> study.

### Conclusion and Limitations

New onset pediatric seizures are one of the commonest causes of hospitalization which imposes not only mental but also financial burden on the parents. In our study we found that incidence was common in older children with male predominance and GTCS being the most common type of seizure followed by focal seizures. CSF analysis, EEG, Neuroimaging plays an important role in evaluating the seizure etiology and thorough history and clinical evaluation is very important before undergoing investigations as they involve significant risks especially CT, which has got risk of radiation exposure. Most commonly CNS infection followed by seizure disorder, intracranial space occupying lesions predominantly NCC, febrile seizures, metabolic disorders were the etiologies found.

From our study we suggest that studying the clinico-etiological profile of seizures can help in better understanding of the disease and help in better management. Larger sample size and long term follow up is required for the better understanding of the etiologies of seizures in context of a developing country.

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