ORIGINAL ARTICLE

Clinical Spectrum and Neuroimaging Findings in Children with Seizures: A five-year Retrospective Study

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Abstract

Objectives

Seizures are the most common neurological illness in the pediatric population and account for 1% of all emergency department (ED) visits and 2% of all visits to children's hospital EDs. Pediatric epilepsy presents with various diagnostic challenges. Neuroimaging, especially structural neuroimaging and preferably MRI brain, plays an essential role in diagnosing, managing, and guiding pediatric epilepsy treatment**.**

The study aimed to estimate the clinical spectrum of seizures in children and examine the neuroimaging findings in children with seizures**.**

Materials & Methods

The study was a hospital-based retrospective observational study. The hospital case records of all children belonging to the age group 1 month to 12 years with 'seizures' were reviewed for 5 years from Jan 2016 to Dec 2020. Clinicodemographic profiles and neuroimaging (CT/MRI) findings were obtained, and descriptive statistics were applied.

Results

A total of 838(11%) children in the age group 1 to 144 months (mean±SD: 32.57±32.65) presented with seizures, of whom 515(61.5%) were boys and 323(38.5%) girls. Of 596(71.1%) children under five years, 409(68.6%) had febrile seizures. Generalized onset-motor seizures were the predominant type of seizures seen in 666(79.4%) children, of whom 434(65.1%) had febrile seizures. Neuroimaging (CT/MRI) was normal in 335(40%) and abnormal

in 124(14.8%) children. Perinatal insult (7%) was the most common abnormality, followed by CNS infections (2.8%).

Conclusion

Neuroimaging, preferably MRI brain, is the most helpful tool for the etiological diagnosis of afebrile seizures.

In our study, seizures secondary to perinatal insult/hypoxic insult followed by infections were major causes. Improvement in peripartum and perinatal care coupled with a targeted Tuberculosis control program may help in reducing these potentially preventable causes

Keywords: Seizures; Children; Neuroimaging

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Seizure' is defined as abnormal neuronal firing leading to a clinical alteration of neurologic function (motor, sensory, autonomic, or psychological) (1). Seizures are the most common neurological illness in the pediatric population and account for 1% of all emergency department (ED) visits and 2% of all visits to children's hospital EDs (2). Approximately 4–10% of children experience at least one seizure (febrile or afebrile) in the first 16 years of life. The incidence is highest in children under 3 years of age, with a decreasing frequency in older children (3). As per World Health Organization (WHO) fact sheet (2019), globally, an estimated five million people are diagnosed with epilepsy (two or more unprovoked seizures) each year (4). The annual prevalence of epilepsy is 0.5–1.0%. The risk of premature death in children with epilepsy is up to three times higher than in the general population, with the highest premature mortality rates found in low- and middle-income countries and rural areas (4). Also, these children have significant morbidities due to physical problems (such as bruising from injuries and fractures related to seizures), higher rates of learning difficulties, and behavioral and mental health issues.

Seizures occurring with fever or accompanying a febrile illness are usually referred to as febrile seizures, and these are the most common cause of acute seizures in young children. The prevalence of febrile seizures in children aged ≤6 years varies in different geographical regions, as reported in various studies (5). Another common cause of acute seizures in children is acute symptomatic seizures (6) that may have a higher prevalence in tropical countries than in Western countries and have a poorer outcome. In some Asian countries, central nervous system infections (CNS), especially neurocysticercosis, are the leading cause of seizures (7, 8). In Sub-Saharan Africa, malaria is the leading cause (9). Pediatric epilepsy presents with various diagnostic challenges. Structural neuroimaging has a vital role in evaluating, managing, and treating children with epilepsy. Neuroimaging techniques such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) can identify etiology, provide prognosis, and help plan appropriate

clinical care. MRI is the imaging modality of choice because of its superior anatomic resolution as it provides much better detail and identifies more abnormalities than CT (10).

In these Islands of ours, we have very scant data, even unpublished, on childhood seizures. Hence, we undertook this study with the following objectives:

i) To estimate the clinical spectrum of seizures in children.

ii) To study the beuroimaging findings in children with seizures.

Knowing common etiologies of childhood seizures in these remote islands may help us plan appropriate preventive and control measures.

Materials & Methods

Patient

In this retrospective hospital-based study, we reviewed the hospital case records of all children belonging to the age group 1 month to 12 years with 'seizure' as one of the diagnoses who were admitted to the Pediatric Ward of Andaman & Nicobar Islands Institute of Medical Sciences (ANIIMS) & GB Pant Hospital, from Jan 2016 to Dec 2020.

Operational definition

'Seizures' included any one of the several disorders, including epilepsy, febrile seizures, first unprovoked seizures, and symptomatic seizures secondary to metabolic, infectious, or other etiologies (e.g., hypocalcemia, meningitis).

'Epilepsy' will be clinically defined by two or more unprovoked seizures occurring in a time frame of longer than 24 hr.

The definition of 'febrile seizure' (FS) was adopted from the International League against Epilepsy (ILAE), which is defined as "a seizure occurring in childhood after 1 month of age associated with a febrile illness not caused by CNS infection, without previous neonatal seizures or a previous unprovoked seizure, and not meeting the criteria for other acute symptomatic seizures". FSs are classified as simple and complex FSs. A simple FS is generalized in nature, with a duration of less than 15 minutes and one episode within 24 hr, whereas a complex FS lasts more than 15 minutes, occurs more than once in 24 hr, or has focal features. Other etiologies were taken as recorded from the final diagnosis and based on clinical findings and laboratory investigation in medical case records and verified with standard reference.

The information, including age, sex, type of seizure, presence of fever, family history, antenatal and perinatal history, developmental history, laboratory tests (complete blood count, C-Reactive Protein (CRP), blood sugar, electrolytes, Calcium), neuroimaging and electroencephalogram (EEG), duration of admission, and final diagnosis, was obtained from the medical records of each patient. In the absence of any information, the parent was contacted over the telephone, and history/ investigations were ascertained. A detailed history was taken to determine seizure semiology and correlated with EEG findings, when available.

According to the 2017 ILAE seizure classification (11), seizure semiology was defined and classified as focal (motor onset, non-motor onset, and focal to bilateral tonic-clonic), generalized (motor and non-motor/absence onset), and unknown onset (motor and non-motor and unclassified).

Neuroimaging (CT/MRI) criteria

Neuroimaging was considered in children with complex febrile seizures, first unprovoked seizure lasting longer than 30 mins, suspected CNS infection, epilepsy, dysmorphic features,

neurocutaneous markers, other congenital anomalies, developmental delay, focal onset seizure, abnormal head circumference, and abnormal neurologic examination.

CT & MRI protocol

CT scan was done using a SIEMENS SOMATOM EMOTION 16 slice machine. The contrast was given in suspected cases of meningitis and space-occupying lesions.

MRI brain with epilepsy protocol was performed in the epilepsy group after the second seizure. The images were acquired using a WIPRO GE Healthcare discovery 1.5 T MR 450W 1.5 TESLA machine. All the patients were placed in a supine position with a head coil. Conventional spin-echo sequences including axial T1WI, T2WI, and FLAIR; coronal T2WI; Sagittal T1WI; axial GRE (Gradient Recalled Echo); and post-contrast images were obtained. DWI using echo-planar imaging was done in all the patients before contrast administration.

Ethical considerations and approval

The permission to perform this study was obtained from the Institutional Ethics Committee of ANIIMS, Port Blair; No. ECR/940/Inst/AN/2017, dated 23-06-20. All measures were taken to protect the privacy and confidentiality of the study subjects.

Data analysis

The study details were recorded in a proforma, and data were generated in an MS Excel sheet. Descriptive analysis was done using Statistical Package for the Social Sciences (SPSS) for Windows Version 26 (IBM, Chicago).

Results

Demographic characteristics of children with seizures

There were 7592 children admitted to the Pediatrics Ward above 1 month of age during the 5-year study period. Of these patients, 838(11%) had seizures as a presenting complaint. There were 515(61.5%) boys and 323(38.5%)girls in the age group 1 to 144 months (mean ± SD: 32.57±32.65). The age and gender distribution of all study recruits is described in Table 1 . These children were broadly categorized in any of the four groups based on the operational definition in the methodology section. The gender-wise distribution of participants in each of these groups is described in Table 2. Among 838 children, 596(71.1%) were under 5 years. The febrile seizure was the most common seizure (68.6%) in this age group. Generalized onset-motor seizures were the predominant type of seizures seen in 666(79.4%) children, of whom 434(65.1%) had febrile seizures. EEG was done in 132(15.8%) cases, with abnormality in 12.8%.

Neuroimaging findings in children with seizures

The neuroimaging data of the patients were evaluated. Cranial CT scan was done in 400(47.7%) children, MRI brain in 132(15.8%) children, and both in 54 children. Neuroimaging (CT/MRI) was abnormal in 124(27%) children. The detailed etiologically relevant abnormalities of neuroimaging are described in Table 3. The most common abnormality found was related to perinatal insult (7%), followed by CNS infections (2.8%), with the most common being Tuberculosis (TB).

Table 1: Age & Gender distribution of subjects

AGE(months)	<6		6-60		61-144		Total
	M n(%)	F n(%)	M n(%)	F n(%)	M n(%)	F n(%)	
	49 (5.8)	35 (4.1)	364 (43.4)	232 (27.6)	102 (12.1)	56 (6.6)	838

Table 2: Seizure type distribution

Seizure type	Male n (%)	Female n (%)	Total n (%)
FEBRILE SEIZURES	261(31.1)	176(21)	437(52.1%)
ACUTE SYMPTOMATIC SEIZURES	41(4.8)	18(2.1)	59(7%)
FIRST UNPROVOKED SEIZURE	20(2.3)	9(1)	29(3.5%)
EPILEPSY	193(23)	120(14.3)	313(37.4%)
TOTAL	515(61.4)	323(38.5)	838

Table 3: Neuroimaging findings of 459 study subjects

NEUROIMAGING FINDINGS	Freq. (n)	(%)
NO SIGNIFICANT ABNORMALITY	**335**	**40**
ANOXIA & HYPOXIC ISCHEMIC ENCEPHALOPATHY(HIE)changes	**59**	**7**
INFECTIONS-	**23**	**2.8**
Tuberculosis(TB)-13/ Meningoencephalitis-5/Meningitis (exc. TB)-4/Neurocysticercosis-1		
VASCULAR	**9**	**1.1**
Ischemic stroke-6/Intracerebral bleed -3		
HYDROCEPHALUS	**6**	**0.6**
Congenital-2/Acquired-4		
MALFORMATIONS OF CORTICAL DEVELOPMENT(MCD)	**5**	**0.5**
Schizencephaly-2/Lissencephaly-2/Pachygyria-1		

DIFFUSE CEREBRAL ATROPHY	5	0.5
INTRAPARENCHYMAL CYST	4	0.4
MESIAL TEMPORAL SCLEROSIS	4	0.4
CNS NEOPLASM	3	0.3
Glioma-1/PNET-1/Meningioma-1		
TRAUMATIC BRAIN INJURY	2	0.2
ACUTE DISSEMINATED ENCEPHALOMYELITIS(ADEM)	2	0.2
FOCAL ATROPHY/GLIOSIS	2	0.2

Discussion

Demographics and clinical seizure types

Most studies show a high incidence of seizures in younger children with a decreasing frequency in the older age group and a higher frequency in males (7,12,13,14). The highest frequency of seizures in our study was also in the 6mths to 5yrs age group with 596(71.1%) children. Febrile seizures (FS) were the most common (52.1%), followed by epilepsy (37.4%). Similar findings were reported in previous studies (2, 12).

Regarding epilepsy, of the total 313 children in our study, 148(46.9%) were in the 6-60 mths age group and 98(31.3%) in the 61-144 mths age group. Anand et al. (15) also demonstrated the highest number of epilepsy patients (57.9%) in the 0-3 years age group.

The prevalence of seizures was higher in males (1.6:1) in all the age groups, similar to other studies (14). Our study reemphasized the fact, as in previous studies, that both FS (16,17-19) and epilepsy (15,20-22) were more frequent in boys than in girls.

Most studies show that generalized seizures are much more common than partial seizures (7, 9, 12, 13, 14, 17, 18, 23). In the current study, generalized onset-motor was the most common (79.5%) seizure semiology, with a higher incidence among febrile children. Focal onset was the next most common semiology seen in 15.2% of children.

Among the 313 epilepsy children in our study, the most common seizure semiology was generalized onset, seen in 190(60%) children. The next most common seizure semiology was focal onset, seen in 112(35.7%) children. In other Indian studies (15,23) done on epilepsy patients, generalized seizures constituted the major seizure group being present in as many as 66.3% and 76.7%.

Neuroimaging correlates of etiological profile

The newer classification of epilepsy (11) emphasizes determining etiology at the outset. This requires the availability of neuroimaging and genetic studies, among others. Usually, the first recommended investigation is neuroimaging, ideally MRI wherever available. This allows the clinician to rule out a structural etiology for the patient's epilepsy.

The diagnostic yield of neuroimaging in new-onset seizures/epilepsy was evaluated in various studies (10) and ranged widely from 10% to 45%. It was uniformly higher in children with high-risk features. In our study, neuroimaging was done in children with complex febrile seizures, first unprovoked seizure lasting longer than

30 mins, suspected CNS infection, epilepsy, dysmorphic features, neurocutaneous markers, other congenital anomalies, developmental delay, focal onset seizure, abnormal head circumference, and abnormal neurologic examination. Overall, clinically significant abnormalities were found in 124(27%) of the 359 children evaluated. Cranial CT scan and MRI brain were abnormal in 46(16.6%) and 29(34.1%) children with generalized onset seizure, respectively, whereas the abnormality in focal onset seizure was observed in 35(31.2%) and 19(63.3%) children.

The most common etiological structural abnormality found in neuroimaging in our children was secondary to Hypoxic-ischemic insult/perinatal insult seen in 59 (7%) cases. Similar observations were made in most studies done in India and other developing countries like Bangladesh and Nepal (14,24,25). This higher rate of perinatal causes in epilepsies indicates that developing countries like India cannot remain complacent in perinatal care. In particular geographical areas like ours, we again stress the need for controlled transport of high-risk cases.

CNS infections were the second most common cause and occurred in 23(2.8%) children. We found CNS TB most common among the various infections, similar to other studies (15,23). Most of our cases were from a community in the Southern group of Islands where TB is endemic.

Neurocysticercosis (NCC) is common in certain regions of India, with a significant impact on the local prevalence rates of epilepsy. We found inflammatory granuloma on neuroimaging in three children, of whom two proved to be Tuberculoma and one (0.1%) NCC. This is in contrast to several other studies (15, 23, 26) from India and other developing countries, which reported a high percentage only similar to CNS TB.

Mesial Temporal Sclerosis (MTS) was seen in four(0.5%) children in our study. In a study from Nagpur (15) (INDIA), of 84 patients, 8.3% had isolated temporal lobe involvement, and MTS was most commonly seen in 57.1% of them. The relatively lower figures for MTS in our study could be due to lower MRI rates (only 121 cases).

There are significant differences regarding the most frequent pathology in Malformations of Cortical Development (MCD) in various studies published in the literature. In our study, of five patients with MCD, two had lissencephaly and schizencephaly, and one had pachygyria. Our findings are similar to those of Sadek et al. (27), who reported that MCD and lissencephaly were most commonly found in 42% of 50 patients. In two other studies (15,28), Focal Cortical Dysplasia was seen in 33.3% and 29.6% of patients, respectively.

Strength and limitations of the study

This is the first study done on childhood seizures with a considerable number of children (838) over a period of 5 years on this far-flung island.

The limitations were that the study was a single-center, retrospective, hospital-based one, and EEG was done on limited subjects. The details of other causes contributing to the seizures, like inborn errors of metabolism, could not be specified due to the nonavailability of current investigations.

In conclusion

Children with seizures comprise a significant group of pediatrics inpatients in developing countries, with GTCS being more common and having various etiologies. A detailed history, including seizure semiology, clinical examination, and relevant supporting laboratory tests, is required in all children. However, imaging modalities,

preferably MRI brain, is the most helpful tool for the etiological diagnosis of afebrile seizures.

In our study, etiologically relevant neuroimaging abnormalities were deducible in 124(14.8%) cases. The most common structural abnormalities were secondary to perinatal/hypoxic insult, followed by infections. Improvement in peripartum and perinatal care coupled with targeted TB control program may help in reducing these potentially preventable causes.

Perinatal insult and CNS infections are the leading cause of seizures in these Islands.

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Ethical clearance: Obtained –Institutional Ethics Committee of ANIIMS, Port Blair; No. ECR/940/ Inst/AN/2017, dated 23-06-20.

Author's Contribution

Data compilation and analysis, literature review and manuscript writing; TLR: Concept and design of study, final editing; TP Data compilation and interpretation. All authors have read final version of the manuscript.

Conflict of interest

None

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