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ROLE OF NEUROIMAGING IN FIRST UNPROVOKED SEIZURES IN CHILDREN: A PROSPECTIVE OBSERVATIONAL STUDY

Paediatrics

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ABSTRACT

A seizure is a common neurological problem that occurs in children. Approximately 1% of children who present with what appears to be a first unprovoked seizure will be assigned a different diagnosis that will potentially alter acute management based on neuroimaging. Hence, the current study was conducted with the main purpose to assess the proportion of children presenting with first unprovoked seizures who have neuroimaging (CT/MRI) abnormalities. This is a hospital based prospective observational study comprised of 72 children aged between 2-months to 12-years with first unprovoked seizures. MRI was done at 1.5 Tesla in most situations; while CT was done in case of nonavailability of MRI. Neuroimaging findings were categorized into normal study and the abnormalities were classified as ring enhancing lesions, neurodegenerative disorders, tumors, cerebrovascular accident, congenital structural defect, calcifications, neurocutaneous syndrome, metabolic disorders and others categorized as miscellaneous. Majority of subjects i.e., 48.6% belonged to 6–9-year age group with male predominance (M:F ratio: 1.6:1). 29.2% cases had abnormal neuroimaging findings. Out of total 72 subjects 53 (83.6%) cases underwent brain MRI and 19 (25.8%) cases underwent brain CT. Out of 53 MRI neuroimaging, 17 (23.6%) had neuroimaging abnormalities. Similarly, out of 19 CT neuroimaging, only 4 had cerebral oedema. Generalized tonic-clonic seizures (GTCS) were the most common type accounted for 93% of patients. The association of altered sensorium with neuroimaging abnormalities was statistically significant ($p = 0.027$). In conclusion, neuroimaging is a valuable adjunct in the diagnostic work-up of childhood seizures, particularly when guided by relevant clinical indicators. Hence, targeted neuroimaging offers the most effective strategy for accurate diagnosis and management of first unprovoked seizures in the paediatric population.

KEYWORDS

First Unprovoked Seizure, Neuroimaging, MRI, Computed Tomography, Children, Neuroimaging Abnormalities

INTRODUCTION

A seizure is a temporary episode characterized by clinical signs and symptoms caused by excessive or synchronous abnormal neuronal activity within the brain.[1] Seizures may occur either without an identifiable trigger or secondary to provoking factors, most commonly brain injury, metabolic derangements, or toxic disturbances affecting cerebral function. Additional precipitating factors include fever, head trauma, drug withdrawal, hypoglycemia, electrolyte imbalance, central nervous system infections, ischemic stroke, intracranial hemorrhage, and pro-convulsant medications such as clozapine. A first unprovoked seizure (FUS) refers to a seizure occurring in the absence of an evident precipitating factor, although advances in diagnostic methods have increased the likelihood of identifying previously unrecognized causes. Such seizures may occur as isolated or recurrent events and may result from either a static lesion, as in remote symptomatic seizures, or a progressive lesion, as seen in progressive symptomatic seizures.[2]

Approximately 5% of children experience convulsions within the first five years of life. Nearly 30% of children presenting with an initial afebrile seizure subsequently develop epilepsy.[3] Between 5% and 10% of children have at least one seizure episode during the first 12 years of life, with the greatest incidence observed in children younger than five years. Epidemiological evidence indicates that nearly 1,50,000 children experience a first unprovoked seizure each year.[4]

The occurrence of a first seizure episode is often distressing and immediately prompts concern regarding its cause and the risk of recurrence. Neuroimaging in children with a first afebrile seizure is primarily undertaken to identify any serious underlying pathology that may require urgent management and to assist in determining prognosis. Findings from multiple studies suggest that the prevalence of abnormal neuroimaging in children presenting with new-onset afebrile seizures ranges from 0% to 21%.[5]

The two principal imaging techniques employed during the initial assessment of seizures are computed tomography (CT) and magnetic resonance imaging (MRI). CT scanning can be completed rapidly, is comparatively inexpensive, and usually does not require sedation; however, it exposes the child to ionizing radiation. CT is mainly used to exclude emergency conditions such as intracranial hemorrhage, brain abscess, or tumors that demand immediate intervention. MRI, in contrast, offers superior visualization of structural abnormalities and does so without radiation exposure.[6]

Literature reports evidenced that both the etiology and frequency of unprovoked seizures may differ in developing countries such as India because of the higher burden of infectious conditions, particularly neurocysticercosis and tuberculosis.[7,8] In addition, neuroimaging is especially important because some children may harbor lesions requiring specific therapy, and these abnormalities are often difficult to identify on clinical examination alone.[9] Examples of such lesions include acute disseminated encephalomyelitis, infarcts due to viral angiopathy, and thromboembolic events. Therefore, evaluating neuroimaging abnormalities in children presenting with a first apparent unprovoked seizure is essential.[4] Furthermore, there is limited information available regarding the utility of neuroimaging in children with first unprovoked seizures in northern Karnataka.

With these viewpoints, present study was conducted to assess the proportion of children presenting with first unprovoked seizures who have neuroimaging (CT/MRI) abnormalities.

METHODOLOGY

Ethical approval

Ethical committee approval was obtained by institutional human ethics committee of Karnataka Institute of Medical Sciences, Hubballi (Reg. No.: ECR/486/Inst/KA/2013/RR-16). A written informed consent was taken from parents or guardians.

Study design and patients

This is a hospital based prospective observational study conducted among children aged 2-months to 12-years with first unprovoked seizures in the Department of Paediatrics, Karnataka Medical College and Research Institute, Hubballi, Karnataka, India. The sample size was calculated using the formula for estimating a proportion:

$$N = \frac{Z^2 pq}{d^2}$$

where Z is the standard normal deviate corresponding to a 95% confidence interval (1.96), p is the estimated prevalence (30% or 0.30), q=1-p(0.70), and d is the allowable error (10% or 0.10). Substituting these values, and after considering a 10% attrition/non-response rate, the final sample size was rounded to 72.

Inclusion criteria
Age: 2-months to 12-years
First unprovoked seizures

Exclusion criteria
Children between 2-months to 12-years having convulsion with a history suggestive of acute antecedent events like trauma, drugs, toxins

Convulsions associated with:
Fever
Cerebral palsy
Neonatal seizures
Seizures due to electrolyte imbalances
Pervasive developmental disorder/intellectual disability

Data collection
A detailed clinical history and physical examination were recorded in a pre-structured proforma including patients age, and gender. Description of seizure such as (i) prodromal symptoms (fever, diarrhoea with dehydration, nausea, vomiting, headache, blurring of vision), (ii) type of seizure (generalized/focal), (iii) duration and progression of seizure, (iv) loss of consciousness, (v) starring look, (vi) frequent blinking, (vii) associated symptoms (up rolling of eye ball, frothing from mouth clinches of teeth, fecal/urinary incontinence), (viii) any diurnal variation, (ix) any precipitating factors (history of drug ingestion, trauma, and toxins), (x) other clinical features were examined and recorded in a proforma. Furthermore, family history of seizure, epilepsy, birth history, developmental history, immunisation status, dietary history was taken.

Neuroimaging was done after stabilization and sedation given if needed to reduce motion artefacts. Neuroimaging was done either as urgent or non-urgent study. MRI was preferred in most situations as it better detected the abnormality compared to other imaging modalities. CT was considered in case of nonavailability of MRI. MRI was performed at 1.5 Tesla. The entire imaging was evaluated by an experienced radiologist and reassessed in cases of doubt with paediatric neurologists. The findings were documented in the proforma. Neuroimaging findings were categorized into normal study and the abnormalities were classified as ring enhancing lesions, neurodegenerative disorders, tumors, cerebrovascular accident, congenital structural defect, calcifications, neurocutaneous syndrome, metabolic disorders and others categorized as miscellaneous.

STATISTICAL ANALYSIS
Data were entered in Microsoft Excel 2021 and statistical analysis was done using IBM Statistical Software for Social Sciences (SPSS) version 22. Categorical variables were represented in the form of percentages, and frequencies. Continuous variables were presented as descriptive statistics (Mean and Standard deviation [SD]). Categorical variables were analysed using the Chi-square test. $p \leq 0.05$ was considered statistically significant.

RESULTS
Majority of subjects i.e., 48.6% belonged to 6–9-year age group followed by 9-12 yrs (29.1%), 3-6 yrs (12.5%), and only 9% belonged to <3 yrs age group. Majority i.e., 62.5% were male gender and 37.5% were belonged to female category with M:F ratio of1.6:1 (Table 1).

Table 1. Demographic and baseline characteristics

Age	Male	Female	Total	Mean Age	Overall Mean Age
2months-3yrs	5 (6.9)	2 (2.0)	7 (9.0)	1.5	7.42
3 – 6 yrs	4 (5.5)	5 (6.9)	9 (12.5)	4.5	
6 – 9 yrs	21 (29.1)	14 (19.4)	35 (48.6)	7.5	
9 – 12 yrs	15 (20.8)	6 (8.3)	21 (29.1)	10.5	
Total	45 (62.5)	27 (37.6)	72 (100.0)		

Values are n (%) unless otherwise stated

The results on distribution of subjects based on final diagnosis were represented in Table 2. Results depicted that majority of patients (70.8%) were diagnosed with seizure disorder without any identifiable abnormality on neuroimaging, indicating that a large proportion of first seizures may not have visible structural causes. However, 29.2% had abnormal neuroimaging findings, underlining the significant role of imaging in detecting potentially treatable or serious underlying conditions. The common abnormal findings include cerebral oedema (8.3%), hypoxic-ischemic encephalopathy (HIE) changes and encephalopathy (4.1% each), cerebral atrophy, structural abnormalities, and infarcts with hemorrhage (2.7% each), and tumor, hydrocephalus, and demyelination (1.3% each).

Table 2. Final diagnosis wise distributions

Final Diagnosis	N (%)
Seizure disorder	51 (70.8)
Cerebral oedema	6 (8.3)
HIE changes	3 (4.1)
Encephalopathy	3 (4.1)
Cerebral atrophy	2 (2.7)
Structural abnormalities	2 (2.7)
Acute infarct with hemorrhage	2 (2.7)
Tumor	1 (1.3)
Hydrocephalus	1 (1.3)
Demyelination	1 (1.3)

HIE, Hypoxic-ischemic encephalopathy

Out of total 72 subjects 53 (83.6%) cases underwent MRI brain and 19 (25.8%) cases underwent CT brain. Out of 53 MRI neuroimaging, 17 (23.6%) had neuroimaging abnormalities, and 36 (50%) showed no obvious abnormalities. Similarly, out of 19 CT neuroimaging, only 4 had cerebral oedema, 15 (20.8%) had normal findings (Table 3).

Table 3. Distribution of subjects based on neuroimaging abnormalities

Neuroimaging	Abnormal	Normal	Total
Brain MRI	17 (23.6)	36 (50.0)	53 (83.6)
Brain CT	4 (5.0)	15 (20.8)	19 (25.8)
Total	21 (29.2)	51 (70.8)	72 (100.0)

Values are n (%), MRI, Magnetic resonance imaging; CT, Computed tomography

Generalized tonic-clonic seizures (GTCS) was the most common type accounted for 93% of patients. Out of this 25% had abnormal neuroimaging, while 68% had normal imaging. Focal seizures accounted for 3.3% of cases out of this 2% had abnormal imaging, and 1.3% had normal. Absence seizures, least common (2.6% of total cases), evenly distributed: 1.3% had abnormal imaging and 1.3% had normal. Overall, the correlation between types of seizure with neuroimaging abnormalities was non-significant ($p = 0.26$) (Table 4).

Table 4. Correlation of types of seizure with neuroimaging abnormalities

Types of Seizures	Neuroimaging		Total
	Abnormal	Normal	
GTCS	18 (25.0)	49 (68.0)	67 (93.0)
Focal seizure	2 (2.0)	1 (1.3)	3 (3.3)
Absence seizure	1 (1.3)	1 (1.3)	2 (2.6)
Total	21 (29.0)	51 (70.0)	72 (100.0)
p-value	0.26		

Values are n (%) unless otherwise stated; GTCS, Generalized tonic-clonic seizures

The results on association of altered sensorium with neuroimaging abnormalities were represented in Table 5. Results showed that the relative risk of having abnormal neuroimaging findings in patients with altered sensorium was calculated to be 2.2, indicating that individuals with altered sensorium were over two times more likely to have abnormal neuroimaging compared to those without altered sensorium. The attributable risk was found to be 25%, suggesting that approximately 25% of the risk of abnormal neuroimaging in individuals with altered sensorium can be attributed directly to the presence of altered sensorium. Moreover, the association of altered sensorium with neuroimaging abnormalities was statistically significant ($p = 0.027$).

Table 5. Association of altered sensorium with neuroimaging abnormalities

Altered Sensorium	Neuroimaging		Total
	Abnormal	Normal	
Yes	11 (15.2)	13 (18.0)	24 (30.0)
No	10 (13.8)	38 (53.0)	48 (70.0)
Total	21 (29.0)	51 (71.0)	72 (100.0)
p-value	0.027		
RR	2.2		
AR	25%		

Values are n (%) unless otherwise stated; RR, Relative risk; AR. Attributable risk

The results on association of outcomes with neuroimaging abnormalities were represented in Table 6. Results revealed that all patients whose abnormalities were detected by CT showed improvement (100%). For patients whose abnormalities were detected by MRI, the outcomes were more varied: more than half showed improvement (52.9%), more than quarter showed partial improvement (35.2), and a small proportion resulted in death (11.7%).

Table 6. Association of outcomes with neuroimaging abnormalities

Outcome	Improved	Partially Improved	Death	Total
Brain CT	4 (100.0)	0	0	4
Brain MRI	9 (52.9)	6 (35.2)	2 (11.7)	17
Total	13	6	2	21

Values are n (%) unless otherwise stated; MRI, Magnetic resonance imaging; CT, Computed tomography

DISCUSSION

Seizures represent one of the most frequent neurological disorders encountered in childhood. A first seizure episode is often highly distressing for parents, and it is essential for healthcare professionals to adopt the most appropriate diagnostic approach and management recommendations in each case.[3] Approximately 1% of children initially thought to have experienced a first unprovoked seizure are ultimately found to have an alternative diagnosis on neuroimaging that significantly changes acute management.[10] Therefore, the present hospital-based prospective observational study was undertaken to determine the proportion of children with first unprovoked seizures who demonstrate abnormalities on neuroimaging (CT/MRI).

In the present study, 48.6% of the children were in the 6–9-year age group, with a predominance of males. These findings are consistent with the observations of Adhikari et al., Chung et al., and Saravanan et al., who also reported a higher occurrence of seizures among school-aged children, with declining frequency in younger age groups and a greater prevalence in boys. The predominance of children aged 6–9 years in the current study may be attributed to age-related idiopathic epilepsies, particularly childhood absence epilepsy, which commonly manifests during this developmental period as the brain matures. Many epileptic syndromes are age dependent and often occur in the absence of an identifiable precipitating factor.[11-13]

In our study, generalized tonic-clonic seizures (GTCS) were the most common presentation, occurring in 93% of the patients. These findings are comparable to those reported by Choudhary et al., in which 89% of children presented with generalized seizures and only 5% had partial seizures.[14] Among the generalized seizure types, tonic-clonic seizures were the most frequent. Similar results have been documented in Indian studies by Bhavani et al. and Ashraf et al.[15,16]

Such seizure patterns are frequently idiopathic or genetically determined rather than associated with structural brain lesions. In addition to GTCS, three children in the present study had focal seizures, while two had absence seizures at the time of admission. The majority of children in the present study, 51 cases (70.8%), had no identifiable abnormality on neuroimaging and were diagnosed as having seizure disorder without visible structural pathology. This suggests that many first unprovoked seizures in children occur in the absence of detectable brain abnormalities. Nevertheless, abnormal neuroimaging findings were observed in 21 of the 72 children (29.2%), emphasizing the importance of imaging in identifying serious or potentially treatable underlying causes.

Among the abnormal findings, cerebral edema was the most frequent, detected in 6 children (8.3%). Hypoxic-ischemic encephalopathy and encephalopathy were each identified in 3 children (4.1%), suggesting a possible perinatal or postictal etiology. Cerebral atrophy, structural abnormalities, and infarction with hemorrhage were each present in 2 children (2.7%), indicating chronic or vascular causes in a subset of patients. Less frequent but clinically important abnormalities included brain tumor, hydrocephalus, and demyelination, each identified in 1 child (1.3%). These findings have major implications for subsequent management and prognosis. Neuroimaging therefore proved useful in detecting clinically significant abnormalities in nearly one-third of the children included in the study. This observation supports current recommendations advocating neuroimaging, particularly MRI, after a first unprovoked seizure in order to exclude structural, infectious, vascular, or neoplastic etiologies, even when neurological examination is otherwise normal. Identification of these abnormalities may influence prognosis, the need for further investigations, and the decision to initiate antiepileptic therapy.

A comparable study by Agarwal et al. reported abnormal neuroimaging findings in 37 children, with hypoxic injury being the most common abnormality, identified in 12 children (32.4%). Of these, 10 had a history of delayed cry at birth. Calcifications were noted in 4 children (10.8%), including 2 cases diagnosed as tuberous sclerosis. One child with Down syndrome had normal neuroimaging findings. Hyperintense signals suggestive of demyelination were observed in 3 cases, although the underlying cause could not be established and hypoxia was presumed. Congenital malformations included one case of schizencephaly, two cases of porencephalic cyst, and one case of pachygyria.[17]

Dua et al. evaluated 161 children, among whom MRI of the brain was performed in 129. Abnormal MRI findings were detected in 48 children (37.2%).[18] Similarly, Chib and colleagues studied 276 children with seizures and performed neuroimaging in 121 children (43.8%). Among those aged 2–16 years, 21 children (25%) had abnormal neuroimaging findings. This indicates that abnormal imaging is more frequently encountered in school-aged children than in younger age groups. Overall, neuroimaging abnormalities were detected in 55 children (34%), with neurocysticercosis being the most common finding, present in 33 children and occurring more frequently in older children.[19]

CONCLUSION

In conclusion, neuroimaging serves as an important component of the diagnostic evaluation of childhood seizures, particularly when guided by appropriate clinical findings. A thorough clinical assessment combined with Targeted neuroimaging based on clinical indicators provides the most effective approach for establishing an accurate diagnosis and planning appropriate management in children presenting with a first unprovoked seizure.

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