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Secondary Seizures in Pediatric Population in Two Tertiary Hospitals in India

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Abstract

Objective: To evaluate the clinical pattern of secondary seizures which includes acute and remote symptomatic seizures among hospitalized patients in two healthcare centers and to assess the outcomes among hospitalized patients having secondary seizures.

Methods: This multicentric cross-sectional study was conducted in two tertiary hospitals in Odisha and Tamil Nadu, India, for a period of four years. A total of 274 patients in the age group between 6 months to 12 years participated in the study. A structured proforma was used to document the clinical pattern and causes of the secondary seizures.

Results: Among the participants in Odisha and Tamil Nadu hospitals, focal seizures constituted 67.5%. Generalized seizures were present in 32.4%. The key causes of seizures in Odisha were malaria, cerebral palsy, and viral meningitis, while in Tamil Nadu, the causes were neurocysticercosis, cerebral palsy, and viral meningitis.

Conclusion: Since the majority of the causes are preventable, it is important to address the issue at the public health level, by providing improved sanitation and adequate awareness on the secondary seizure and its causes. It is also important that the physicians are well conversant with the early case detection and treatment of primary diseases causing secondary seizures.

Keywords: Convulsion, encephalitis, malaria, secondary seizures

Introduction

There are many causes attributed to seizures and it is now well recognized that seizure is a symptom and not a disease. A seizure is defined as transient occurrence of signs and symptoms, resulting from abnormal, excessive or synchronous neuronal activity in the brain. According to the World Health Organization (WHO), secondary seizures are defined as seizures whose underlying cause is known. Secondary seizures in this study include those conventionally called as acute symptomatic seizures and remote symptomatic epilepsy. Incidence of seizures during the first five years is about 5%, and around 4-10% of children experienced at least one seizure episode in the first 16 years of life. The prevalence of childhood seizures varies between 5.2-8.1 per 1000 population. The most common type (60%) of seizures are convulsive, of which two-thirds begin as focal seizures (which may then become generalized), while one-third begin as generalized seizures. The remaining 40% of seizures are non-convulsive.[1]

Although seizures have been classified in many ways according to their site of origin, electroencephalogram (EEG) abnormalities, types of seizures, and response to therapy, a broad-based classification developed by Gastaut is applicable globally.[2] Furthermore, the International League Against Epilepsy

(ILAE) 2017 has provided a broad classification of epilepsy as focal, generalized, and unknown onset, with additional etiological classification that includes structural, genetic, infectious, metabolic, immune, and unknown etiology. Seizures with unknown causes presumed to be of genetic in origin, while symptomatic seizures, either of genetic causes or acquired causes like hippocampal sclerosis, perinatal and infantile causes, cerebral trauma, tumor or cerebrovascular causes, provoke seizures secondary to provoked factors and are cryptogenic in nature where presumed symptomatic nature in which the cause has not been identified.[3]

Seizures are considered as one of the non-specific symptoms expressed in a variety of many different pathologies. In most cases, seizure phenomenology depends upon the cortical location of the lesion rather than on specific population. Also, early recognition of the treatable causes of this common neurologic symptom and the institution of proper and adequate treatment, will ensure normal physical, mental and psychological development of the child.[4] From the perspective of the clinical patterns of secondary seizures, it can be challenging to identify of a single underlying pathology of the seizure. A brain tumor may produce seizures that are similar to other intracranial pathologies, such as infections and birth injury, and the treatment is incomplete unless there is a correlation between the clinical and pathological aspects of seizures. As far as possible, the underlying pathology should be investigated for better management of secondary seizure disorders.[5] The present study was carried out to evaluate the clinic pathological profile of secondary seizures in pediatric population and to assess the outcomes of hospitalized pediatic patients with secondary seizures.

Methods

The present study was carried out as a multi-centric cross sectional study in two tertiary care teaching hospitals with a total bed capacity of 1,000 in Odisha and Tamil Nadu, respectively. The study was conducted for a period of four years of October 2012-2014 and Nov 2016-2018. Children in the age group of 6 months to 12 years were taken up for the study. Children with generalized convulsion with or without neurological deficit, clearly appreciable focal seizures with or without neurological deficit, intermittent quivering movements affecting one or more extremities with altered sensorium, facial grimace with altered sensorium, staring look with altered sensorium, chewing and sucking motion with sensorium deficit and slight posturing or barely perceptible tremor with disturbance in tone and reflex activity, and irregular movements with constant crying and irritability with known definite underlying cause for seizures were included in this study. All cases were included on the basis of history and examination of a senior pediatric consultant or pediatric neurologist. Idiopathic generalized epilepsy and conditions mimicking seizure disorders like apneic spells, tremors, and syncopal attacks were excluded. Approval was obtained from the Institutional Ethics Committee prior to the data collection. Detailed explanation on the study was given to each participant's parent or guardian and informed consent was obtained from the parent prior to the data collection. All pediatric patients who were admitted to the respective hospitals during the study period was taken purposively as the subjects of this study. A total of 264 patients participated: 168 patients participated in Odisha and 96 participated in Tamil Nadu. A structured proforma was used to obtain the history and clinical information regarding the subjects. Particulars regarding the course in the hospital, laboratory parameters, and outcomes were also documented. Data were entered into and analyzed using SPSS ver.20 software. Descriptive statistics were used. The comparison of seizure profile with risk factors was evaluated using the chi square test with a p value of <0.05 considered statistically significant. Ethical approval for this study has been granted by the health research ethics committee from the Communication of Decision of the Instuitional Ethics Committee (IEC)/Institutional Review Board (IRB), Indian Council of Medical Research, under IEC/IRB:-43/12.

Results

Most subjects were in the age group of 3.6-7 years in both teaching hospitals (41.6%). Females constituted the majority of the population in Odisha and Tamil Nadu (57.2%). Most subjects in both locations belonged to lower socioeconomic status and to rural areas. The most common type of seizures in studied cases were found to be partial seizures, which were seen in 185 (67.51%) cases, followed by generalized seizures (32.4%). Amongst those with partial seizures, simple partial seizures were most common and were seen in 67

Table 1 Background Characteristics and Type of Seizures

Demographic Details and Type of Seizures	Characteristics	Odisha & Tamil Nadu	
		n	%
Age (in years)	0.6–3.5	53	19.3
	3.6–7	114	41.60
	7.1–10.5	60	21.8
	10.6–12	35	12.7
Sex	Males	107	39.05
	Females	157	57.2
Socioeconomic status	Lower	137	50
	Middle	73	26.6
	Upper	54	19.7
Location	Urban	101	36.8
	Rural	163	59.4
Type Of Seizures	Generalized	**89**	33.71%
	GTCS	50	18.94%
	Tonic	22	8.33%
	Atonic	6	2.27%
	Clonic	9	3.41%
	Myoclonus	2	0.76%
	Focal	**175**	66.29%
	Aware	76	28.79%
	Impaired awareness	25	9.47%
	Focal to bilateral tonic Clonic	74	28.03%

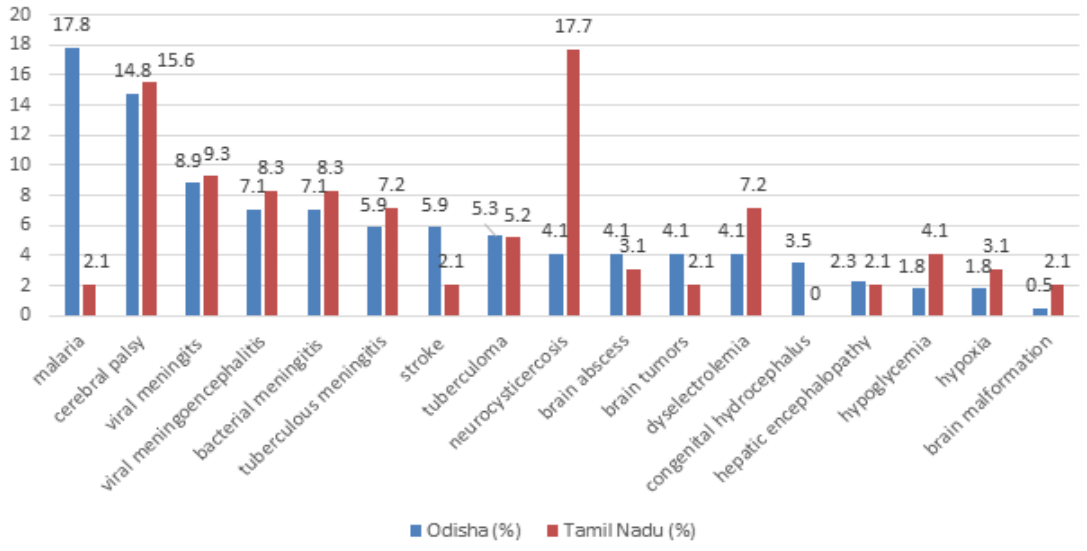

Fig. 1 Causes of seizures in Odisha and Tamil Nadu

Table 2 Clinical Presentation of Infective Causes

Symptom	No of cases (%)	Sign	No of cases (%)
Malaria			
Fever	29 (90.6)	Pallor	11 (34.3)
Lassitude	26 (81.2)	Icterus	5 (15.6)
Convulsions	32 (100)	hepatosplenomegaly	8 (25)
Altered sensorium	17 (53.1)	Meningeal signs	3 (9.3)
Decreased urination	11 (34.3)	Papilledema	4 (12.5)
Viral Meningitis			
Fever	22 (91.6)	Meningeal signs	19 (79.1)
Convulsions	24 (100)	Papilledema	8 (33.3)
Viral Meningoencephalitis			
Fever	8 (40)	Meningeal signs	5 (25)
Altered sensorium	18 (90)	Papilledema	3 (15)
Convulsions	20 (100)		
Loose stools	7 (35)		
Vomiting	4 (20)		
Bacterial meningitis			
Fever	14(70)	Meningeal signs	17 (85)
Altered sensorium	8 (40)	Papilledema	10 (25)
Convulsions	20(100)		
Neurocysticercosis			
Fever	2 (8)	Meningeal signs	5 (20.8)
Altered sensorium	7 (29.1)	Papilledema	3 (12.5)
Convulsions	24 (100)		
Brain Abscess			
Fever	7 (70)	Meningeal signs	8 (80)
Altered sensorium	7 (70)	Papilledema	5 (50)
Convulsions	10 (100)		

(27.7%) cases, whereas amongst those with generalized seizures generalized tonic-clonic seizures were the most common and seen in 50 (18.94 %) patients (Table 1).

The predominant causes of the seizures in Odisha were malaria, cerebral palsy, and viral meningitis, while in Tamil Nadu, the predominant causes were neurocysticercosis, cerebral palsy and viral meningitis. (Fig. 1).

From the clinical presentation for infective causes, it was demonstrated that fever was the most important symptoms and meningeal signs were the most important signs for most of the infective etiology. Convulsion being the inclusion criteria were seen in all cases (Table 2).

For the congenital etiology, the variation in head size either microcepahly or macrocepahly was the predominant sign. For those with metabolic etiologies, convulsions and altered sensorium were the dominant symptoms and most of the cases manifested with generalized systemic signs (Table 3).

The majority of the diagnosis in Odisha was based on CT scan, while the MRI scan is predominantly used in Tamil Nadu. The other investigations which were done to establish the etiology of seizures were complete blood count, rapid malarial antigen test, serum electrolyte test, hepatic and renal function tests, random blood sugar levels, and CSF examination in selected cases. The outcomes of various causes of secondary seizures was determined by using electroencephalograms in three successive follow up visits in 3 month interval [3, 6 and 9 months] after the discharge.

Table 3 Clinical Presentation of Congenital, Metabolic, and Other Causes

Clinical Presentation		Symptom	Odisha & Tamil Nadu n (%)	Sign	Odisha & Tamil Nadu n (%)
Congenital Causes	Cerebral palsy (n=40)	Convulsions	40(100)	Microcephaly	40 (100)
		Fever	5 (12.5)	Increased tone	31 (77.5)
		Tonic posturing	27 (67.5)	Hepatosplenomegaly	0 (0)
	Brain malformation (n=3)	Convulsions	3 (100)	Microcephaly	3(100)
		Increased tone	2 (66.6)	Hypertonia	2 (66.6)
	Congenital hydrocephalus (n=6)	Convulsions	6 (100)	Macrocephaly	6 (100)
		Increased head size	6 (100)	Macewens and transillumination	6 (100)
		Altered sensorium	6 (100)	Papilledema	3 (50)
	Electrolyte Imbalance (n=14)	Convulsions	14 (100)	Signs of dehydration (sunken eyes, delayed skin pinch, dry mucosa)	5 (35.7)
		Altered sensorium	14 (100)		
		Loose stools	14 (100)		
		Vomiting	7 (50)		
		Decreased urination	6 (42.8)		
Metabolic causes	Hypoglycemia (n=7)	Convulsions	7 (100)	Convulsions	7 (100)
		Altered sensorium	7 (100)	Altered sensorium	7 (100)
	Hypoxia (n=6)	Convulsions	6 (100)	Crepitations on auscultation	6 (100)
		Altered sensorium	6 (100)	Tender hepatosplenomegaly	5 (83.3)
		Hurried breathing	6 (100)		
		Fever	4 (66.6)		
Other Causes	Stroke (n=12)	Weakness of body and limbs	12 (100)	Hemiplegia	10 (83.3)
		Convulsions	12 (100)	Facial palsy	10 (83.3)
	Tuberculoma (n=14)	Convulsions	14 (100)	Meningeal signs	3 (21.4)
		Fever	4 (28.5)	Papilledema	3 (21.4)
		Altered sensorium	7 (50)		
	Brain tumors (n=9)	Convulsions	9 (100)	Meningeal signs	6 (66.6)
		Altered sensorium	6 (66.6)	Papilledema	3 (33.3)
	Organ failure (n=7)	Convulsions	7 (100)	Icterus	7 (100)
		Altered sensorium	7 (100)	Meningeal signs	2 (28.5)
		Yellowish discoloration of body	7 (100)	Papilledema	2 (28.5)

Although significant drop outs of more than 50% of patients were observed, there was an overall significant improvement of outcome, i.e., seizure free or seizure reduction along with EEG normalization, during the follow up period based on the evaluation using the EEG in both the centers. The outcome was better in children with acute causes of secondary seizures and also in causes in where no permanent brain injury was seen compared

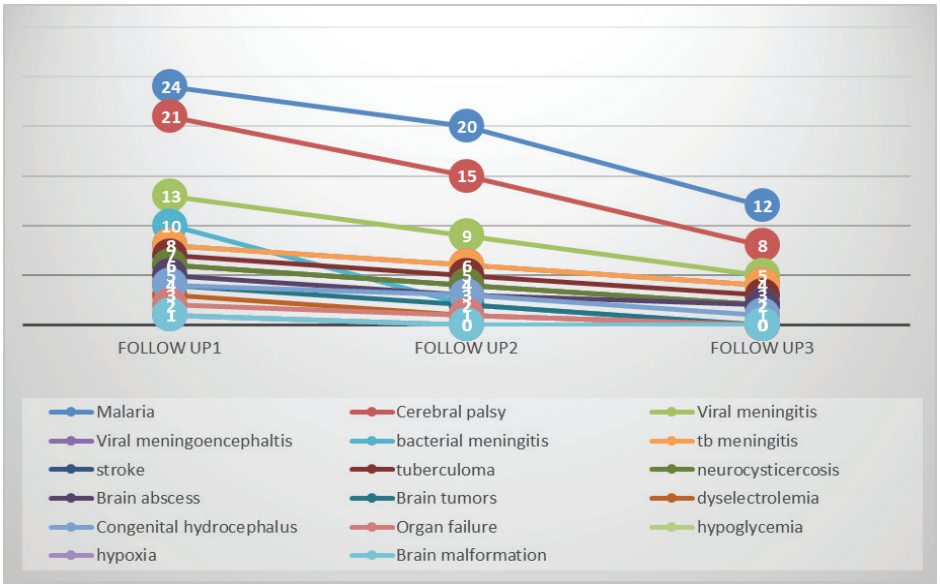

Fig. 2 Outcomes During Follow Up (Odisha)

to remote symptomatic causes like cerebral palsy (Fig. 2 and Fig. 3).

Discussion

Secondary seizures are rampantly increasing in developing countries, including in India. However, there is considerable paucity in the availability of literature. The present study was carried out as a multicentric study in Odisha and Tamil Nadu on 168 and 96 patients, respectively. In this study, the incidence of seizures was more in early childhood between the ages of 3.5 to 7 years in both centers. Similar findings were observed in a study done by Kotsopoulos *et al.* and Neubauer *et al.* [4, 5] Therefore, the need for early detection of the symptomatology is high among younger children. The majority of the subjects were diagnosed with partial seizures

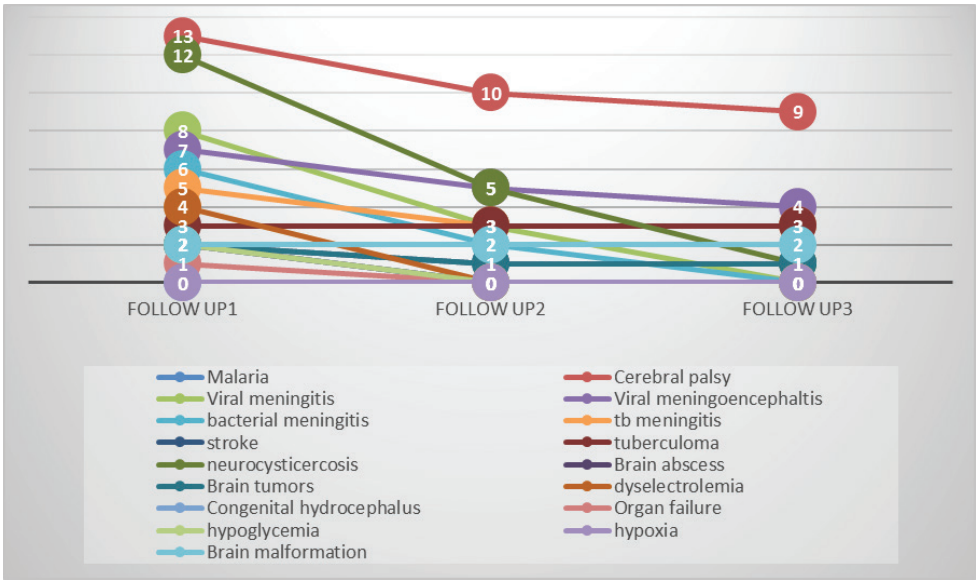

Fig 3 Outcomes During Follow Up (Tamil Nadu)

(71.5% in Odisha and 57.2% in Tamil Nadu). The findings are similar to the studies done by Unver *et al*.[6], where the prevalence of partial seizures is 56.5%.

The dominant causes of seizures among the study population are infective cause, essentially parasitic infections, with malaria as the strongest cause for seizures in Odisha (17.8%) while neurocysticercosis was the most common cause in Tamil Nadu (17.7%). Symptomatic infective etiology was present in 47.1% of the subjects. In a review done by Vezzani *et al*.[8], infections of the Central nervous system constituted the predominant cause for seizures similar to this study.[7] In another study done by Gowda *et al*., the predominant cause for seizures was structural abnormalities, while TORCH infections contribute 7.2% of the seizures. The reason for the high prevalence of malaria induced seizures in Odisha is due to the epidemiological vulnerability of the state. Odisha has several rural and tribal districts that are endemic to falciparum malaria. In a study done by Das *et al*.[9], the prevalence of cerebral malaria was found to be 18.5% among pediatric population in Odisha and 44.4% of the deaths in the pediatric age group was attributed to seizures in malaria. There has been a steady rise in the prevalence of seizures associated with neurocysticercosis in recent years. In various studies carried out in South India, the incidence of seizures was as as high as 94.8% among children with neurocysticercosis. This has been largely attributed to the changing lifestyle patterns resulting in formation of solid cystic granuloma by the Taenia solium parasite. [10]

According to a study by Nelson *et al*. the incidence of nonfebrile convulsions was highest in the first year of life, especially in the first month. Children with neurological or developmental abnormality assessed in the first year of life did not have their first seizure earlier than children without any abnormality. Neurological abnormalities in the first year of life before any seizure, and the presence of minor motor seizures, are associated with an increased rate of mental retardation and cerebral palsy at age of seven, but early age at onset appears to have little prognostic value regarding intellectual function, cerebral palsy, and epilepsy.[11]

Malaria and neurocysticercosis were the most common infective pathologies seen in studied cases. In various developing countries infective pathologies remain common cause of secondary seizures. Other than infective causes, non-infective causes such as cerebral palsy and dyselectrolytemia were the common causes of secondary seizures in these children.

Based on the study findings, it may be considered that secondary seizures are not recurrent, unlike primary idiopathic seizures, when the underlying cause is treated properly. Recurrent secondary seizures are observed in patients with residual brain damages due to primary disease or due to persisting primary disease and these children have much poorer outcomes. Age of onset and cause of secondary seizures have found to have important effect on the outcome of secondary seizures so our study is not compatible with their study since the trend secondary seizures is different from primary idiopathic seizures.[12]

This study is limited in terms of a relatively small number of patients; thus, a study with a larger number of pediatric patients will further substantiate the findings of this study. Moreover, in this study, neuroimaging such as computerized tomography or MR imaging could not be done in all cases. The present study has emphasized on the role of infectious etiology, specifically malaria as a cause of secondary seizures. Majority of the causes of secondary seizures in pediatric age group in our study were found to be either preventable or treatable. Precise etiological diagnosis will help in proper management of children having secondary seizures.

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