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Study of Clinico-Etiological profile of seizures in Kolar District of Karnataka, India

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Abstract

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Keywords:

Epilepsy, Seizure, Convulsion, clinical profile, Neurocysticercosis All children between 1 month to 18 years, admitted with new on set undiagnosed febrile or a febrile convulsive seizure disorder to R.L. Jalappa Hospital and Research Centre, Kolar are included in this study. The study was conducted over a period of one year from Dec 2013 to Jan 2015 with sample size of 150. The mean age of onset of seizure in study group was 5.19 \pm 4.37 years. The age group at which maximum onset of seizures found was between 1-5 years of life. Febrile seizure (65.9%) was the most common cause of seizure below 5 years of age and Neurocysticercosis (50%) in the age group 6-18 years. Females were more susceptible to seizure disorders than males. The most common clinical presentation of seizures was generalized tonic-clonic type (56.6%). The most common etiology was infectious (66.1%). Idiopathic generalized epilepsies (45%) were most common type of epilepsy. Mean temperature on admission to hospital in febrile seizure patients was 101.43⁰F. Mean age for febrile seizure was 24.05 months. Further, studies on large scale over longer duration should be carried out, to put forth the diagnostic guidelines and management plans based on clinical presentation and etiological causes in a specific age group.

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INTRODUCTION

Seizure is a common problem evaluated in pediatric emergency departments which is transient occurrence of signs and symptoms due to the abnormal, excessive, or synchronous neuronal activity in the brain characterized by abrupt and involuntary skeletal muscles activity. (Trinka *et al.*, 2015).

The clinical diagnosis of epilepsy usually requires

the occurrence of at least two unprovoked seizures 24 hrs apart or one unprovoked seizure and enough EEG and clinical information to convincingly demonstrate an enduring predisposition to develop recurrences.

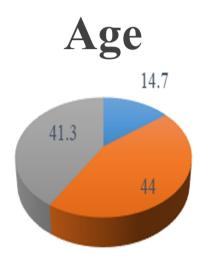
Approximately 4-10% of children experience at least 1 seizure (febrile or afebrile) in the 1st 16 years of life. The cumulative lifetime incidence of epilepsy is 3%, and more than half of the cases start in childhood. The annual prevalence is 0.5-1.0% globally. (Johnston, 2015)

Thus, the occurrence of a single seizure or of febrile seizures does not necessarily imply the diagnosis of epilepsy. (Johnston, 2015) Status epilepticus refers to continuous or recurrent seizure activity lasting longer than 30 minutes without recovery of consciousness in between. (Friedman and Sharieff, 2006)

The age and neurodevelopmental maturity status determine the clinical manifestations and the type of seizure disorders encountered. (Kalra, 2011)

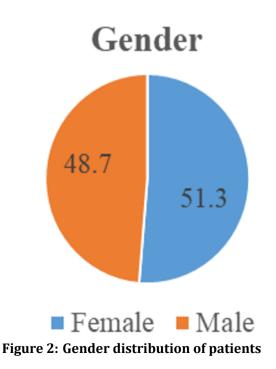
Although the outlook for most children with symptomatic seizures or those associated with epilepsy is generally good, seizures may signal a potentially serious underlying systemic or central nervous system (CNS) disorder that requires thorough investigation and management. (Johnston, 2015) The type of seizure, its etiology, manifestations and progression varies from age to age.

This study was planned in rural tertiary level hospital with the aim to study the clinico-etiological profile of seizures in children among 1 month to 18 years of age of Kolar District, Karnataka. It also helps in prognostication and outcome.

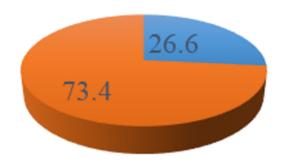


■ Infants (< 1 year) ■ 1 to 5 years ■ 6 to 18 years

Figure 1: Age distribution of patients



Type of Seizures



■ Focal ■ Generalized

Figure 3: Type of Seizures

Fever distribution

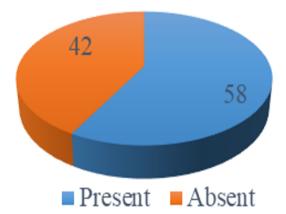
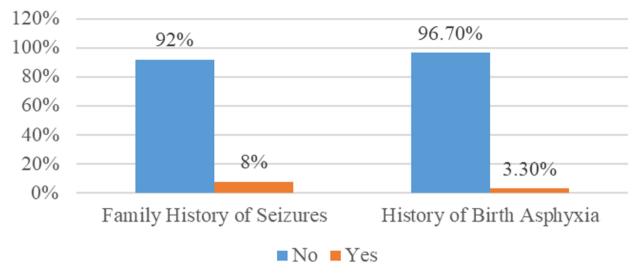


Figure 4: Number of patients who had seizure associated with fever

MATERIALS AND METHODS

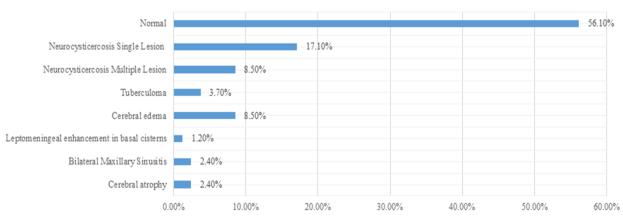
Sample size estimation

R.L. Jalappa Hospital and Research Centre is being a tertiary care center and total number of admissions for year 2012-13 were 3242 of which, 324 cases were admitted with seizures, among them 216 were new onset seizures. Based on this value, sample size was estimated at 6.66% expected proportion with 5% absolute error. At 95% confidence interval a minimum sample size of 96 was obtained. Considering 10% non- response rate sample size required was 96+10=106.

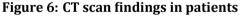


Risk factors for Seizures

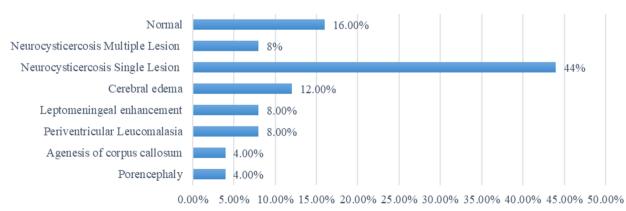
Figure 5: Risk factors for Seizures

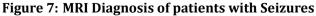


CT scan findings in patients









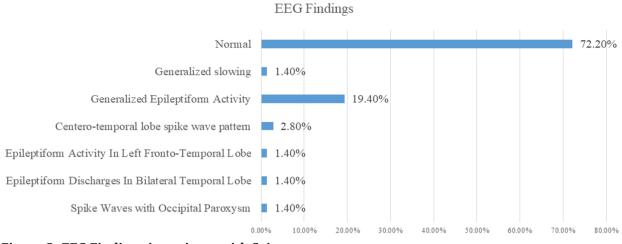


Figure 8: EEG Findings in patients with Seizures

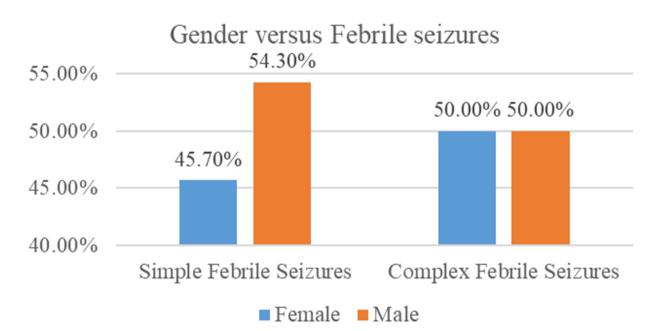


Figure 9: Gender distribution of febrile seizure patients

		Cases	Percent
Parents	Consanguineously married	16	10.7
	Non-Consanguineous	134	89.3
	Total	150	100.0

Table 2: Motor Manifestations of Seizures in the patients studied

	Number	Percent
Tonic-clonic	85	56.6
Tonic	41	27.3
Clonic	24	16
Total	150	100.0
	Tonic Clonic	Tonic-clonic85Tonic41Clonic24

		Cases	Percent
Loss of Consciousness	No (Conscious)	12	8.0%
during seizure episode	Yes (Unconscious)	138	92.0%

Table 3: Events during Seizure episode

Table 4: Post ictalphenomenon in seizure subjects

Level of Consciousness at admission					
Awake	88	58.7%			
Response to verbal stimulus	50	33.3%			
Response to painful stimulus	6	4.0%			
Unresponsive	6	4.0%			
Neurological deficits					
Absent(No)	144	96.0%			
Present(Yes)	6	4.0%			

Table 5: Neurological manifestations in patients

		Cases	Percent
Head Circumference	Microcephaly	6	4%
	Normal	144	96.0%
Signs of upper motor neuron	Absent	144	96.0%
type of leison	Present	6	4.0%
Clinical signs of meningitis	Absent	143	94.0%
	Present	9	6.0%

Table 6: Laboratory findings in patients

		Cases	Percent
Malaria Parasite in Peripheral	Negative	145	96.7%
Smear/Rapid diagnostic test	Positive	5	3.3%
Hyponatremia	Absent	149	99.3%
	Present	1	0.7%
Hypocalcemia	Absent	144	96.0%
	Present	6	4.0%
Widal Test Positive	No	148	98.7%
	Yes	2	1.3%
Abnormal CBC	No	127	84.6%
	Yes	33	15.4%
Urine culture Report	Candida	1	0.7%
	E.coli	7	4.7%
	Normal	142	94.7%
Tests for tuberculosis	Normal	146	97.3%
	Hilar nodes present in chest X	2	1.3%
	ray		
	Mantoux Positive	3	2%
	Sputum for AFB	1	0.7%

Age in Mor	nth	N	Mean	SD	Min	Max	Range	
Febrile sei	zures							
Simple	Febrile	46	25.17	15.53	6.10	59.1	53.00	
Seizures								
Complex	Febrile	12	19.77	10.01	8.13	36.50	28.37	
Seizures								
Total		58	24.05	14.65	6.10	60.83	54.73	

Table 7: Age distribution of febrile seizure patients

Table 8: Temperature at admission in febrile seizure patient

•		-			
Temperature in degree Fahrenheit	of N	Mean SD	Min Max	Range	Quartile Range
1 0111 01111010					
Febrile seizures					
Simple Febrile Seizures	46	101.65 1.015	100.00 105.00	5.00	1
Complex Febrile Seizures	12	100.58 0.514	100.00 101.00	1.00	1
Total	58	101.43 1.027	100.00 105.00	5.00	1

Mean temperature on admission to hospital in febrile seizure patients was 101.43^oF.

Table 9: Etiological Diagnosis of patients with Seizures

				Total
			Cases	Percent
Etiological	Febrile Seizures	Simple febrile seizure	46	30.7%
Diagnosis		Complex febrile seizure	12	8.0%
	Infectious	Neurocysticercosis	34	22.7%
	Causes	Encephalitis	19	12.7%
		Pyogenic meningitis	7	4.7%
		Tuberculoma	2	1.3%
		Tuberculous meningitis	2	1.3%
		Cerebral Malaria	1	0.7%
	Metabolic	Hypo Calcemic seizure	6	4.0%
	Causes	Hypoglycemic seizures	1	0.7%
		Hyponatremic seizures	1	0.7%
	Cerebral palsy		4	2.6%
	Congenital anoma	alies	2	1.3%
	Not found		13	8.7%
Total			150	

Table 10: ILAE Classification of seizure types in patients

		Cases	Percent
IIAE Classification of	Generalized Tonic-clonic	85	56.6%
seizure types	Generalized Tonic	25	16.6%
	Simple Partial Seizure	12	8.0%
	Complex Partial Seizure	28	18.6%

Epilepsies and Epileptic syndromes	Cases	%	Total
Situation-related seizures	58	44.6	130(86.6%)
1. 1.	67	51.6	
2.2.	05	3.8	
3. 3.			
Generalised epilepsy	09	60	15(10%)
1.1.	06	40	
2.2.	00		
3. 3.			
Localisation related epilepsy (LRE)	03	60	5(3.4%)
1. 1.	02	40	
2. 2.			
Total	150		150

Table 11: Showing ILAE Classification of epilepsies and epileptic syndromes

			Types of Seizure		Total
			Partial	Generalized	
Etiological	Febrile Seizures	Simple febrile seizure	0	46	46
Diagnosis		Complex febrile seizure	0	12	12
	Infectious Causes	Neurocysticercosis	34	0	34
		Encephalitis	0	19	19
		Pyogenic meningitis	0	7	7
		Tuberculoma	2	0	2
		Tuberculous meningi-	0	2	2
		tis			
		Cerebral Malaria	0	1	1
	Metabolic Causes	Hypo calcemic seizure	0	6	6
		Hypoglycemic seizures	0	1	1
		Hyponatremic seizures	0	1	1
	Cerebral palsy		0	4	4
	Congenital anomalies		0	2	2
	Not found		4	9	13
	Total		40	110	150

 χ 2 = 51.72, df = 3 ,p < 0.001*

In the study duration i.e from December 2013 to January 2015 total of 150 cases with new onset seizures were admitted and were included to the study.

Method of data collection

Method

Patient's detailed history was obtained from the informant who has witnessed the seizure episode. All details obtained from history, examination and investigations were recorded in a predefined case proforma.

In clinical history more emphasis was given on the points, which are helpful in classification and diagnosis of seizures. Age is one of the important characters, as different seizure types are presented in a specific age group. Age of patients was divided in 3 groups as <1 year (infant), 1 to 5 years (toddlers and preschool children) and 6 to 18 years (school going and adolescents). Each patient's sex and consanguinity were also noted. Details of the seizure episode were recorded as, type of convulsion that is, generalised or focal, motor manifestation as tonic, clonic or tonic-clonic, autonomic

Etiological Diagnosis	Age Infants (< 1 year)		1 to 5 years		6 to 18 years	
	Count	% Count	%	Count	%	
Cerebral Malaria	0	0.0%	1	1.5%	0	0.0%
Cerebral palsy	1	4.5%	3	6.2%	0	0.0%
Complex febrile seizure	2	9.0%	10	15.4%	0	0.0%
Encephalitis	0	0.0%	3	4.6%	16	26.6%
Hypo calcemic seizure	4	18.2%	2	3.1%	0	0.0%
Hypoglycemic seizures	0	0.0%	1	1.5%	0	0.0%
Hyponatremic seizures	0	0.0%	0	0.0%	1	1.6%
Neurocysticercosis	0	0.0%	4	6.2%	30	50.0%
Not found	0	0.0%	4	6.2%	9	15.0%
Pyogenic meningitis	4	18.2%	1	1.5%	2	3.3%
Simple febrile seizure	10	45.4%	36	54.5%	0	0.0%
Tuberculoma	0	0.0%	0	0.0%	2	3.3%
Congenital anomalies	1	4.5%	1	1.6%	0	0.0%
Tuberculous meningitis	0	0.0%	0	0.0%	2	3.2%

Pearson Chi-square value = 132.2, df = 26, p = <0.00001

			Total	
			Cases	Percent
Anti –	None		5	3.3%
Convulsant	Calcium		6	4.0%
used	Clobazam proph	58	38.6%	
	Monotherapy	Carbamazepine	33	22.0%
		Valproate	22	14.7%
		Levitiracetam	1	0.7%
		Phenytoin	12	8.0%
		Phenobarbitone	9	6.0%
	Polytherapy	Phenytoin and phenobarbitone	3	2%
		Multiple anticonvulsants	1	0.7%
		(phenytoin,phenobarbitone and val- proate)		
	Total		150	

components like vomiting or bowel-bladder incontinence, level of consciousness was measured by using AVPU scale (Advanced Life Support Group, 1997), duration of convulsion, associated symptoms like cyanosis or fever, post-ictal level of consciousness,focal neurological deficit, number of seizure episodes, that is 1,2, >/= 3 (multiple), interval between repeated seizure episodes was within 24 hours or 24 hours apart.

Lumbar puncture was done in any child who presents with a seizure and fever and < 1 year, fever with meningeal signs and symptoms (neck stiffness, Kernig and/or Brudzinski signs) or History suggestive of neuro infection or meningitis (Hirtz *et al.*, 2000) Lumbar puncture was done after fundus examination, to rule out increased intracranial pressure, under aseptic precautions. EEGs were done on computerised "Neuropage plus" machine using 23 electrode system. All EEGs were done at least 24 hours after last episode of convulsion (Hirtz *et al.*, 2000). Patients were classified according to the International Classification of Epileptic Seizures (Johnston, 2008).

T-+-1

RESULTS AND DISCUSSION

Age distribution of patients studied

Majority of subjects studied were in the age group of

1 to 5 years 66(44.0%). (Figure 1)

Gender distribution of patients

Majority of patients were Females 77 (51.3%). (Figure 2)

Distribution of patients born to consanguineously married parents

Majority of patients were born to non – consanguineous parents. (Table 1)

Type of Seizures in the patients

Majority of patients (73.4%) had generalized seizure. (Figure 3)

Motor Manifestations of Seizures in the patients

In this study, majority (56.6%) patients had Tonic clonic seizures. (Table 2)

Patients who had seizures associated with fever

58% of patients studied had seizures associated with fever. (Figure 4)

Events during Seizure episode

In the study 92.0% of patients had Loss of Consciousness during seizure episode. (Table 3)

Post ictal phenomenon in seizure subjects

58.7% were awake at admission to hospital and 4% had Neurological Deficits. (Table 4)

Risk factors for seizures

8% had Family History of Seizures and 3.3% had History of Birth Asphyxia. (Figure 5)

Neurological manifestations in patients

4% had microcephaly, 4% had signs of UMN leison, 6.0% had signs of meningeal irritation. (Table 5)

Laboratory findings in patients

In the study 3.3% showed malarial parasite in peripheral smear, 0.7% had hyponatremia, 4% had hypocalcemia. (Table 6)

CT scan findings in patients with seizures

25.6% showed signs of Neurocysticercosis (Parietal NCC was common site). (Figure 6)

MRI Diagnosis of patients with seizures

52% showed signs of Neurocysticercosis. (Figure 7)

EEG Findings in patients with seizures

22.2% were abnormal pattern. Generalized epileptiform activity was the most common pattern observed in EEG. (Figure 8)

Gender distribution of febrile seizure patients

Majority (79.3%) patients had simple febrile seizures with male predominance. (Figure 9)

Age distribution of febrile seizure patients

Mean age for febrile seizure was 24.05 months. (Table 7)

Temperature at admission in febrile seizure patient

Mean temperature on admission to hospital in febrile seizure patients was 101.43^oF. (Table 8)

Etiological Diagnosis of patients with Seizures

Infectious causes were the most common causes for seizures in the study (42.7%), followed by Febrile seizures (38.7%) and other causes (Metabolic and CP). In 8.7% Etiological diagnosis was not found. (Table 9)

ILAE Classification of seizure types in patients

Majority of patients (56.6%) had as Generalized Tonic-clonic seizures. (Table 10)

ILAE Classification of epilepsies and epileptic syndromes

Situation related seizures were the most common (86.6%) in the present study. (Table 11)

Association between Etiological Diagnosis and Types of seizures

Neurocysticercosis was the most common cause for focal seizures and Simple febrile seizure was the most common cause for generalized seizure. This observation was statistically significant. (Table 12)

Age wise distribution of etiology of seizures

There was significant association between etiological diagnosis and age. In < 1-year infants & 1 to 5 years, most common etiology was imple febrile seizures, 45.4% & 54.5% respectively. In 6 to 18 years age group, most common etiology was Neurocysticercosis (50.0%). (Table 13)

Anticonvulsants used in treatment of patients with Seizures

During the 1 year study period, total of 150 patients were analyzed. Distribution of cases according to age, was done into 3 groups - <1 year(infants),1-5 years(toddlers and preschool children),6-18 years(school going and adolescents). Out of 150 patients, 22 (14.7%) patients were between age group 1 month to <1 years age, 66 (44%) patients between 1 to 5 years and 62 (41.3%) patients were from age group 6 year to 18 years. Mean age of onset of seizure was 5.19 ± 4.37 years, Median age of onset of seizure was 4 years. Female patients were 77 (51.3%) and males were 73 (48.7%) out of 150 patients studied.

Out of 20 cases with epilepsy, 4 (20%) cases were born to consanguineously married couple. This indi-

cates that consanguinity has a role in occurrence of epilepsy. Family history of seizures was found in 12 (8%) out of 150 cases. History of seizure was present in siblings in 4 (33%) cases and in cousins in 8 (67%) cases out of 12. Majority of children 67 (44.7%) had single episode of convulsion and 31(20.7%) had multiple convulsions. In postictal state, consciousness was intact in 88 (58.7%) cases and 6(4%) were unresponsive. 87(58%) patients had fever in the present study population. These findings were consistent with study done by (Adhikari *et al.*, 2013) in Nepal, who found that 53.3% of cases with seizures had fever in their study population. (Adhikari *et al.*, 2013).

Neurocutaneous markers were found in 2 cases and dysmorphic facial features were found in 2 (1.3%) cases out of 150, which include low set ears and ear tag in both patients. In all of these cases no significant syndromic association was found on evaluation. On central nervous system examination of 150 cases studied, signs of UMN type of lesion were found in 6 (4%), clinical signs of meningitis in 9 (6.0%) (5 females and 4 males), scissoring sign in 2 (1.3%) and decerebrate posturing in 3 (2%) cases. All cases with meningitis were associated with high grade fever. Fundus examination was abnormal in 4 (2.6%) cases of 150 cases, which includes bilateral papilledema in all 4 cases. Abnormal blood reports were found in 33 (22%) cases of 150 patients. These cases include 9(27.2%) cases of meningitis, 8 (24.2%) cases of UTI, 5 (15.1%) cases of malaria, 2 (6%) cases (Widal test positive) of enteric fever. Out of 46 CSF samples analyzed, abnormal CSF findings were found in 21 (14%), which includes 2 (9.5%) cases of tuberculous meningitis, 7 (33.3%) cases of pyogenic meningitis and 12 (57.1%) cases of encephalitis. Thus, CSF analysis was helpful in diagnosing the above conditions.

Cranial CT scan was done in 82 cases, out of which 36 (43.9%) were abnormal. MRI brain was done in 25 (16.6%) cases out of 150. It was abnormal in 22 (88%) cases. The most common brain lesions detected were neurocysticercosis (NCC) in 13 (59.0%) cases. In our study 58 (38.6%) cases out of 150 had abnormal brain images. EEG was done in 72 cases, out of which 20 (27.7%) were abnormal. Most common EEG finding was generalised epileptiform activity, seen in 15 (75%) cases. Epileptiform foci localised to one or more hemisphere of brain was reported in 5 (25%) cases. Febrile seizures were seen in 58 (38.6%) of 150 cases, of which 27 (46.6%) were female and 31 (53.4%) were male patients. Maximum cases of febrile seizures were in second year of life. Minimum age was 6 months and maximum age was 5 years with mean age 24.05

months. In our study, the mean temperature at admission to hospital in febrile convulsion patients was $101.43^{\circ}F \pm 1.027^{\circ}F$. The minimum temperature noted was $100^{\circ}F$ and maximum temperature noted was $105^{\circ}F$. Maximum number of patients had temperature between 101 to $102^{\circ}F$ which includes 42(72.4%) cases out of 58.

Out of 58 cases of febrile convulsion, 46(79.3%) cases were simple febrile convulsions and 12 (20.6%) cases were complex febrile convulsions. This indicates that simple febrile convulsions were the most common type in present study. Among febrile seizure patients,45(77.5%) had upper respiratory tract infection (URTI),8 (13.7%) cases had urinary tract infection (UTI) ,4 cases (6.8%) had malaria and 2(3.4%) had enteric fever. UTI was more common in female children. Out of 137 cases in which etiology was identified, upper respiratory tract infection (URTI) was most common infection present in 45 (32.8%) cases. In URTI, there was sudden rise in temperature causing febrile seizure mostly simple febrile seizures.

Pyogenic meningitis was one of the infectious causes, which was present in 7 (5.1%) cases. These findings were consistent with study by (Joffe et al., 1983), who found that pyogenic meningitis was present in 4.56% of study group. (Joffe et al., 1983) Among the Metabolic causes, hypocalcemia was the leading cause seen in 6(4.3%) cases. Hypocalcemia lead to acute symptomatic seizures, which includes 4 cases from age less than 1 year and 2 cases from 1-5 years of age. Mean age of patients with hypo calcemic seizures was 10.32 months \pm 4.84 months (minimum age 4.07 months and maximum age 18.23 months). These findings, were consistent with the study conducted by (Feyzullah, 2008) found that hypocalcemic convulsions were occurring with mean age 6.3 months \pm 5.9 months. (Feyzullah, 2008)

Cerebral palsy (CP) was seen in 2.6%. In MRI brain, 2 (33.3%) patients had periventricular leucomalacia (PVL). All cases of CP had symptomatic generalized epilepsy and mental retardation

ILAE Classification by seizure type was done in 150 cases, most common type was generalized which includes generalized tonic clonic (GTC) in 85 (56.6%) cases (39 females and 46 males), generalized tonic (GT) in 25 (16.6%) cases. Partial seizures were seen in 40(26.6%) of 150 cases, out of which 12 (30%) cases were simple partial seizures and 28 (70%) were complex partial seizure (CPS). In a study conducted by (Adhikari *et al.*, 2013), they found that partial seizures occurred in 19.7% cases. (Adhikari *et al.*, 2013) In a study done by (Taheri *et al.*, 2009),

partial seizure type was found in 22% cases. (Taheri *et al.*, 2009)

Out of 130 cases of situation related seizures, febrile seizures were present in 58 (44.6%), acute symptomatic seizures in 67(51.6%) and status epilepticus in 5 (3.8%). Of 20 cases with epilepsy, generalized epilepsies were found in 15 (75%) cases.9 (45%) cases were idiopathic generalized epilepsies, 6 (30%) cases were symptomatic generalized epilepsies, localisation related epilepsies (LREs) were found in 5 (25%) of which, symptomatic LREs were present in 2 (40%) cases and idiopathic LREs in 3 (60%) cases.

All these were more common in age group > 1 years. This is a statistically significant finding. (p=0.001). Anticonvulsant monotherapy was used in 77 (51.4%) cases and 4 (2.7%) required polytherapy to control seizures. Clobazam was used as a prophylaxis for febrile seizures in 58(38.6%) cases. Carbamazepine was used in 33(22%) cases and valproate in 22 (14.7%) cases out of 150. Intravenous Calcium Gluconate was given in 6 (4%) cases. (Table 14)

CONCLUSIONS

Febrile seizures were the most common cause of seizures below 5 years and neurocysticercosis in older children. Neuroimaging should be advised in all afebrile children for diagnosis of neurocysticercosis in places where neurocysticercosis is endemic. Children diagnosed with epilepsy require long term follow up studies including neuropsychologic studies. Further studies on large scale over longer duration should be carried out, to put forth the diagnostic guidelines and management plans based on clinical presentation and etiological causes in a specific age group.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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