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Research Article

The study of etiological profile in new onset seizures in Indian scenario

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ABSTRACT

Background: A seizure (Latin word which means "to take possession of") is a paroxysmal event due to abnormal excessive or synchronous neuronal activity in the brain. Seizure is a medical emergency and about 1 in 10 persons will experience a seizure in their lifetime. Etiological contribution to seizures in developing countries is different from developed countries. Epilepsies related to malaria, neuroinfections, tuberculosis, HIV, meningitis, trauma and perinatal difficulties more prevalent in India and other developing countries. Neurocysticercosis is the most common cause of seizures/epilepsy in the developing countries and designated as a "biological marker" of the social and economic development of a community. In India, Single Small Enhancing CT Lesions (SSECTL) being the most common radiological finding and dying cysticercus larva in histopathological studies. Aim: To study the etiological profile in new onset seizures.
Methods: This was an observational and prospective study. The present study enrolled 100 patients above 15 years of age with new onset seizures. All the patients and their relatives were interviewed regarding history and thorough clinical examination was done. Routine blood investigations, blood urea, serum creatinine, blood sugar, liver function tests, serum electrolyte were done. Special investigations like electroencephalography (EEG), CT scan brain, MRI, and lumbar puncture were done in selected cases.
Results: Out of 100 patients included in the study, neuroinfection is leading cause of seizure in 36%, Cerebrovascular accidents (25%) and metabolic in (12%). Majority of seizures in neuroinfections were due to neurocysticercosis in 15 patients (42%) followed by meningoencephalitis in 14 patients (38%). Among Cerebrovascular accidents, stroke accounted for 84% (21) (Infarct-12, Haemorrhage-9), followed by cerebral venous thrombosis 12% (3). Out of 12 patients with metabolic seizures, hypoglycaemia and hyponatremia constituted 33% each.
Conclusions: Etiological spectrum of seizures includes neuroinfection, CVA, tumour, metabolic, poisoning and alcohol withdrawal. Neuroinfection accounted for significant number of seizures in all the age groups. Neurocysticercosis is the most common etiology among neuroinfections. Cerebrovascular accidents common in 4th & 5th decades. Limitation: Patients <15 years with new onset seizures were not included in the study.

Keywords: Cerebral venous thrombosis, Cerebrovascular accidents, Electroencephalography (EEG), Lumbar puncture, Neurocysticercosis, Psychogenic seizures

INTRODUCTION

Seizures are common in the general population and about 1 in 10 people will experience a seizure in their lifetime.[1,2] Community-based surveys in India have shown epilepsy with incidence of 50 per 100000[3,4] and a prevalence of 5.59 per 1000.[5] A seizure[1] (Latin word which means "to take possession of") is a paroxysmal event due to abnormal excessive or synchronous neuronal activity in the brain. Epilepsy[1] refers to a clinical

phenomenon rather than a single disease entity which describes recurrent seizures. Auras[1] are subjective "internal" events that are not directly observed. Automatisms are involuntary, automatic behaviours such as chewing, lip smacking, swallowing, or "picking" movements of the hands. Seizures are a result of a shift in the normal balance of excitation and inhibition within the CNS.[1,6] Precipitating factors can be psychological, physical stress, sleep deprivation, sedative drugs, alcohol withdrawl or by repeated stimulation from sub convulsive electrical pulses known as "kindling phenomenon".[1]

Seizures are classified into partial and generalised seizures. Depending on the presence of cognitive impairment, partial seizures can be simple and complex. Partial seizure activity begins in a very discrete region of cortex and spread to neighbouring regions i.e. seizure initiation and a propagation phase. Sufficient activation and recruitment of neurons leads to loss of surrounding inhibition and propagation of seizure activity into contiguous areas. Partial seizures cause motor, sensory, autonomic or psychic symptoms without impairment of cognition. The phenomenon described by Hughlings Jackson and known as "Jacksonian march," represents the spread of seizure activity over a progressively larger region of motor cortex. Post epileptic paresis (Todd's paralysis)[6] evolves in minutes to hours. Partial seizures manifest as auras like paraesthesias, flashing lights, flushing, sweating and piloerection. Partial seizures arising from the temporal or frontal cortex may cause alterations in hearing, olfaction like unusual odors or psychic symptoms like sense of impending change, detachment, depersonalization, déjávu, or illusions like micropsia or macropsia. Complex partial seizures are accompanied by a transient impairment of consciousness and recovery occurs within seconds to an hour. Focal seizures can spread to involve both cerebral hemispheres and produce a generalized seizure. Epilepsia partialis continua[6] consists of repetitive focal muscle contractions of the fingers and corner of the mouth, persisting for days or weeks without loss of consciousness and is often refractory to medical therapy.

Generalized seizures arise at some point in the brain and rapidly engage neuronal networks in both cerebral hemispheres. Status epilepticus is defined as a seizure that is repeated frequently and recovery of consciousness between attacks does not occur. Generalized seizures can be a. Absence b. Tonic-clonic c. Atonic and d. Myoclonic. Typical absence seizures are characterized by sudden, brief lapses of consciousness without loss of postural control which lasts for only seconds with consciousness returning as suddenly as it was lost and there is no postictal confusion. Absence seizures are usually accompanied by subtle bilateral motor signs such as rapid blinking of the eyelids, chewing movements and clonic movements of the hands. The electrophysiologic hallmark of typical absence seizures is a generalized, symmetric, 3-Hz spike and wave discharge that begins and ends suddenly superimposed on a normal EEG.[6] Generalized tonic-clonic seizures are common in 10% of persons with epilepsy. The seizure usually begins abruptly without warning, although vague premonitory symptoms proceed seizure. The initial phase of the seizure is tonic contraction of muscles of expiration and larynx producing a loud moan or "ictal cry." Respirations are impaired, secretions pool in the oropharynx and cyanosis develops. Contraction of the jaw muscles causes biting of the tongue. A marked enhancement of sympathetic tone leads to increases in heart rate, blood pressure, and pupillary size. After 10-20 sec the tonic phase of the seizure typically evolves into the clonic phase produced by the superimposition of periods of muscle relaxation (<1 mt) on the tonic muscle contraction. Postictal phase is characterized by unresponsiveness, muscular flaccidity and excessive salivation that can cause stridorous breathing. Bladder or bowel incontinence may occur. Patients gradually regain consciousness over minutes to hours with postictal confusion. The EEG during the tonic phase of the seizure shows a progressive increase in generalized low-voltage fast activity, followed by high-amplitude, polyspike discharges. In the clonic phase, the high-amplitude activity is typically interrupted by slow waves to create a spike-and-wave pattern. The postictal EEG shows diffuse slowing that gradually recovers as the patient awakens.

Atonic seizures are characterized by sudden loss of postural muscle tone lasting 1-2 seconds. Consciousness is briefly impaired without postictal confusion. The EEG shows brief, generalized spike-and-wave discharges followed immediately by diffuse slow waves that correlate with the loss of muscle tone. Myoclonus is a sudden and brief muscle contraction that may involve one part of the body or the entire body. A normal physiologic form of myoclonus is the sudden jerking movement observed during sleep while pathologic myoclonus is most commonly seen with metabolic disorders, degenerative CNS diseases, or anoxic brain injury. The EEG shows bilaterally synchronous spike-and-wave discharges synchronized with the myoclonus.

Etiological contribution to seizures in developing countries is different from developed countries. The etiology of epilepsy varies with different age groups. Congenital and genetic causes are common in early childhood. In infancy metabolic and perinatal insults are the leading causes. In older children and young adults, inherited predisposition, alcohol, drug abuse and trauma are important causes. Major etiology of seizures in elderly being subdural haematoma, stroke, degenerative disorders like Alzheimer's disease, malignant gliomas and brain metastases. Seizures in a post-partum women should prompt consideration for cerebral venous thrombosis.[7] Epilepsies due to neuro-infections, malaria, tuberculosis, HIV, meningitis, trauma and perinatal difficulties more prevalent in India[5] and other developing countries.[6] Neurocysticercosis[8] is the single most common cause of seizures/epilepsy in the developing countries and designated as a "biological marker" of the social and

economic development of a community.[9] Single Small Enhancing CT Lesions (SSECTL) <25 mm in size being the most common radiological finding[10] with dying cysticercus larva seen in histopathological studies in India. In India, 40% of focal seizures are due to neurocysticercosis with higher prevalence in Punjab, Haryana, U.P. and Delhi. Seizures ceases to recur once the lesion resolves on CT.[11] Seizure is important neurological complication in bacterial and tuberculous meningitis in India. In one study 50% of the patient with CNS tuberculosis had seizures.[12] New onset seizures are found in 3-17% of all Human Immunodeficiency Virus (HIV) infected patients.[13]

Malignant tumors are more likely to occur after 30 years of age. Epilepsy is seen in 10% of patients with brain tumor. Tumor with seizures in childhood is uncommon because most childhood tumors arise in non-epileptogenic areas like cerebellum, brainstem and diencephalons. Seizure increase incidence and prevalence of cerebrovascular accidents after the age of 60 years. Seizures occur in 50-75% of patients with cerebral venous thrombosis during or after pregnancy. The risk of early post traumatic seizures is about 2.1%. 50 to 60% of patients who develop post traumatic epilepsy do so within 1 year of injury and approximately 85% by 2 years.

Metabolic abnormalities account for 9% of acute seizures. Metabolic abnormalities such as uremia, hyperglycemia, hypoglycemia, hyponatremia (<115 meq/L)[14] hypocalcemia, hypomagnesemia (0.8 meq/L) and withdrawal from sedative hypnotic agents /alcohol may induce seizures . Alcohol abuse may be precipitant of status epileptics in 9-25% of cases which may sometimes be the first-ever seizure type. Seizure risk is strongly dose dependent of alcohol.[15]

Hans Berger recorded the first human EEG on paper in 1924. Conventional EEG remains a major technique for investigating epilepsy which records changing voltage fields at the scalp surface that result from on-going synaptic activity in the underlying cortex as a continuous graph. Spontaneous brain wave activity is recorded for 20 minutes with an additional 10 minutes of sleep record. Sleep and sleep deprivation provoke abnormal focal or generalized alterations in EEG activity.

The availability of CT scan, MRI and CSF serology have made accurate diagnosis possible and changed the management of seizures from symptomatic lifelong therapy to etiological short duration therapy. Various newer imaging methods of identifying ictal foci are Positron Emission Tomography with flurodeoxy glucose (FDG-PET), Single Photon Emission Computed Tomography (SPECT) and cerebral angiography.

Management of seizure includes treatment of underlying etiology, avoidance of precipitating factors, suppression of recurrent seizures by prophylactic therapy and addressing psychological and social issues. Failure of therapy in a newly diagnosed epilepsy is mainly due to poor compliance. Epilepsy is resistant to medical therapy in 20% of patients. Seizure control is very good with high remission rates in the early years of treatment. About ¼th of patients do go on to develop chronic seizures. The first two years of treatment appeared to be crucial as the pattern of chronicity usually be established within this period. It is also apparent that treatment of chronic seizures is very difficult hence the need for early effective treatment for epilepsy should be stressed upon. Overall goal of treatment is to prevent seizures.

Aim of study: The aim is to study the etiological profile in new onset seizure.

METHODS

This is prospective and observational study. Ethical clearance was obtained from the institution. Informed consent was taken from the patients and their relatives in their own language before data were collected. 100 Patients above 15 years of age with new onset seizures were included in the present study. Patients with episodes like hyperventilation, TIA, psychogenic seizures, movement disorders like choreoathetosis and tic disorder were excluded from the study. Routine blood tests, blood glucose, serum electrolytes, serum calcium, lipid profile, V.D.R.L. test for syphilis, X-ray of the chest, thigh and skull were done. Special investigations like fundus examination, lumbar puncture, CT scan brain, MRI and Electroencephalography (EEG) were done whenever necessary.

RESULTS

The study included 100 patients with new onset seizures. The results of study are shown in tables & figures below.

Figure 1 below shows age distribution in the study. Out of 100 patients included in the study, 10% of the patients were in the age group of 15-19 years, 45% of patients were in the age group of 20-39 years, 33% of patients were in the age group of 40-59 years and 12% were in the age group of 60 years and above.

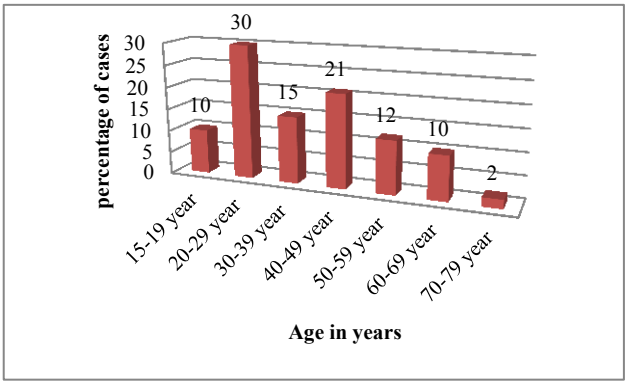

Figure 1: Showing age distribution in the study.

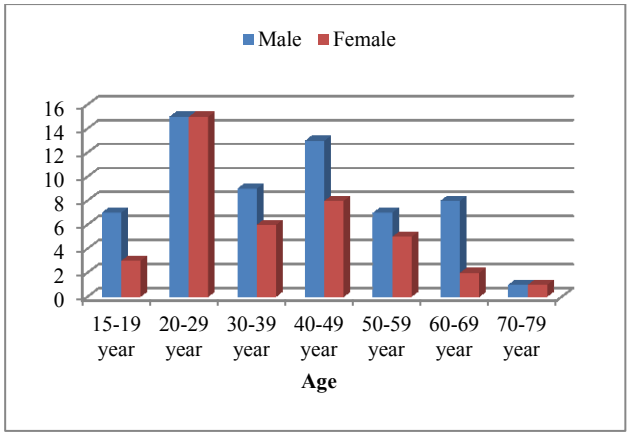

Figure 2: Showing sex distribution in relation to age.

Figure 2 above shows sex distribution in relation to age. Out 100 patients, 60 were males and 40 were females with peak incidence of males 15 patients (25%) and females 15 patients (37.5%) in the age group 20-29 years. Male to female ratio was 1.5:1.0

Table 1: Distribution of etiologies in patients with seizures.

Etiologies	n=100	%
Neuroinfection	36	36.0
Meningoencephalitis	14	14.0
Neurocysticercosis (NCC)	15	15.0
Cerebral malaria	6	6.0
Tuberculoma	1	1.0
Cerebrovascular accidents	25	25.0
Infarct	12	12.0
Haemorrhage	9	9.0
Cerebral venous thrombosis	3	3.0
SAH	1	1.0
Metabolic	12.0	12.0
Hypoglycaemia	4	4.0
Hyperglycaemia	2	2.0
Hyponatraemia	4	4.0
Hypocalcemia	2	2.0
Poisoning	**7**	7.0
Op compound	**5**	5.0
o-Tricyclic antidepressants	1	1.0
Rodenticide	1	1.0
Alcohol related	6	6.0
Idiopathic	6	6.0
Tumours	4	4.0
Secondaries	2	2.0
Meningioma	1	1.0
Acoustic neuroma	1	1.0
Eclampsia	4	4.0

Table 1 above shows various etiologies in patients with new onset seizures. Out of 100 patients, neuroinfection is leading cause of seizure which accounted for 36%, Cerebrovascular accidents (25%) and metabolic (12%) followed by poisoning (7%) alcohol related in 6, tumours in 4 and eclampsia in 4 patients. Among 36 patients with neuroinfection, majority of seizures were due to neurocysticercosis in 15 patients (42%) followed by meningoencephalitis in 14 (38%) and cerebral malaria in 6 (16%). Among 25 patients with cerebrovascular accidents, stroke accounted for 84% (21) (Infarct-12, Haemorrhage-9), followed by cerebral venous thrombosis 12% (3). Out of 12 patients with metabolic seizures, hypoglycaemia and hyponatremia constituted 33% (4) each. Out of 7 patients with poisonings, organophosphorus poisoning (OP Poisoning) accounted for 71%.

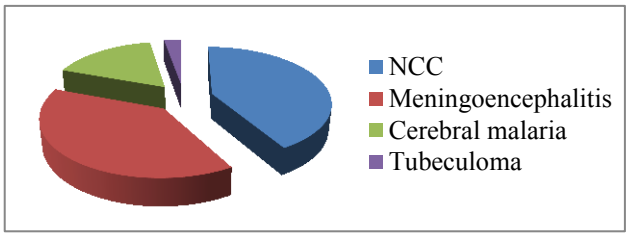

Figure 3: Showing various neuroinfections.

Figure 3 above shows various types of neuroinfections. Out of 100 patients, neuroinfection is leading cause of seizure which accounted for 36%. Among 36 patients with neuroinfection, majority of seizures were due to neurocysticercosis which accounted in 15 patients (42%) followed by meningoencephalitis in 14 (38%) and cerebral malaria in 6 (16%) and tubeculoma in 1 patient (3%).

Table 2: Various types of neurocysticercosis with seizures.

Neurocysticercosis	n=15	%
Solitary cystic granuloma	10	66
Calcified granuloma	4	27
MREL	1	7

Table 2 above shows various types of neurocysticercosis with seizures. Out of 15 patients with seizures due neurocysticercosis, solitary cystic granuloma was seen in 66% (10), calcified granulomas in 27% (4) of patients, and MREL (Multiple ring enhancing lesions) in 7% (1) of patients.

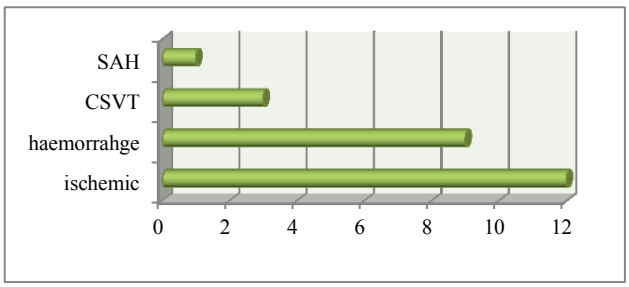

Figure 4: Showing types of cerebrovascular accident.

Figure 4 above shows types of cerebrovascular accidents (CVA) in new onset seizures. Out of 25 patients with CVA, 12 patients had infarct, haemorrhage in 9 patients, Cerebral Sinus Venous Thrombosis (CSVT) in 3 and SAH in one patient.

Figure 5 below shows different metabolic abnormalities in the study. Out of 12 patients with metabolic seizures, hypoglycaemia and hyponatremia constituted 33% (4) each and hyperglycemia and hypocalcemia in 2 patients each.

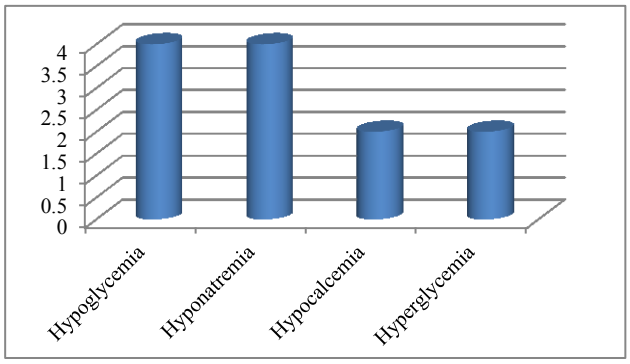

Figure 5: Showing various metabolic abnormalities.

Figure 6 below shows various etiologies in relation to sex. Out of 60 male patients, seizures in 23 patients were because of neuroinfection 38.3%, followed by CVA 21.7% (13), metabolic 13% (8), and alcohol related 10% (6). Seizures due to alcohol withdrawal occurred in all males (100%). Among 13 male patients with CVA majority of seizures were because of infarct 53.8% (7), followed by haemorrhage 38.4% (5). In females, out of 40 patients, majority of seizures were because of neuroinfections 32.5% (13), followed by CVA 30% (12), eclampsia 10% (4) and metabolic 10% (4).

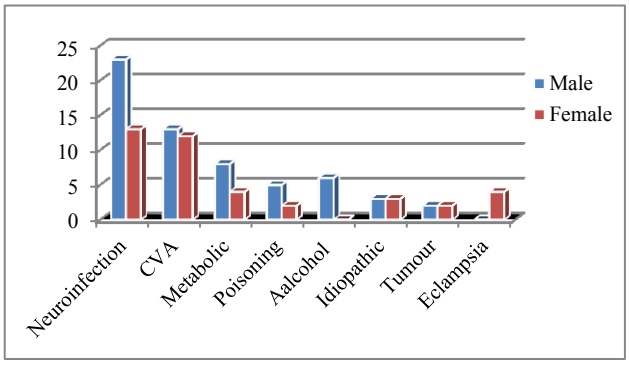

Figure 6: Etiologies in relation to sex distribution.

Table 3: Various etiologies in relation with age group.

Etiology	Age in years							Total
	<20	20-29	30-39	40-49	50-59	60-69	>70	
Neroinfection	5	12	10	8	1	-	-	36
CVA	-	3	2	5	9	4	2	
Infarct	-	-	2	3	5	2	-	
Haemorrhage	-	-	-	2	4	1	2	25
CVT	-	3	-	-	-	-	-	
SAH	-	-	-	-	-	1	-	
Metabolic	-	-	1	3	2	6		12
Poisoning	-	5	1	1	-	-	-	7
Alcohol related	1	2	-	3	-	-	-	6
Idiopathic	3	3	-	-	-	-	-	6
Tumour	-	2	1	1	-	-	-	4
Eclampsia	1	3	-	-	-	-	-	4
Total	10	30	15	21	12	10	2	100

Table 3 above shows various etiologies in relation with age group. Out of 10 patients in age group 15-20 years most common etiology is neuroinfection 50% (5), followed by idiopathic 30% (3). Most common etiology is neuroinfection 40% (12), followed by poisonings 16% (5) in 20-29 years age group. In 30-39 years, out of 15 patients common etiology is neuroinfection 66% (10), followed by CVA 13% (2). In 40-49 years, out of 21 patients, neuroinfection in 38% (8), followed by CVA 23% (5), metabolic 14% (3) and alcohol related 14% (3). CVA 75% (9) commonly seen in 50-59 years age group followed by metabolic cause 16.6% (2), and neuroinfection 8% (1). In 60-69 years age group, most common etiology is metabolic 60% (6) followed by CVA 40% (4) and in patients >70 years CVA was the only etiology seen. The major etiology for seizures seen in 2nd and 3rd decades was neuro infections upto 61%, metabolic seizures 50% were seen in 6th decade. CVA 52% seen in 5th and 6th decades, poisoning's 71% common in 2nd decade and 100% of CSVT occurred in 2nd decade constituting the major cause of stoke.

DISCUSSION

Seizures are common disorders found all over the world and are encountered frequently during medical practice. Etiological spectrum of seizures in developing countries is different from developed countries. Presently CNS infections like HIV (Human Immunodeficiency Virus), neurocysticercosis, malaria, bacterial and tuberculosis meningitis account for significant number of cases in developing countries. These etiologies vary from region to region with in India. The present study "Etiological profile of new onset seizures" was carried out to know various etiologies in adults of this region who presented to hospital attached to Siddhardha medical college, Vijayawada.

The present study included 100 patients with new onset seizures as per the criteria mentioned in the materials and methods. Etiological spectrum depends on age, sex, geography and medical setting. In the present study out of 100 patients, 10% of patients were in the age group of 15-19 years, 45% of patients were in the age group of 20-39 years, 33% of patients were in the age group of 40-59 years and 12% were in the age group of 60 years and above as shown in Figure 1 which correlated with study done by Sridharan R, Murthy BN.[3] Age specific prevalence rates of epilepsy in India were higher in the younger age group mostly in the first 3 decades as in a study by Sridharan R., Murthy BN study.[3] The major etiology for seizures seen in 2nd and 3rd decades was neuroinfections upto 61%, metabolic seizures 50% in 6th decade. CVA 52% in 5th and 6th decades, poisonings 71% common in 2nd decade and 100% of CSVT occurred in 2nd decade constituting the major cause of stoke as shown in Table 3.

In the present study out 100 patients, 60 were males and 40 were females, with male to female ratio of 1.5: 1.0 as per Fig: 2 which correlated with study done by Sridharan R, Murthy BN.[3] In the present study various etiologies in relation to sex showed 38.3% of neuroinfection in males and 32.5% in females, CVA in males (21.7%) & 30% in females, metabolic causes 13% in males & 10% in females as shown in Figure 6. The results in our study were comparable to the observations of Sridharan R, Murthy BN study[3] relation to age and sex prevalence.

In present study out of 100 patients, neuroinfection is leading cause of seizure, which accounted for 36%, cerebrovascular accidents (25%) and metabolic (12%) followed by poisoning (7%) alcohol related in 6, tumours in 4 patients and eclampsia in 4 patients as shown in Table:1. Out of 36 patients with neuroinfection, majority of seizures were due to neurocysticercosis in 15 patients (42%) followed by meningoencephalitis in 14 (38%) and cerebral malaria in 6 (16%) as per Figure 3. Out of 15 patients with seizures due neurocysticercosis, solitary cystic granuloma was seen in 66% (10), calcified granulomas in 27% (4) of patients, and MREL (Multiple ring enhancing lesions) in 7 % (1) of patients as shown in Table 2: The different studies have shown that neuroinfections accounted for 2% of patients in Sander et al. study, 15% in Hauser et al., 77% in Murthy JMK and Ravi Y[16] study and 32% in a study by Narayan JT and Murthy JMK.[17] In the present study neuroinfection in 36% patients was the most common etiology and the results were comparable to the Indian studies.[16,17]

Among 25 patients with cerebrovascular accidents, stroke accounted for 84% (21) (Infarct-12, Haemorrhage-9), followed by cerebral venous thrombosis 12% (3) as shown in Table 1 & Figure 4. CVA occurred in 15% of the patients in Sander et al.[18] study, 18% in Hauser et al, 14% in study by Murthy JMK and Ravi Y[16] and 21% in a study by Narayan JT and Murthy JMK.[17] In this study CVA occurred in 25% and the results were comparable to the Indian studies.[16,17] Seizures due to Cerebro Venous Thrombosis (CVT) was reported in 3% of patients in this study and when compared with Narayan JT and Murthy JMK[17] study similar results were seen.

Out of 12 patients with metabolic seizures, hypoglycaemia and hyponatremia constituted 33% (4) each and hyperglycemia and hypocalcemia in 2 patients each as shown in Figure 5. In this study alcohol related seizures occurred in 6% of patients and these results were comparable with studies as 9% of the patients in Sander[18] et al. study, 11% in Hauser et al, and 9% in Narayan JT and Murthy JMK.[17] The results of alcohol realted seizure rates in the present study were comparable to Indian studies.

CONCLUSION

Seizure being a medical emergency, its etiological determination is quite important in expediting the management and helping in the prevention of seizures. Etiological spectrums of seizures vary from region to region which includes neuroinfection, CVA, tumour, metabolic, poisoning and alcohol withdrawal. Neuroinfection and cerebrovascular accidents accounted for significant number of seizures in all the age groups. Neurocysticercosis is most common etiology among neuroinfections in new onset seizures. Management of seizure is always multi modal which constitutes treatment of underlying etiology, avoidance of precipitating factors, suppression of recurrent seizures by prophylactic therapy and addressing a variety of psychological and social issues.

Limitations of the study

Patients <15 years with new onset seizures were not included in the study.

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Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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