

Original Research Article

Clinical and etiological profile of epilepsy: a hospital based study from rural population of North India.

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Abstract: Objectives: To determine the clinical and etiological profile of epilepsy along with the distribution of various epilepsies and epileptic syndromes in the people with epilepsy (PWE) in view of limited published data from rural population of North India. **Methods:** We conducted a cross sectional, hospital based study among 590 patients. The diagnosis of epilepsy and epileptic syndromes was established under the guidelines of the International League Against Epilepsy 2010. **Results:** Of 590 patients, 388 (65.8 %) were male. Their age ranged from 6 months to 93 years. Mean age was 27.19±17.5 years. Age of onset of epilepsy was most frequent in second and third decade .79.1 % had only one type of seizure and focal seizure (61.9%) being the commonest type. Most cases (50.2 %) had underlying structural - metabolic causes. A specific electroclinical syndrome diagnosis could be made in 27.6 % and 7% had a distinctive constellation .The leading cause of epilepsy in pediatric patients was pre-/perinatal insults; in adults and elderly group it was presumed genetic (epilepsy with generalized tonic- clonic seizures alone) and stroke respectively. **Conclusion:** The most common etiologies of epilepsy in our setup were central nervous system (CNS) infections, presumed genetic and pre-/perinatal insults. Sincere efforts must be made to prevent the occurrence of epilepsy with prevention and effective treatment of infections like neurocysticercosis and tuberculosis along with up gradation of the pre/ perinatal care.

Keywords: Epilepsy; Etiology; Classification; Seizures.

INTRODUCTION

Epilepsy is one of the most widely recognized chronic neurological disorders. Worldwide, around 70 million individuals are supposed to be suffering from epilepsy and among them about 90% reside in developing nations (Ngugi, A. K. *et al.*, 2010). In addition, the relatives and companions of people with epilepsy (PWE) also bear the burden of this condition; more than 500 million people are indirectly affected by epilepsy (Kale, R. 2002). In this way, epilepsy imposes a large economic burden on global health care systems and is a noteworthy public health problem in low- and middle-income countries (WHO. 2005). It is estimated that there are more than 12 million PWE in India. The knowledge of clinical profile of epilepsy patients from various human populaces is essential to widen the accessible information and to give standard baseline data.

underdeveloped states of India and provide accommodation to around 16.50% Indian populace, further most population reside in rural and remote area with limited medical resources .Despite of all these alarming facts ,no such study has been conducted so far particularly from our rural area. Furthermore, in developing countries, hospital-based studies are rare, and the present study will fill a void in literature. Given this etiological distribution, prevention strategies tailored to different age groups may be an efficient way for reducing the occurrence of seizures.

The present study was aimed to determine the clinical and etiological profile of epilepsy along with the distribution of various epilepsies and epileptic syndromes in PWE.

MATERIAL AND METHODS

Uttar Pradesh which is one of the largest and

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We performed a Cross sectional, hospital based study, from June 2017 to March 2018. Our institute is located in a rural and remote area of Etawah district; with a catchment area of 2311 km.² It caters to the population of approx.6.5 million people of surrounding 11 districts.

All the patients who experienced epilepsy, admitted in indoor department or outpatient clinic were recruited during the study phase after obtaining their informed consent and approval from the institutional ethical Committee.

Inclusion Criteria:

- All the people with epilepsy attending the neurology department.

Exclusion Criteria:

- Patients with neonatal seizures.
- Patients with non epileptic events, isolated unprovoked seizure, acute symptomatic seizures and those who had seizures resulting from special pathologic conditions (e.g. febrile convulsions).

The diagnosis of epilepsy and epileptic syndrome was established under the guidelines of the International League against Epilepsy 2010 (Berg, A. T. *et al.*, 2010). Epilepsy was defined as two unprovoked seizures occurring at least 24 h apart (Commission on Epidemiology and Prognosis International League against Epilepsy1993).

932 patients having epileptic seizures and epilepsy were evaluated in our hospital during this period. We exclude acute symptomatic seizures cases and isolated unprovoked seizure (342) remaining 590 patients fulfilled the inclusion criteria.

The information retrieved included patient's age, gender, religion, education, employment: Employed, self-employed (farmer /shopkeeper) or unemployed (never employed, student and homemaker) address, family history, birth history, perinatal insults, history of febrile seizures. Per capita income was calculated by using BG Prasad socioeconomic classification 2016 (Khairnar, M.R. *et al.*, 2016).

For grouping syndromes age at onset was categories into infant (<1 year), child (1–12 years), adolescent (12–18 years), and adult (>18 years) and elderly above 60 years.

Details of seizures such as age of onset, frequency of seizures (Daily- approximately 1 or more seizures in a day, Weekly -at least one seizure/ week but less than 5/ week, Monthly- 1-8 seizures/ month, annual 1-2 seizures/ year, Sporadic-one seizure in two years), semiology of seizures, cause of epilepsy, history of status, history of febrile seizures, history of antiepileptic drug, neurological findings were recorded by preformed questionnaires.

All the patients who fulfilled the inclusion criteria were subjected to routine EEG (electroencephalogram). Local or generalized slow waves in the EEG recording were considered as non-specific abnormalities, while local or generalized paroxysms sharp waves, spike waves; sharp and slow waves, spike and slow waves were teemed as epileptiform discharges.

All the patients underwent brain imaging in the form of Magnetic resonance imaging (MRI) of brain/ computerized tomography (CT) scan of the brain (plain scan in all patients and contrast-enhanced CT whenever considered necessary) based on clinical indications and affordability.

Patients who had characteristic brain lesion in imaging and/or metabolic abnormality were classified under "epilepsies attributed to structural-metabolic cause." For those whose epilepsy could not be classified into any of the electroclinical syndromes or distinctive constellations, were classified as epilepsy with unknown cause.

Statistical Analysis:

The data collected was encoded and entered in MS Excel and IBM SPSS Version 23. Results were represented in graphs and tables. Data were expressed as percentage, mean, median, and standard deviation & Interquartile range.

RESULTS

Five hundred and ninety eligible patients were included in the study; among them 388 (65.8 %) were male. Their age ranged from 6 months to 93 years. Mean age was 27.19±17.5 years. Total pediatric population (below 12 years) was 99 (16.8 %), adults were 447 (75.8%) and elderly (> 60 years) were 44(7.4%). Majority of patients were Hindu (93%). 67% of patients belong to lower socio economical status (class V), 20% belongs to middle socio economical status (class III) and 10 % belong to lower middle class (class IV). Majority of them were self employed 73.5 %. 40% had education up to primary class, 17% were illiterate and only 23 % had education up to college.

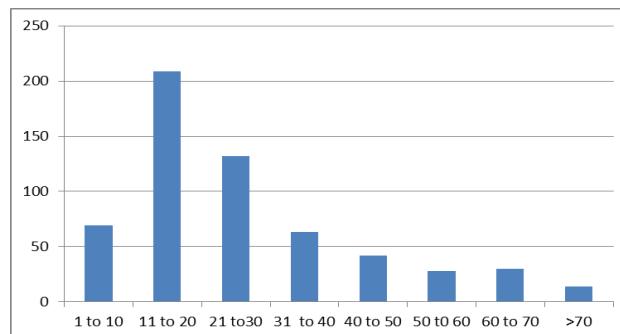


Fig 1: Age wise distribution of study subjects

Age of onset of epilepsy was most frequent in second (35.4%) and third decade (22.3%) of life. (Fig 1) 18 % patients suffered from at least one episode of status epilepticus. History of febrile seizures was present in only 3% of patients. Positive family history of epilepsy was present in 10% of cases. Most common trigger was stress in 62% followed by sleep deprivation in 38.5 % other triggers were emotional stress and

watching TV. Frequency of seizures is mostly monthly followed by annual and sporadic.

Majority of the patients were on monotherapy 60%. The MRI of brain was carried out in 450 patients and was abnormal in 280(62.2%). Only computerized tomography (CT) scan of the brain was done over 140 cases and was abnormal in 72 (51.4%). The electroencephalography recorded in 520 (88.1%) cases, showed epileptiform discharges in 312 cases.

The seizure characteristic of patients enrolled in the study is shown in Table 1 and Figure 2.

Table 1: The seizure characteristic of patients enrolled in the study

Age of seizure onset	Infancy	31	5.5
	Childhood	199	34
	Adolescent	141	23.5
	Adults	181	30.5
	Elderly	38	6.5
Frequency of seizures	Daily	45	7.5
	Weekly	68	11.5
	Monthly	170	29
	Annual	149	25.2
	Sporadic	158	26.8
History of status epilepticus	Yes	105	18
	No	485	82
History of febrile seizures	Yes	17	3
	No	573	97
Triggers for epilepsy	Stress situation	123	62
	Menstruation cycle	2	1
	Exertion(physical/mental)	8	4
	Sleep deprivation	76	38.5
	Emotional stress	36	18
	Watching TV	36	18
	Alcohol	8	4
Family history	First degree relatives	45	7.6
	Second degree relatives	12	2
	Other	2	0.4
	None	531	90
Drug history	Monotherapy	353	60
	Polytherapy	237	40
EEG (n=520)	Normal	208	40
	Abnormal	312	60
MRI brain (n= 450)	Normal	170	37.7
	Abnormal	280	62.2
CT brain only (n= 140)	Normal	68	48.6
	Abnormal	72	51.4

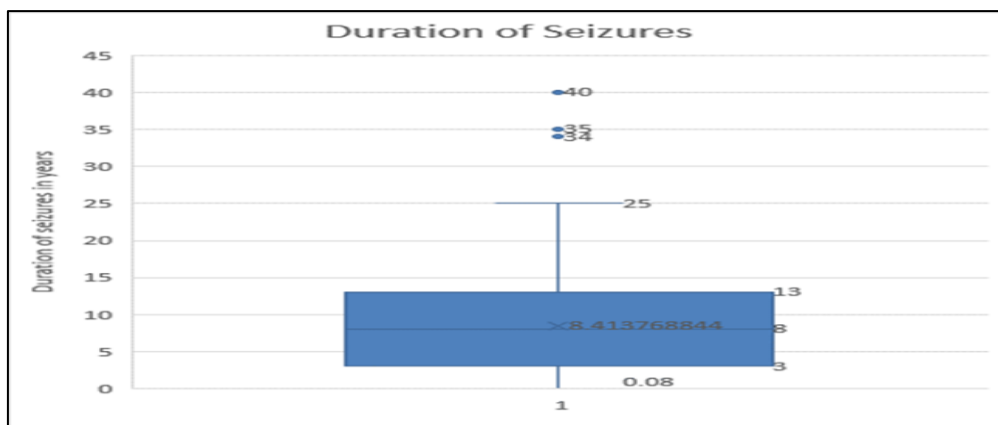


Fig. 2 Duration of epilepsy in years

Table 2: Distribution according to Type of Seizures

Type of seizures	Patients with 1 type of seizures (N=466) 79.0%		Patients with multiple seizures (N=124) 21.0 %
	n	%	n
Generalized seizures	178	38.2	134
	Tonic-clonic	148	64
	Absence	7	10
	Tonic	19	6
	Atonic	0	3
	Myoclonic	2	52
	Myoclonic atonic	2	1
Focal seizures	283	60.7	121
	Focal motor	4	9
	Focal motor with dyscognitive features	83	62
	Focal with Bilateral Convulsive seizures	196	50
Epileptic spasms	5	1	1

Of 590 patients, 466 (79.0 %) had only one type of seizure. Among them the commonest seizure type was focal seizures in 283 (60.7%), including focal seizures evolving to bilateral convulsive seizures in 196 (42.0%), focal motor seizures with dyscognitive features in 83 (17.8%) and focal motor seizures in 4(8%). The second common seizure type was generalized seizures in 178(38.2%) in which

generalized tonic-clonic seizures were in 148 (32.4 %) cases and generalized tonic seizures in 19 (4.1%) cases. 124(21.0%) patients had multiple seizure types, the common seizure types were generalized tonic-clonic, focal with dyscognitive features and myoclonic. Most common combination was generalized tonic-clonic and myoclonic seizures (Table 2).

Table 3: Distribution of various epilepsies in ILAE 2010 classification

Electroclinical syndromes	162 n	27.5 %
West syndrome	6	1
Early-onset childhood occipital epilepsy	1	0.1
Epilepsy with myoclonic atonic seizures	3	0.5
Childhood absence epilepsy	7	1.1
Lennox-Gastaut syndrome	1	0.1
LKS-CSWS	1	0.1
Juvenile absence epilepsy	2	0.3
Juvenile myoclonic epilepsy	41	7
Epilepsy with generalized tonic clonic seizures alone	95	16.1
Progressive myoclonic epilepsy	5	.8
Distinctive constellations	42	7
Mesial temporal lobe epilepsy with hippocampal sclerosis	40	6.8
Rasmussen syndrome	1	.1
Hemiconvulsion-hemiplegia epilepsy syndrome	1	.1
Structural-metabolic causes	296	50.2
Malformations of cortical development	20	3.4
Neurocutaneous syndromes	1	.1
Bain Tumors	10	1.7
Intracranial infections	101	17.1
Trauma	53	9
Angioma	1	.1
Pre-/perinatal insults	61	10.3
Stroke	49	8.3
Epilepsy of unknown causes	90	15.2

Distribution of various epilepsies in ILAE 2010 is shown in Table 3. A specific electroclinical syndrome diagnosis could be made in 27.6% (162/590).The five most common electroclinical

syndromes were epilepsy with generalized tonic clonic seizures alone in 95(16.1 %) ,juvenile myoclonic epilepsy in 41 (7%), childhood absence epilepsy 7(1.2 %), west syndrome in 6(1%), progressive myoclonic

epilepsy 5(.8%). Distinctive constellations were relatively uncommon and constituted only 7.0% (42/590) cases. 50.2% of the cases had underlying structural -metabolic causes. Among them important causes were intracranial infections 101(17.1 %) (Post encephalitic sequale 35 + calcified lesions 66), pre-/perinatal insults 61 (10.3%), trauma 53 (9%), stroke 49

(8.3%), malformation of cortical development 20 (3.4 %). Four patients had dual pathology (three patients had JME with single calcified lesion; one patient had mesial temporal lobe epilepsy with calcified lesion). However, 15.2 % of our cases were classified as having epilepsies of unknown cause.

Table 4: The first three leading causes of CSE in each specific age group

Age group (n, %)	The first n (%)	The second n (%)	The third n (%)
<12 years 99 (16.8)	Pre-/perinatal insults - 26(26.6%)	Epilepsy of unknown cause – 22(22.2%)	Epilepsy with GTC alone-10(10.1%)
12-60 years 447(75.8)	Epilepsy with GTC alone-84(18.8%)	Epilepsy of unknown cause – 63(14.1%)	Intracranial infections -56(12.5%)
>60 years 44(7.4)	Stroke- 26(59%)	Trauma- 6(13.6%)	Epilepsy of unknown cause-5(11%)

Table: 5 Percentage distributions of patients in ILAE 2010 classification categories in various studies

Authors	Type of study	Number of patients	Electroclinical syndromes	Distinctive constellations	Structural-metabolic causes	Epilepsy of unknown causes
Uttam <i>et al.</i> , 2013	Hospital based All Age	500	19.6	12.6	51.8	16
Khoo <i>et al.</i> , 2012	Hospital based Children	527	27.5	2.1	46.9	23.5
Syvetsen <i>et al.</i> , 2015	Population based	1771	20.3	–	43.3	36.4
Present study	Hospital based All age	590	27.6	7	50.2	15.2

The different age groups had different epilepsy etiologies. The leading cause of epilepsy in pediatric patients was pre-/perinatal insults in 26.3 % cases; among the adult group was epilepsy with generalized tonic clonic seizures alone in 18.8 %. Whereas stroke was the leading cause among elderly patients (Table 4).The most common causes of epilepsy in our setup were central nervous system (CNS) infection, epilepsy with generalized tonic clonic seizures alone and pre-/perinatal insults.

DISCUSSION

The fact that the prevalence of epilepsy in rural and underserved areas is twice where health care facilities are already lacking clearly signifies the urgent need to strengthen epilepsy services in these areas. However, there are dearth of literature on epidemiology and etiology of epilepsy from rural area of developing countries particularly from our region.

In our study commonest seizure type was focal seizures in 60.7% cases. Most of the hospital-based studies from India have recorded a higher frequency for partial epilepsies: 57 and 80% (Mani, K.S., & Rangan, G. 1990; Joshi, V. *et al.*, 1977; Murthy, J.M.K. *et al.*, 1998). While the community-based studies recorded a higher frequency for generalized seizures ranging from 79 to 54. 5% (Mani, K.S. *et al.*, 1998; Koul, R. *et al.*, 1988; Satishchandra, P. *et al.*, 1996). This is in consistent with the findings from other developing countries (Danesi, M.A. 1985; Senanayake, N. 1993; Velez, A., & Cobos, J.E. 2006).

We found onset of epilepsy to be the most frequent in second decade and third decade. Previous studies also revealed that the onset of epilepsy most commonly occurred in the first 2 or 3rd decades of a patient's life. Mathai *et al.*, reported 80% of the patients had onset in the first 2 decades of life (Mathai, K.V. 1986), Kaul *et al.*, from rural Kashmir, found 91% of active epilepsy cases had onset of seizures before the age of 30 years (Koul, R. *et al.*, 1988). Various other studies from India also reported a higher prevalence during the 2nd decade (Mani, K.S. *et al.*, 1998; Bharucha, N.E. *et al.*, 1988; Banerjee, T.K. *et al.*, 2010) while a recent estimate from Raina *et al.*, have reported a higher prevalence in the 4th decade (Raina, S.K. *et al.*, 2011).

Similar to Hauser *et al.*, Mani *et al.*, and Banerjee *et al.*, from India also reported a bimodal incidence with peaks during early childhood and during 70s and 80s of life (Hauser, W.A. *et al.*, 1993; Mani, K.S. *et al.*, 1998; Banerjee, T.K. *et al.*, 2010) .The second peak in elderly was not found in our study. The majority of the elderly, especially in our rural setup, are poorly educated and living a neglected life without special care which might have lead to many seizures being unrecognized and untreated. Old people living in distant villages were not able to avail medical facilities due to lack of awareness and concern toward health and poor transport facilities in remote areas.

In our study we found majority (50.2 %) of cases had underlying structural -metabolic causes followed by electroclinical syndrome comparable to other studies (Table 5) (Khoo, T.B. 2010; Uttam, A. K. *et al.*, 2013; Syvertsen, M. *et al.*, 2015).

Age is an important factor in the distribution of etiologies, and the leading cause of epilepsy in different age groups. The common cause of epilepsy in pediatric patients was pre-/perinatal insults; in adults and elderly group it was epilepsy with generalized tonic-clonic seizures alone and stroke respectively. In the early pathogenesis of epilepsy a complex relations between genes and environment was found to be involved. Perinatal injury, newborn distress, head trauma, neonatal hypoglycemia and malnutrition were reported as significant risk factors of epilepsy in children in India (Attumalil, T.V. *et al.*, 2011; Udani, V. 2005). In the elderly population stroke is the most common cause of seizures (Luhdorf, K. *et al.*, 1986; Verma, A., & Kumar, A. 2017). The rate of seizures after stroke changes broadly in the literature (2.7–42.8%) because of diverse incorporation criteria, study outlines, and detection modes (Conrad, J. *et al.*, 2013).

Overall the most common causes of epilepsy in our group were CNS infection, presumed genetic (epilepsy with generalized tonic clonic seizures alone) and pre-/perinatal insults. Among the CNS infection post encephalitic sequale and calcified lesions were the most common causes. A hospital-based study from south India, among 1,117 patients' established CNS infections accounted for 17.4% of cases and focal calcified lesion accounted for 8 % of symptomatic localization-related epilepsies (Murthy, J.M.K. *et al.*, 1998). Another study from a tertiary care center in India, autopsied 100 cases of status epilepticus identified neuroinfections and stroke as important etiological factors (Sinha, S. *et al.*, 2010). Other studies from India also reported CNS infections and pre-/perinatal insults as most common cause of epilepsy (Uttam, A. K. *et al.*, 2013; Misra, U.K. *et al.*, 2008).

Despite noteworthy advances in prevention and control of communicable and infectious diseases in India, infections are still a most important cause. Thus, appropriate comprehension of the causes and risk factors of epilepsy are essential for successful management of epilepsy in India where majority of patients are inadequately treated or not treated at all.

Our study is limited by relatively small sample size. Comparison between different groups could not be possible. Despite of these constraints this report provides valuable data on clinical and etiological profile of epilepsy from a rural populace of a developing country which is underserved and already deprived of their basic needs.

CNS infection, pre-/perinatal insults are potentially preventable causes. Efforts should be made to prevent the occurrence of epilepsy with prevention and effective treatment of infections like neurocysticercosis and tuberculosis. Upgrading the pre/perinatal care by improving awareness and infrastructures seems to be highly effective. The present studies provide baseline data from rural population for future studies and may guide the development of strategies for managing epilepsy in developing countries.

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Conflict of Interest:

None of the authors has any conflict of interest to disclose.

Ethical Approval:

The study is in accordance with the ethical standards of the institution.

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines

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