



Seizures Scenario in a Tertiary Care Teaching Hospital in Odisha, India- A Retrospective Study

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Authors' contributions

This work was carried out in collaboration between all authors. Authors PSS, SK and SP did the study design and wrote the protocol for data collection. Authors AKS, BCSP and VNVPS did the primary data collection. Authors AKS, BCSP and MS did literature searches and analyses of study was by authors PSS and MS. All authors read and approved the final manuscript.

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ABSTRACT

Purpose: Seizures being one of the major causes of morbidity and mortality in many developing countries still the etiological profile is less documented in many regions. This retrospective study aimed to understand regionally identified etiologies of seizure in Odisha, an eastern coastal province of India.

Methods: Data was retrieved from medical records of seizure patients those who were admitted during between August 2012 to December 2014 in a university teaching hospital. Information about demographics, clinical presentations, imaging studies, and diagnoses were extracted manually from

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each of the case sheets for analysis.

Results: A total of 519 cases of seizures were admitted in various wards during the above period; a majority were male (63.2%). Presentation was more afebrile (62.04%) than febrile (37.96%), where either forms were predominantly found in children over adults ($p = <0.05$). Among cases with afebrile seizures, the recorded leading causes were hypertensive neuropathy (4.98%), metabolic encephalopathy (3.42%), viral encephalopathy (3.1%), neurocysticercosis (2.8%), and status epilepticus (6.21%). Among cases with febrile seizures, the major etiology was due to an infection (23.35%) where respiratory tract infection was the most common form.

Conclusion: This is the first ever report where etiological profile of febrile and afebrile forms of seizures are identified in Odisha where seizure is a continuing problem. Scenario at one hospital might be the tip of iceberg that tempts to explore the base by either prospective or record based multi-center studies to find more accurate regional burdens of seizure and its causes.

Keywords: Seizure; febrile seizure; afebrile seizure; neuropathy; encephalopathy; neurocysticercosis; medical record; Odisha.

1. INTRODUCTION

Seizures are symptoms of a brain malfunction, which happen because of sudden, abnormal electrical activity in the brain. Recurrent seizures are called epilepsy or seizure disorder, which is one of the most common neurological disorders affecting people of all age groups. According to WHO ~50 million people are affected by epilepsy worldwide and nearly 80% of them lives in low and middle income countries [1]. Majority of the global burden of epilepsy is contributed by the two most populous countries India and China [2]. Recent study suggested there are more than 12 million individuals in India lives with epilepsy, which contributes nearly one sixth of the global burden [3]. Usually the geographical variations are thought to be the determinants that influence the common causes in a particular region; several studies from India showed that prevalence rate varies at different times and places [4]. Mostly, central nervous system (CNS) infections are one of the major causes of acquired epilepsy and seizures in developing countries [5,6]. In cases of viral encephalitis, meningitis and neurocysticercosis (NCC) recent onset seizures are more commonly reported [7–9].

Seizures account for about 1% of all emergency visits and about 2% of visits in children emergency department as reported in a hospital based report from a developed country [10]. Seizures are the most common pediatric neurological disorder 4 to 10% of children suffers at least one episode of seizure in the first 16 year of life [11]. In most of the studies febrile seizures are more often seen in pediatric population specifically in the age group younger than 5 year [5,10]. However, there is probably a lack of data

on seizures scenario from any comprehensive countrywide study available from the developing world like India. There are only limited studies on cause and outcome of acute seizures in India [12,13].

There is a potential need to understand the patterns of seizures as well as its etiologies in a study population specifically at the tertiary care hospital level; thereby appropriate preventive and/or interventional measures could be implemented in accordance with the causative factors. However, there are probably a number of factors that limit any prospective study in a resource poor setting particularly in developing countries. Heavy patient load, funding limitations, unavailability of neuroimaging facilities, as well as patient unawareness are few noted reasons in most of the underdeveloped regions in India. In this study we therefore attempted to analyze the etiological spectrum and associated other clinical symptoms in patients with seizures, which was done retrospectively on the medical record data from a previously unexplored province in India.

2. MATERIALS AND METHODS

This was a retrospective hospital based study conducted in a University teaching hospital in the capital city of the state of Odisha (India). This study was approved by the Institutional Research Ethical committee of Kalinga Institute of Medical Sciences, KIIT University (Odisha, India). During the period from August 2012 to December 2014 a total of 519 patients who were admitted with major presenting complain of seizures were included in the study.

Cases were admitted in our hospital under different clinics viz., pediatrics, general medicine

& neurology, psychiatry, ENT, O&G, orthopedics, ophthalmology, and cardiology. The following information was obtained from the medical records of each patient age, sex, type of seizure, associated symptoms (fever, vomiting, cough, diarrhea, headache and other systematic complications) and residential location.

Records of cases with major presenting complain of seizures those were admitted into any of the above clinical departments were included in the study. Only cases with record of residing in Odisha state for more than one year were included. Exclusion criteria-records of cases with current address outside Odisha state were excluded. Outpatient cases without hospitalization were also excluded.

On the basis of types of seizures, patients were divided into two groups with and without fever. Patients with temperature more than or equal to 38°C were considered in Group 1 and patients with temperature less than 38°C were considered in Group 2. Seizures type classification, clinical manifestation and associated symptoms was as per the definitions proposed by International League Against Epilepsy (ILAE) and the International Bureau of Epilepsy (IBE) [14]. Febrile Seizure was defined by 1993 the international league against Epilepsy as, “an epileptic seizure occurring in childhood after one month of age, associated with febrile illness not caused by an infection of the CNS without previous neonatal seizure or previous unprovoked seizure, and not meeting criteria for other acute symptomatic seizure”.

Other etiologies including meningitis, encephalitis, NCC were diagnosed on the basis of recorded clinical and laboratory investigations and verified with standard references [15,16]. Additionally patients were divided into two age groups- pediatric (≤ 18 years) and adult (>18 years). Variables including age, sex, types of seizures associated symptoms, EEG findings, neuroimaging findings, and residential location were analyzed within the study population. These variables were also compared with children with different age groups. Data was extracted from medical records and entered in a MS-Excel data sheets. The statistical analysis was done using MedCalc statistical software freely available online (<https://www.medcalc.org/calc/>). Comparisons of proportions were calculated in order to analyze differences between sub-groups. The odds ratio (OR), z statistic, and 95% confidence interval parameters were calculated.

Test was found significant when P value was obtained to be <0.05 .

3. RESULTS

There were a total of 519 cases whose medical files were studied; all these cases of seizures were admitted in the different wards of Kalinga Institute of Medical Sciences Hospital in Odisha (India). Majority of the patients (60.88%) were admitted in the pediatric department followed by medicine & neurology (35.26%), and psychiatry (2.31%). Record showed 2 patients each from ENT, O&G, and orthopedics departments. There was one case each from ophthalmology and cardiology departments (Table 1). We observed that predominantly males (63.2%) were affected with seizures in comparison to females (36.8%) (Table 2).

There was a wide age range the minimum and maximum being 1 month and 84 years respectively. We divided the patient age groups as pediatric (≤ 18 years) and adults (>18 years) where the majority patients were under pediatrics age range (70.33%). The distributions of cases with seizures under different age ranges are presented in Table 3. Among under five children, majority (24.08%) were newborns within the age range 1 month to 23 months whereas 20.04% cases were between >2 to 5 years age. Data shows there were only 9 cases of age more than 70 years and out of them 2 were above more than 80 years.

Table 1. Cases of seizures admitted in different wards in the tertiary care hospital

Departments	Numbers (n=519)	Percentages
Pediatrics	316	60.88
General medicine & Neurology	183	35.26
Psychiatry	12	2.31
ENT	2	0.38
O&G	2	0.38
Orthopedics	2	0.38
Ophthalmology	1	0.19
Cardiology	1	0.19

Table 2. Gender-wise distribution of seizures cases

Gender	Number of subjects (n=519)	Percentage
Male	328	63.2
Female	191	36.8

The data extracted from the patient files revealed that majority of the patients with seizures admitted into our hospital were from Khurda district where the hospital is located and neighboring districts (Table 4). There were 26 cases where no information about the particular region in Odisha was indicated.

Table 3. Age group wise distribution of admitted cases with seizures

Age groups	Numbers (n=519)	Percentages
< 2 years	125	24.08
2-5 years	104	20.04
>5-18 years	136	26.2
Pediatrics total	365	70.33
>18-30 years	75	14.46
>30-50 years	39	7.52
>50-70 years	31	5.97
>70 years	9	1.73
Adults total	154	29.67

Table 4. District wise distribution of admitted patients with seizures

Districts	Numbers (n=519)	Percentages
Khurda	365	70.32
Puri	30	5.78
Dhenkanal	24	4.62
Cuttack	18	3.46
Keonjhar	13	2.50
Nayagarh	12	2.31
Angul	10	1.92
Balasore	4	0.77
Bhadrak	3	0.57
Jagatsinghpur	3	0.57
Balangir	2	0.38
Jajpur	2	0.38
Mayurbhanj	2	0.38
Sambalpur	2	0.38
Ganjam	1	0.19
Koraput	1	0.19
Sundargarh	1	0.19
NOT known*	26	5.00

* Of total 519 cases, medical record showed 26 cases to be from Odisha but no district information was available

On an overall basis there was a predominance of afebrile seizures (62.04%) over febrile seizures (37.96%) (Table 5). The details of the breakdown of the pediatric and adult age groups presenting with either febrile or afebrile seizures are shown in the Table 6.

Of 322 cases presenting with afebrile seizures 127 (39.44%) cases had a diagnosis as per the hospital record. No definite diagnosis was established in rest 195 of 322 (60.56%) cases. We observed status epilepticus (SE) recorded in 20 of 322 (6.21%) cases. Other major underlying conditions in a decreasing order were hypertensive neuropathy (stroke), metabolic encephalopathy, viral encephalitis, NCC, atrophy, congenital epilepsy (Table 7).

Table 5. Seizures cases presenting with or without signs of fever

Clinical categories	Number of subjects (n=519)	Percentage
Afebrile	322	62.04
Febrile	197	37.96

Non-epileptic attack disorder (NEAD) was recorded in 5 of 322 (1.55%) cases. Other than viral encephalitis and NCC, other infectious causes included tuberculoma, amebic encephalopathy, and *Angiostrongylus* brain infection. There was one case each diagnosed as meningoencephalitis, and post encephalitis seizures disorder. Other less common non-infectious cases included Diabetic peripheral neuropathy, hypoxic-ischemic encephalopathy, alcohol withdrawal syndrome, drug dependent pseudo seizure, h/o trauma, schizophrenia, ICSOL (unspecified calcified granulomas, and proencephalic cyst), cerebral palsy, and dapsone hypersensitivity syndrome.

Among the febrile cases, the majority (23.35%) was due to an infectious cause (Table 8). Among the infectious causes respiratory infections were recorded in 4.58% cases. Viral infection was recorded in 3.04% cases, which presented with fever and seizures. So also 1.52% cases having diagnosed with enteric fever. There was one case of pyrexia of unknown origin (PUO). Also one case of febrile seizure due to insect bites as in the record though no information about the insect was found.

When febrile vs. afebrile presentations of the cases with seizure were analyzed, a statistically significant association was found in case of pediatric subjects comparison to adults (*p value*<0.0001). However no statistical difference was detected when frequencies of presentations of febrile vs. afebrile seizures were analyzed in male and female patients (Table 9).

Table 6. Age group distribution of in-patients with seizures presenting with or without signs of fever

Age groups	Afebrile		Febrile	
	N=322	Percentage	N=197	Percentage
< 2 years	41	12.73	84	42.63
2-5 years	41	12.73	63	31.98
>5-18 years	113	35.1	23	11.68
Pediatrics total	195	60.56	170	86.29
>18-30 years	62	19.25	13	6.6
>30-50 years	33	10.25	6	3.05
>50-70 years	23	7.14	8	4.06
>70 years	9	2.8	0	0
Adults total	127	39.44	27	13.71

Table 7. Diagnostic profile of cases presenting with afebrile seizures

Diagnosis	Number (n=322)	Percentage
Epilepsy (Status epilepticus)	20	6.21
Hypertensive Neuropathy (Stroke)	16	4.98
Metabolic encephalopathy	11	3.42
Viral encephalitis	10	3.1
Neurocysticercosis	9	2.8
Atrophy	7	2.17
Congenital epilepsy	5	1.55
Diabetic peripheral neuropathy	5	1.55
Hypoxic-Ischemic Encephalopathy	5	1.55
Non-epileptic attack disorder	5	1.55
Alcohol withdrawal syndrome	4	1.24
Drug dependent pseudo seizure	4	1.24
Trauma	4	1.24
Meningoencephalitis	3	0.93
Post Encephalitis Seizures Disorder	3	0.93
Schizophrenia	3	0.93
Tuberculoma	3	0.93
Calcified granulomas (Unspecified)	2	0.63
Cerebral palsy	2	0.63
<i>Angiostrongylus</i> infection	1	0.31
Amoebic encephalopathy	1	0.31
Dapsone hypersensitivity syndrome	1	0.31
Proencephalic Cyst	1	0.31
Old case of Meningomyelocele	1	0.31
Snake bite	1	0.31
Undefined	195	60.56

4. DISCUSSION

The current retrospective study based on medical records provided the scenario of seizure cases in Odisha (India), which was never explored before. Thus the present data might aid in an appropriate disease management and/or preventive plan in future as applicable based on the major contributors recorded in this province which is the gateway to Eastern part of India. The data analysis revealed the highest incidences of seizures in

Khurda district of Odisha in which our hospital is located; however, patients with seizures were also originated from 16 other districts of this state.

In the present record based study, we found seizures incidences are higher in males than females. Also previous population-based epidemiological studies suggested the prevalence and incidence of seizures and epilepsy to be slightly higher in males than in females [17,18].

Table 8. Diagnostic profile of cases presenting with febrile seizures

Diagnosis	Number (n=197)	Percentage
URTI	16	8.12
Respiratory infection (Undefined)	9	4.58
Viral	6	3.04
Malaria	4	2.03
LRTI	4	2.03
UTI	4	2.03
Enteric fever	3	1.52
Total number of cases with an infectious cause	46	23.35
Atypical febrile seizure	4	2.03
Hypovolemic shock	1	0.51
Pyrexia of unknown origin (PUO)	1	0.51
Postencephalitic seizure disorder	1	0.51
Febrile seizure due to insect bite	1	0.51
Acute febrile illness with no established diagnosis	143	72.58

Table 9. Association of febrile and afebrile seizures with respect to age and sex

		Afebrile (n=322)	Febrile (n=197)	Odds ratio (95%-CI)
		Number (%)	Number (%)	z statistics P value
Age group	Paediatric	195 (60.56)	170 (86.29)	0.243 (0.153 to 0.387) z=5.967 p <0.0001*
	Adult	127 (39.44)	27 (13.71)	
Gender	Male	199 (61.81)	129 (65.48)	0.852 (0.589 to 1.234) z= 0.844 p= 0.3988
	Female	123 (38.19)	68 (34.52)	

* Statistically significant

Majority of patients with febrile seizures were children where we found more incidences in the age group <5 years in comparison to higher age group (5-18 years) children. Previous studies as reported elsewhere even showed higher frequencies of seizures in younger children than older ones [6,10]. Additionally we observed majorities of febrile seizures cases were recorded to affect the newborns among <5 years children.

We estimated afebrile seizures to be the predominant form over febrile seizures on an overall data analysis. We observed a majority of our patients with afebrile seizures were children. However previous studies from elsewhere reported that febrile seizures are the most common clinical form of seizures among children [5,10]. The higher incidences of seizures in children compared to adults were estimated to be statistically significant in both febrile and afebrile conditions.

A recent population based study of comorbidities on epilepsy addressing association with various

somatic, psychiatric and neurodevelopmental conditions with epilepsy [19]. We observed majority of cases were epileptic while some other underlying conditions were included viz., hypertensive neuropathy (stroke), metabolic encephalopathy, viral encephalitis, NCC, atrophy, and congenital epilepsy.

In new onset of seizures several hypertension has been implicated [19,20]. We observed 4.98% cases were associated with hypertensive neuropathy or stroke. Viral encephalitis was also strongly associated with seizures [21], In our study we found 3.1% cases associated with viral encephalitis those who presented with afebrile seizures.

NCC is one of the leading risk factor in *Taenia solium* endemic countries it is estimated that seizures occur nearly in 80% of people affected with NCC [22,23]. Similarly our study noted 2.8% of cases were associated with NCC. Though never extensively studied, however NCC has also been previously reported from Odisha either in form of case studies [24–26] or case series

[27]. Hence NCC could be considered as a differential particularly in children presenting with afebrile seizures especially with a radio-imaging supportive diagnosis in tropical developing countries or areas endemic for taeniasis/cysticercosis as recommended in a previous report [28].

Psychogenic nonepileptic seizures are episodes of abnormal experience and observable behavior that superficially resemble epileptic seizures [29]. Psychogenic seizure or non-epileptic seizure, or pseudo-seizure, are all described under the common terminology non-epileptic attack disorder (NEAD) [30]. A diagnosis of NEAD appeared to have no significant impact on health-related quality of life as reported elsewhere [31]. In our study, we found NEAD in 1.55% among the afebrile seizure cases. When the diagnosis is either never established or established with no known etiology, then the treatment management becomes difficult.

The comorbidity of diabetes and epilepsy was indicated in several studies [19,32]. We also found some of the cases of seizures (1.55%), which were associated with diabetes.

Alcoholism and drug abuse have been identified as common mental health problems in patients having epilepsy [33]. Some other studies have shown that alcohol withdrawal can also trigger the seizures onset in patients [34,35]. We also observed 1.24% cases those seem to be associated with alcohol withdrawal syndrome.

In the current retrospective study, among the cases, which presented with febrile seizures, the major etiology was due to an infectious cause. We found mostly febrile seizures, which seem to be associated with infectious disease viz., upper respiratory tract infection (URTI), viral infection, malaria, lower respiratory tract infection (LRTI), urinary tract infection (UTI) and enteric fever. The details of other causes contributing towards seizures such as, inborn errors of metabolism could not be specified due to lack of adequate information. Probably prospective studies are required to find out more details regarding the problem of multi-centric seizures in Odisha province.

SE is defined as seizures lasting for more than five minutes without regaining consciousness [36]. SE is a neurological emergency with significant morbidity and mortality [37]. Multiple SE events, ranging from two to six per patient

was reported previously in India [37]. We noticed SE could be established only in 6.21% cases that to be with afebrile seizures among our cases as per records. Previous study from India showed an acute symptomatic etiology in 58.6% of entire cohort (n=126) in a hospital based screening study [36]. In that study a significantly higher percentage of patients with refractory SE had an etiology of CNS infections than non-refractory SE group, and amongst the CNS infections, viral encephalitis was one of the major etiology. In our study among of cases with febrile seizures, only 3.04% had a diagnosis of viral infection. And no confirmed diagnosis was established in 143 cases of which 2 cases had SE (*data not shown*).

Seizures still remain a major public health problem although most of its underlying conditions are preventable and treatable. Usually seizure cases are predominantly observed in developing countries over the developed world that might be due to the low socioeconomic conditions, and large gaps in treatment availability to the community. Therefore socioeconomic disadvantage and health problems are common in people with epilepsy [32]. The socioeconomic inequity, huge treatment gap, and the poor epilepsy healthcare delivery system in India are some of the reasons are responsible for the large disease burden. However the present record based study could not provide detailed information on the epidemiological aspect of seizure distribution or so in the study region, which was beyond our scope. In the context of seizures, one recent study from India reported the treatment gap might also causes large disease burden in a population [4]. Hence it is essential to explore different seizures determinants in provinces where no or least information is available previously. Nevertheless we only realized that besides the epidemiological aspects, retrospective hospital record based studies are very crucial while addressing the problem of epilepsy in a particular region particularly identifying the etiologies and their incidences over a time period in a particular region.

5. CONCLUSION

This is the first ever report where the etiological profile of febrile as well as afebrile forms of seizures are identified in Odisha state that is a previously unexplored region of India where seizures is a continuing problem. Both febrile and afebrile seizures occurring predominantly in

pediatric age group over adults were found to be statistically significant. The information extracted from medical records documented at one hospital may be tip of the iceberg which tempts us to explore the base by further conducting multi-center studies either prospectively or by analyzing medical records for a larger patient population in order to establish a more accurate burden of different causes of seizures in this region. Also attention should be given on the preventable causes particularly in cases with recent onset seizures.

CONSENT

This was a retrospective study. However, at the time of admission into the hospital, all patients (or other approved parties) had declared no objection on sharing of clinical information for academic research and/or publication purpose.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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