

## Study of Patients with First unprovoked Seizure in the Eastern Part of Nepal

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### Abstract

#### Background

About 5-10% of the population get at least one seizure in their lifetime. Treatment is started in patients with first unprovoked seizure if the risk of seizure recurrence is predicted to be high. If patients with first seizure are not treated 40-50% of patients develop recurrence within 2 years of the initial seizure. Starting treatment may cause reduction in the risk of recurrence by almost one half. The aim of the study was to identify the factors causing recurrence in patients with first unprovoked seizure

#### Materials and methods

It is a prospective study conducted at Nobel Medical College from March 2015 to March 2019. Patients who presented to Nobel Medical College with first unprovoked seizure were enrolled in the study with follow up during the hospital visit.

#### Results

Eighty six patients participated in our study. Recurrence of seizure occurred in 21(24.4%) patients within the study period of 4 years. Abnormal Electroencephalography was significantly associated with recurrence of seizure in patients with first seizure. (P value<0.001) Neuroimaging abnormality was also associated with increased risk of seizure recurrence (P value<0.001). Starting an antiepileptic after first seizure reduced the risk of further seizure.

#### Conclusion

Recurrence of seizure was observed in almost a quarter of patients within the study period of four years. Recurrence risk was higher in those patients with abnormal EEG and in those patients with identified cause than those patients whose seizure was assumed to be idiopathic.

**Key words:** Seizure, Electroencephalography, epilepsy



### INTRODUCTION

Seizure is defined as transient occurrence of signs and /or symptoms due to abnormal excessive hypersynchronous neuronal activity in the brain. About 5% of the general

population develops at least one seizure in their lifetime. Epilepsy occurs in 1-2% population [1]. Previously Epilepsy was defined if a person had two or more episodes of unprovoked or reflex seizures which occurred more than 24 hours apart [2]. Reflex seizures are sensory evoked or stimulus sensitive seizures. New definition of epilepsy includes this presentation but it also includes patients who have one unprovoked or reflex seizure and has at least 60% probability of having another seizure in the following 10 years. Almost one third of patients with first seizure get a second attack of seizure [3, 4]. The recurrence risk in patients with first unprovoked seizure varies which may be due to variation in study design or difference in demographic profile. Thirty five percent of patients with a first unprovoked seizure develop a second attack of seizure in the next 3 to 5 years [5-7].

The common causes of seizure in the Nepalese population have been identified to be different from that in the western population.

This study was conducted in patients with first unprovoked seizure at a Tertiary care Hospital. The patients with first unprovoked seizure were followed up for a period of four years. The primary aim of the study was to identify the risk of recurrence in those patients taking note of the factors that increased the risk of having second seizure following a first unprovoked seizure.

### Materials and Methods

All the patients who presented to Nobel Medical College Neurology Department with history of first unprovoked seizure from March 2015 to March 2019 were included in the study. Those patients with acute symptomatic seizure were excluded from the study. Acute symptomatic seizure is the type of seizure which occurs with obvious precipitating factor for seizure like alcohol or drug withdrawal, hypoglycemia, acute brain trauma or acute infection. Information regarding age, sex, duration of seizure before coming to hospital and starting antiepileptic medication, status epilepticus, and family history of seizure, CT/MRI and electroencephalography finding were recorded. The patient's seizures were categorized by etiology [8] as idiopathic or remote symptomatic (seizure in patients with a history of CNS insult) such as head injury, stroke [9], CNS infection [10] or static encephalopathy from birth [11, 12]. During each visit of the patients they were asked if they had recurrence of their seizure. Patients who did not visit hospital were inquired about recurrence of the seizure through telephone.

The definition of single seizure included status epilepticus and multiple seizures within a day. Patients with acute symptomatic seizures were excluded from the study.

Patients who did not give informed consent and those patients with acute symptomatic seizure were excluded from the study.

Seizure was defined as unprovoked if it occurred without obvious precipitating factor for seizure like drugs, alcohol and hypoglycemia.

Either CT scan or MRI of the brain and Electroencephalography were done in all patients with first seizure.

Informed consent was obtained from all the patients who took part in the study.

Ethical clearance for the study was obtained from Institutional Review Board of Nobel Medical College.

Analysis of the data was done using SPSS software. If P value  $\leq 0.05$  the result was considered statistically significant.

## RESULT

Table 1: Baseline characteristics of the study population (n=86)

|  |               |
|--|---------------|
| Men  | 61(71%)       |
| Age of study patients                                      | 34 $\pm$ 16.7 |
| Seizure type   |               |
| Focal  | 21(24.4%)     |
| Generalized  | 65(75.6%)     |
| Age at first seizure                                       | 34 $\pm$ 17   |
| Duration of seizure before seeking medical help(In months) | 5 $\pm$ 4     |
| History of epilepsy in first degree family member          | 18(21%)       |
| Seizure recurrence   | 21(24.4%)     |
| No recurrence of seizure                                   | 65(75.6%)     |
| Abnormal EEG   | 36(42%)       |
| (CT or MRI)Abnormal  | 46(53.5%)     |
| Medication   |               |
| Started  | 70(81.4%)     |
| Not started  | 16(18.6%)     |

Most of the study population were male 61(71%).Most of the patients were young with mean age at seizure onset of 34.Generalised seizure was reported in 65(75.6%) patients while 21(24.4%) patients had focal seizure. Eighteen patients reported having family history of epilepsy in their first degree relative. Recurrence of seizure occurred in 21patients (24.4%) while 65patients (75.6%) were seizure free. Antiepileptic Medication was started in 70(81.4%) patients while in 16(18.6%) patients no drug was started. Electroencephalography was normal in 50(58%).However EEG was abnormal in 36(42%) of patients. Neuroimaging (CT/MRI) revealed the cause of seizure in 46(53.5%) patients.

Table 2: Age of study population (years)

| Age in years | Year      |
|--------------|-----------|
| $\leq 20$    | 20(23.2%) |
| 21-40        | 38(44%)   |
| 41-60        | 22(25.6)  |
| $\geq 60$    | 6(7%)     |

Most of our study patients were young .Only 6(7%) of our patients were older than 60 years.

Table 3: seizure duration before coming to hospital

| Seizure duration      | Number of patients |
|-----------------------|--------------------|
| $\leq 1$ month        | 65(75.4%)          |
| 1 month to < 6 months | 6(7%)              |
| > 6 months to< 1 year | 10(11.6%)          |
| > 1 year              | 5(5.8%)            |

Most of the patients (75.4%) came to hospital within a month of the onset of the first seizure. Few (5.8%) patients reported more than 1 year of onset of the seizure.

Table 4: Causes of first seizure

| CT/MRI finding                             | Number of patients |
|--|--------------------|
| Normal                                     | 40(46.5%)          |
| Neurocysticercosis and calcified granuloma | 25(29%)            |
| stroke                                     | 14(16.3%)          |
| Infection such as tuberculoma              | 2(2.3%)            |
| Brain tumor                                | 3(3.5%)            |
| Brain atrophy                              | 1(1.1%)            |
| Others                                     | 1(1.1%)            |

Most of our patients (46.5%) had normal neuroimaging findings.Neurocystercosis and calcified granuloma was the most common abnormality detected on brain imaging followed by stroke. Brain tumor, neuroinfection like tuberculoma and vascular malformation of the brain was detected in minority of patients presenting with first seizure.

Table 5: Reurrence of seizure (N=86)

| Antiepileptic medication(AED) | Total number of patients | Recurrence of seizure |
|-------------------------------|--------------------------|-----------------------|
| AED Started                   | 70                       | 15(21.4%)             |
| AED not started               | 16                       | 6(37.5%)              |

Antiepileptic medication was started in those patients in whom the risk of recurrence was predicted to be high. Those patients in whom antiepileptic medication was started had abnormal neuroimaging finding, abnormal physical examination, abnormal EEG, family history of epilepsy in the first degree relative, focal onset of seizure or presented in a state of status epilepticus. Recurrence of seizure was observed in 15(21.4%) of patients in whom antiepileptic medication was started whereas 6(37.5%) of patients in whom antiepileptic medication was not started had recurrence of seizure.

## DISCUSSION

Many studies have tried to evaluate the risk of recurrence following a first unprovoked seizure and also identify the factors which cause the seizure to recur. In our study we find risk for recurrence following a 1st seizure to be 24.4% at 4 years. Earlier studies have reported seizure recurrence following 1st seizure from 31% to 71% [13-19]. Such variation may be due to difference in study design, characteristics of population studied and mean duration of follow-up. Patients with mild form of seizure are less likely to come for medical help after the first occurrence.

In our study Neuroimaging was done in all patients with new onset seizure. As MRI is the neuroimaging modality of choice to identify the cause of seizure it was performed whenever patient could afford for it .CT Scan of the brain was done in the emergency room and when the patient could not afford for MRI or whenever there was contraindication to doing MRI because of metallic implant in the patient. The cause of seizure could be identified in 46.5% of patients based on neuroimaging (CT scan or MRI) scan of the brain or analysis of the cerebrospinal fluid when meningoencephalitis was suspected. Recurrence of seizure was found to be 60% in those patients with identified causes. This was much higher than

the patients with idiopathic seizure in whom the recurrence risk was 20% over the study period of 4 years. Calcified granuloma and neurocystercosis were found to be an important cause of first seizure. Finding abnormality on the neuroimaging had significant association with recurrence of the first seizure (P Value<0.001). Other causal factors for seizure which were found in our patients included stroke, vascular malformation, head trauma, brain tumors and degenerative brain disease like alzheimer's disease. We did not include patients with acute symptomatic seizure in our study which has been known to occur in close temporal relationship with an acute CNS insult. Acute symptomatic seizure are caused by factors like hypoglycemia, hyponatremia, hypocalcemia, hypomagnesemia, uremia and acute brain injury. Drug withdrawals especially alcohol, barbiturate and benzodiazepine are associated with withdrawal seizure. The use of illicit drugs like cocaine and amphetamine have been known to provoke seizure. Most of those factors do not lead to chronic epilepsy so they were excluded from our study.

In the present study electroencephalography was done in all the patients who presented with history suggestive of seizure. EEG is very helpful in the diagnosis, classification of seizure as focal or generalized and may even identify specific epileptic syndrome. Routine EEG records interictal epileptiform activity which includes spikes, sharp waves, spike and wave discharges and polyspike and wave discharges. An EEG in addition to its diagnostic role helps in determining prognosis following a first seizure. An abnormal EEG has been found to predict seizure recurrence. Abnormal Electroencephalography was also shown to have a significant association with seizure recurrence following first seizure (P value<0.001). In our study a generalized sharp wave pattern and a focal abnormality on EEG influenced recurrence rate. Abnormal EEG was shown to an important risk factor for seizure recurrence in the study done by Kim et al [20].

In our study antiepileptic medication was prescribed to those patients in whom risk of recurrence was assumed to be high. This included patients with abnormal neuroimaging finding; family history of epilepsy in first degree relative, focal onset of the seizure, abnormal physical examination and abnormal electroencephalography finding and patients who presented in status epilepticus. Abnormal neurological examination was associated with increased risk of seizure recurrence. Recurrence of seizure was observed in 21.4% of patients in whom antiepileptic medication was started. In those patients in whom antiepileptic medication was not started recurrence of seizure was observed in 37.5% of patients. Starting an antiepileptic medication after a first seizure was significantly associated with lowered risk of seizure recurrence (P Value <0.001). The earlier study The MESS trial which was done in patients with first seizure showed 30% reduction in the rate of recurrence in those patients in whom treatment was started as compared to patients in whom treatment was deferred until they had another seizure.[20]

In our study we did not find Todd's paralysis as a significant predictor of recurrence. History of status epilepticus was also not associated with increased the risk of recurrence. Similarly, age at seizure onset, sex of the study population did not predict seizure recurrence.

Family history of epilepsy was found in eighteen (21%) patients. Risk of seizure recurrence was higher in those patients who had a positive family history of epilepsy though it was not statically significant.

## CONCLUSION

About 5 -10% of the general population develop at least one seizure. Recurrence of the first seizure was observed in almost a quarter of patients within the study period of four years. Recurrence of first unprovoked seizure was observed to be higher in those patients in whom the cause of seizure could be identified and in those patients who had abnormal EEG. Similarly starting antiepileptic medication also decreased the risk of recurrence.

**Conflict of Interest:**None

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***Bottom Note:***

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