Risk of seizure recurrences after first unprovoked seizure during childhood

Mohamed S. Bessisso, *DCH, MD,* ***Mahmoud F. El Said,*** *MBBCH, CABP,* ***Naema A. Almula,*** *MBBCH, CABP,* ***Samer B. Azzam,*** *MBBCH, CABP,* ***Hani A. Sweid,*** *MD,* ***Mariam G. Al-Ali,*** *MBBCH, CABP.*

ABSTRACT

Objective: To find out incidence of seizure recurrence and its risk factor after the first unprovoked attack in children below 12 years of age.

Methods: A prospective study was carried out between 30th April 1996 - 1st May 1997 with the aim to find out the incidence of seizure recurrence and its risk factor after the first unprovoked attack in children below 12 years of age. All patients aged between 2 months - 12 years who presented with first unprovoked seizure at Hamad General Hospital, Doha, Qatar were studied. Seizures due to fever, metabolic causes, post-traumatic,and myoclonic seizures, infantile spasms, absence epilepsy and pseudo-seizures were excluded. All patients were followed for a minimum of one year. Possible risk factors such as sex, age, family history of epilepsy, delayed development, focal onset, clustered onset (two or more attacks within 24 hours), abnormal neurological findings and epileptogenic activity of electroencephalography were considered.

Results: There was a total of 33 patients (14 male and 19 female), 11 patients (33%) had recurrence. Significant risk factors for seizure recurrence were abnormal encephalograms (p=0.009), positive family history (p=0.03) and cluster onset (p=0.04). Presence of one or more risk factor (p=0.01) was significant. The other risk factors were not statistically significant.

Conclusion: The incidence of seizure recurrence is higher in-patients who have one or more risk factors. The patient and the family should be aware about possibility seizure recurrence and should be involved in the decision of starting treatment after first attack.

Keywords: Epilepsy, seizures, electroencephalogram, computer tomography, magnetic resonance image.

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Prevalence of non-febrile seizures in childhood ranges from 5.2 to 8.1 /1000.[1,2] While the risk of seizure recurrence ranges from 29%[3,4]to 81%[5]. Usually parents are concerned about the possibility of seizure recurrence, later development of epilepsy and optimal time of initiation of treatment. Knowledge of natural history of patients and risk factors are prerequisite for making decisions regarding long term treatment. Commencement of treatment after the first attack should be individualized. In some cases treatment is started after the first attack, if the parents are very anxious, or the patient had a significant neurologic disorder. Possibility of seizure recurrence and drug side effect should be clearly discussed with the patient and or the parents. This is particularly important because of intellectual and behavioral drug side effect.[6]

Methods. ***Subjects:*** Thirty three patients aged 2 month - 12 years who had a first unprovoked attack between the 30th April 1996 to 1st May 1997 were prospectively included. All provoked seizures (i.e. fever, central nervous system infection, trauma and metabolic causes), myoclonic seizures, infantile spasms and absence seizure were excluded.

From the Department of Pediatrics, Hamad General Hospital, Doha, Qatar.

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Address correspondence and reprint request to: Dr Mohammed A. Bessisso, Department of Pediatrics, Hamad General Hospital, PO Box 3050, Doha, Qatar. Fax. 00 974 439 2204. E-mail: mbessisso@hotmail.com

Table 1 - Risk factors for seizure recurrence in-patient with or without recurrence.

	Patients with recurrence	Patients without recurrence	Total (%)	p value
Male	5	9	14	0.06
Female	6	13	19	
Age:				
1-6 months	3	2	5 (15)	
6-24 months	2	8	10 (30)	
2-6 years	5	4	9 (27)	
7-12 years	1	8	9 (27)	
EEG abnormal	7	4	11 (33)	0.009
EEG normal	4	18	22 (67)	
Family history +ve	6	4	10 (30)	0.03
Family history -ve	5	17	23 (70)	
Type of seizure:				0.07
partial	4	4	8 (32)	
generalized	7	18	25 (68)	
Clustered seizure +ve	5	3	8 (32)	0.04
Clustered seizure -ve	6	19	25 (68)	
Abnormal development +ve	3	8	11 (33)	0.16
Abnormal development -ve	1	21	22 (67)	
Radiology: abnormal	2	1	3 (21)	0.19
Radiology: normal	3	8	11 (79)	

History, clinical examination, and laboratory work-up: Peri-natal, developmental and family histories were looked for in addition to neurological and systemic examination. Family history of epilepsy and febrile convulsion were considered significant if they occurred in a 1st and 2nd degree relative or both. All patients were examined and followed by a pediatric neurologist. Initial work up for all patients included; serum electrolytes, liver function tests, complete blood count and electroencephalogram (EEG) record in awake patients (7) and sleep patients (27) (repeated in one patient) or both. The EEG was considered abnormal if there was focal, multifocal or generalized paroxysmal activity. Other investigations such as cerebrospinal fluid study, computerized tomography (CT) scan or magnetic resonance imaging (MRI), serum amino acids or urine organic acids were performed if indicated.

Seizure classification: Seizure classification was done in accordance with the international classification into partial with or without secondary generalization and generalized tonic, clonic, or tonic clonic. Verification of seizures were according toeye witness account and the EEG abnormality. Clustered onset (two attacks or more within 24 hours) was considered to be one seizure. Seizures were considered idiopathic in absence of developmental delay, neurological abnormality or underlying lesion on radiological work up. Remote symptomatic seizures were considered if there were one or more of the above three factors.

Risk factors: Age at onset of seizure, sex, positive

family history of convulsions, delayed development, partial seizures, cluster onset, abnormal neurological examination, abnormal EEG findings, and abnormal radiological finding were considered for this study.

Follow-up: The patients were seen initially at a pediatrics emergency center and later referred to pediatrics neurology division for further assessment and follow up. The patient's and relatives or both were interviewed at three months interval either through clinical visits or telephone calls. We followed up patients until April 1998. Antiepileptic drugs were not given after first attack, except in 5 patients. Recurrence was defined as an attack of seizure after 24 hours of the initial seizure.

Results. The study group included 33 patients, 14 male: 19 female (ratio 0.7:1). The mean age was 4 years (range 2 months - 12 years) (Table 1). We used contengency table test for statistical analysis.

Over all recurrence risk: Recurrences occurred in 11 patients (33%), 5 females and 6 males. The mean time interval of recurrence was 2 months (range 2 days to 6 months). The overall risk of recurrence rate was highest in the first month 12%, followed by 9% in the 2nd month, and 6% in the 3rd month, and 6% between the 4th and 6th months. Twenty patients had 1 risk factor or more, 50% (p 0.01) of them had recurrence.

Mean ages: The mean age at first seizure was 4 years. Five patients (15%) were below 6 month, 10 patients (30%) between 6 month and 2 years, 9 patients (27%) between 2 and 6 years and 9 patients (27%) between 6 and 12 years. The mean age for patients with a recurrence was 3 years, which was lower than patients without recurrence (4.6 years). Recurrence occurred in 3\5 (60%) of patients below 6 months, 2\10 (20%) of patients between 6 months and 2 years, 5\9 (55%) of patients between 2 and 6 years and 1\9 (11%) of patients between 6 and 12 years. Significant predictors of recurrence: abnormal EEG, clustered onset and positive family history were found to be significant. Abnormal EEG were found in 11 patients (33%), out of that 7 patients (63%) had recurrence compared to 4 patients (18%) out of 22 patients with normal EEG (p=0.009). Positive family history was found in 10 patients (30%), and 6 patients (60%) got a recurrence compared to 5 patients (23%) out of 22 patients with negative family history (p=0.03). Clustered onset occurred in 8 patients (24%), and 5 patients (62%) had a seizure recurrence, compared to 6 patients out of 25 patients (24%) with generalized onset (P=0.04). Four patients with recurrence had positive family history combined with abnormal EEG.

Low significant risk factors: delayed development, abnormal neurological examination, focal seizures, abnormal neurological finding. Three out of 4 patients (75%) with delayed development and abnormal neurological examination had a recurrence compared to 8 out of 29 patient (27%) with normal development and neurological examination (p=0.059). Four out of 8 patients (50%) with focal seizures had a recurrence compared to 7 out of 25 patients (28%) with generalized onset (p=0.07). Computerized tomography scans and MRI or both were performed on 14 patients. Two out of 3 patients (66%) with abnormal findings had a recurrence, compared to 3 out of 11 patients (27%) with normal radiological findings (p=0.19).

Discussion. Recurrence rate (33%) in our study after the first unprovoked seizure was similar to some studies (29% and 30%)[3,4,7], but less than in other reports[5,8,9] (69%, 71% and 81%). This wide variation can be explained by many factors: study design (prospective or retrospective), duration of follow-up, type of seizure studied, whether seizures were provoked or not and if treatment was started after first attack or not. Retrospective studies, which included patients with recurrence, can miss those who have single attack without recurrence. Only 45% of patients seek medical advice at the first seizure.[10] More than 65% of patients, who have one attack or more, have a recurrence.[11] Studies, which included patients with a seizure recurrence, had a high incidence of recurrence. In a prospective study[9], a recurrence rate (71%) was reported, patients with past history of seizure recurrences were included which affected the result. Only children with first seizure were included prospectively in our study to avoid that bias. The duration of follow up varies considerably among the studies. We elected a two years period follow up (with a minimum period one-year) since the current treatment practice is to stop treatment after two years seizure free period. The key risk factors for recurrence in our study was epilepetogenic EEG activity, family history of epilepsy and clustered onset. Sixty three perscent of patients (7\11) with abnormal EEG activity had a recurrence, but other studies[3,7,12-15] reported from 34% up to 60% a risk of recurrence with abnormal (epileptogenic and non epileptogenic) EEG activity. The high percentage in our study (63%) can be explained on the basis of inclsion of only epileptiform activity as abnormal EEG. This is similar to a risk of 58% found in other studies[3,13,15] with epileptiform abnormalities, which are more significant than non-epileptiform abnormalities (risk 37%). Sixty percent of patients (6/10) with positive family history had a recurrence compared to 17% (5/23) with normal family history (p=0.03). An increased incidence of a recurrence in-patients with positive family history were reported.[3,7,11,112] Shinner et al[3] reported 86% of patients with positive family history and abnormal EEG had a recurrence. Other studies[6,9,10,15] reported no statistical significance of

family history. The controversy is due to definition varieties of positive family history. Some studies considered only 1st degree relatives. Fifty percent of patients (4/8) with partial seizure had a recurrence which is higher than (32%) in-patients (8/25) with generalized seizures, however this was not statistically significant (p=0.07), and agrees with studies.[8,11,16] In contrast to other reports[3,9,13,14], in which partial seizures were associated with a high risk of recurrence. We think that the high risk of recurrence with partial seizure is due to associated risk factors. Shinner et al[3] showed that idiopathic partial seizures with normal EEG were not associated with significant increase in risk of recurrence. Clustered onset in our study has a significant risk for seizure recurrence (p=0.04), and is similar to results reported by Hauser et al[11], but differ with other.[3] Similar to other studies[3,7,9,11-14] sex and age were not predictors of recurrence risk; Hirtz et al[9] reported a higher risk of recurrence in children below 2 years who had focal seizures. The mean age in children who had a recurrence was 3 years, which was lower than 4.6 years in children without recurrence; however this was not statistically significant. Five patients have had remote symptomatic findings, and out of those three patients had a recurrence (p=0.16). Several studies[3,7,9,12,13,17,18] reported a high risk of recurrence in neurologically abnormal patients. The non-significance reported in our study might be due to small number of patients with remote causes. Treatment after the first seizure was avoided; except in five patients; two of them had a recurrence. In general, our policy is to avoid treatment after the first attack, however this is modified sometimes due to parental anxiety, social background or significant neuro-developmental anomalies. Our study showed non-significance of treatment on seizure recurrence (p=0.7), similar to previous studies[9,11,13,14], however this does not mean that drugs are ineffective against epilepsy but could be biased by inappropriate drug, improper dose and poor compliance. In a prospective study[19] treatment was associated with a significant reduction in risk of recurrence. The efficancy of anti-convulsant treatment decreasing the risk of recurrence or not, still needs well-controlled studies. A prospective double blind study using properly selected medication drugs with a serum blood level in the therapeutic range is needed. Not only the risks of seizure recurrence but also side effect of medication should be taken into account. It is exceedingly important to know risk factors for seizure recurrence after first unprovoked attack, as this permits a better evalation and management.

Recurrence rate is higher in presence of some risk factors such as abnormal EEG, positive family history and clustered onset; the probability of seizure recurrence after the first attack should be discussed with the patient and family. The decision of starting treatment after the first seizure attack should be out weighed against drugs side effect. Some families prefers starting to avoid both physical and psychological trauma or both.

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