ORIGINAL ARTICLE

PATTERN OF CHILDHOOD EPILEPSY AND OUTCOME DETERMINANTS AT TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA

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ABSTRACT

Background: *Epilepsy is the most common cause of neurologic disability throughout the world. The majority of the cases live in developing countries. In Ethiopia epilepsy is an important public health problem; however, little information is available on childhood epilepsy.*

Objective: *The objective of this study is to assess the clinical profile and treatment outcome of childhood epilepsy.*

Methods: *A cross sectional study of 246 epileptic children who were followed up for at least 6 months in a seizure clinic at Tikur Anbessa Specialized Hospital was conducted over a 6 month period, February1-October 31, 2007. Using a structured and pretested questionnaire, data on Socio-demographic information, age at onset of seizure, frequency of seizures before start of AED ,duration of seizure before start of treatment , description of seizure, risk factors for seizure, EEG reports, and the prescribed treatment were collected, entered and analyzed with SPSS 12.0 software. Adjusted odds ratio with 95% confidence interval and P-value were calculated for predictors of poor seizure remission.*

Results: *There were149 (60.6%} male and 97(39.4 %) female epilepsy patients with a mean age of 7.1± 2.9.years, and the median age at onset of seizure 3.5± 2.7 years. Fifty-five (22.3%) had their first seizure at or before 1 year of age. There was a delay before presentation to hospital with mean and median interval of 0.81±1.18 and 0.3 year, respectively. Generalized epilepsy was the most common type of epilepsy present in 171(69.5%) of the patients. Partial seizure and multiple seizure types were seen in (15.9%) and (14.6%) of the patients, respectively. The majority (63%) of the patients were on monotherapy. Eighty -one (32.1%) of the patients had poor seizure remission. Further bivariate analysis revealed that seven factors were independently correlated with seizure remission. These were(1) multiple seizure types(OR=6.76, 95%CI: 3.08-14.82,P=0.0001),(2) a high frequency of seizures(OR=6.75, 95%CI:3.46-13.18, P=0.0001),(3)poor cognitive development(OR=4.35, 95%CI: 2.20-8.61, P=0.006) (4) associated motor abnormality(OR=2.60 95%CI: 1.35-4.97, P=0.004)(5), Cerebral palsy(OR 0.23 CI 0.08-0.66,P=0.006) (6) polytherapy{OR 13.72 CI 7.22-26.06,P=0.0001),and (7) poor compliance to treatment (OR 12.59 CI 6.16-25.73,P=0.0001).*

Conclusion and Recommendation: *This study shows a high rate of poor seizure remission despite anticonvulsant therapy. The findings confirm the need for more specialized neurological care for children.*

Key Words: *Epilepsy, Children, Predictors of poor seizure remission*

INTRODUCTION

Epilepsy is the most common cause of morbidity in children worldwide, 80% of whom live in developing countries where diagnostic and therapeutic facilities are poor (1, 2).A large proportion of patients with epilepsy do not get treatment because drugs are not available or may not be taken for cultural, political, and socioeconomic reasons (2,3).

In Ethiopia, epidemiologic surveys confirm that epilepsy is common (4-9) with a prevalence of 5.2%. In a study done in north west Ethiopia, centered on a locality with a population of 60,000, epilepsy was the most common cause of neurological disability with a prevalence of more than 0.5% and with only 1.6% ever treated(4). The incidence was found to be 64/100,000 population as reported in a community based study conducted in rural central Ethiopia (8).

Similarly, in a health center-based study done in northwest Ethiopia, 87% 0f the epileptic patients were not treated previously with any antiepileptic drug (AEDs), and more than 90% claimed to be unaware that drug treatment existed (5).

In Ethiopia, only few hospital-based data concerning childhood epilepsy are available (6). Moreover, there is very little information on the types of epilepsy or on their clinical presentation, Electroencephalogram (EEG) findings, or clinical outcomes of childhood epilepsy which are important for planning management. The objective of this study is to obtain a baseline profile of epilepsy in children, to determine clinical outcomes, and to identify clinical and therapeutic indices/ factors that may predict poor seizure remission.

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METHODS

Study Area and Period: The study was conducted from February 1 to October 31, 2007, within the Pediatric Seizure Clinic of Tikur Anbessa Specialized Hospital, university teaching hospital, Addis Ababa, Ethiopia. The hospital serves as a referral center for health centers and hospitals in Addis Ababa and different regions of the country and provides out-patient and inpatient services to the majority of children in Addis Ababa. The seizure clinic runs once per week.

Study Design

A Hospital-based cross-sectional study based on retrospective analysis of childhood epilepsy over a 6-month period was conducted.

Sample size and Study population:
All children with epilepsy who were followed up at the seizure clinic during the study period were recruited.

Exclusions: In order to obtain a proper assessment of the clinical outcome, only children with epilepsy who had been followed up in the seizure clinic for at least 6 months with adjusted AED treatment were included in the study.

Sampling techniques
Data Collection: A standard pre-tested questionnaire was used to collect data comprising socio-demographic information, age at onset of seizure, frequency of seizures before start of AED ,duration of seizure before start of treatment , description of seizure, risk factors for seizure, EEG reports, and the prescribed treatment. Patient records were reviewed and parents/care takers interviewed in order to assess the clinical profile of the patients, the degree of compliance with prescribed treatment, and outcome of therapy.

Study Variables
Dependent variables: The dependent variable measured was outcome of seizure control/poor seizure remission.

Independent variables: The independent variables measured were age at early onset of seizures, rate of seizures before treatment, motor and cognitive developmental status of child, seizure type, and risk factors for epilepsy, management strategy, and compliance to anticonvulsants.

Data processing and analysis: SPSS (version12.0) software was used to process and analyze data. Mean, median, and percentages were calculated to describe the characteristics of the study population. Bivariate analysis was done and Odds ratio with 95 % confidence intervals and p-values were calculated to show the magnitude of association between potential predictors of poor seizure remission and $.P < 0.05$ was considered to be statistically significant.

Ethical consideration: Ethical clearance was obtained from the Department of Pediatrics and Child Health, AAU. The necessary explanation about the purpose of the study and its procedure was given, and verbal consent was obtained from the children's parents or guardians.

Operational Definitions

- Age at onset of seizures: Seizure onset at or before 12 months of age was considered early.
- Poor seizure remission as an outcome of treatment was defined as the presence of any seizure attack during the 6 months since the last day of follow-up despite adjustment of AED according to the individual patient's condition. Judgment of poor remission was based on the medical records, and caregivers' interviews.
- Seizure was defined as 'frequent' if one or more attacks per week occurred.
- Associated gross motor developmental abnormality/disability was categorized into: Severe-Major if daily activities of living (such as toileting, dressing, or feeding) were impaired; Mild-Signs of motor deficits, but child is functioning independently and/or appropriately for age.
- EEG finding was considered 'Abnormal' by the presence of interictal or ictal epileptiform discharges and/or abnormal background activity with focal or generalized, excessive slow or fast waves, reported to be abnormal for the child's age.
- Clinical and Etiological classification of epilepsy is according to the International League Against Epilepsy(10)

RESULTS

Socio-demographic Profiles, Description of Epilepsy, Associated Features and EEG Findings

A total of 246 patients, (60.6% male and 39.4% female) were included and analyzed. The mean age was 7.1± 2.9.years, and median age at onset of seizure was 3.5 ± 2.7 years (range 2 months' to 12 years). About 55 (22.3%) had their first seizure

before 1 year of age. The duration of seizure before diagnosis ranged from 1 day to 7.5 years with the mean and median time interval before presentation of 0.81±1.18 and 0.3 years, respectively. The rate of seizures was high in 140(56.9%) of cases and the majority (63%) of patients had not been on anticonvulsant therapy.

Associated gross motor disability was present in 47 (16.2%) of the patients and 41(16.7%) had poor cognitive development. Electroencephalogram was performed in 151(61%) of cases. Abnormal features were found in the EEG tracings from 141(93%) children. Of these, (62%) had abnormal background activity and 37(24.5%) had localized epileptiform discharges.

More than 57% of the epileptic children were diagnosed on the basis of both clinical and EEG findings, while clinical judgment was the only criterion in the rest of the cases. The majority (69.5%) of the children were clinically diagnosed to have generalized epilepsy, followed by partial (15.9%), mixed seizure types (14.2%) and unclassifiable (0.4%). The classification and frequency of the different seizure types is shown in Table I.

Table I: Clinical Seizure types in children with epilepsy, Tikur Anbessa Specialized hospital, February 1-October 31, 2007, Addis Ababa.

Seizure type	No	%
Generalized	**171**	**69.5**
Tonic-clonic	141	57.3
Myoclonic	10	4.1
Tonic	9	3.7
Absence	6	2.4
Clonic	4	1.6
Atonic	1	0.4
Partial	**39**	**15.9**
Complex partial	21	8.5
Secondarily generalized	16	6.5
Simple partial	2	0.9
Mixed/ Multiple seizures	**35**	**14.2**
Unclassifiable	1	0.4

Table II: Type of Epilepsy, Seizure history, Developmental status, and EEG findings, treatment adherence and outcome, February 1-October 31, 2007, Tikur Anbessa Specialized Hospital, Addis Ababa.

Characteristics	Frequency	%
Etiological classification		
Symptomatic epilepsy	47	19.1
Idiopathic epilepsy	199	80.9
Total	246	100
Seizure history		
Age at onset of seizures		
Before and at 12 months	55	22.4
After 12 months of age	191	77.6
Total	246	100
Rate of seizures		
High rate of seizures	140	56.9
Low rate of seizures	106	43.1
Total	246	100
Developmental status		
Motor development		
Normal motor function	199	68.6
Major motor disability	23	7.9
Minor motor disability	24	8.3
Total	246	100
Cognitive development		
Poor	44	17.9
Normal	202	82.1
Total	246	100
EEG Tracings		
Abnormal	141	93
No abnormality detected	10	7
Total	151	100
Compliance to AEDs		
Yes	199	77.6
No	55	22.4
Total	24	100
Seizure remission		
Poor	81	32.9
Good	165	67.1

Risk factors for epilepsy: Symptomatic epilepsy was diagnosed in 47(19.1%) of the children but 156 (80.9%) had no risk factors for epilepsy. About 26 (9%) had CNS infection which was the most common possible etiologic factor identified Family history of epilepsy was found in 15 (6.1%).A history of perinatal asphyxia and neonatal seizures was present in 16(6.1) and 11(4.5%) of the patients, respectively. (Table III)

Table III: Risk factors for childhood epilepsy, February 1-October 31, 2007, Tikur Anbessa Specialized Hospital, Addis Ababa.

Risk factors	Frequency	%
Family history	15	6.1
Cerebral palsy	17	6.9
CNS infection	26	10.5
Febrile seizures	8	3.2
Neonatal seizure	11	4.5
Perinatal asphyxia	16	6.1
CNS anomalies	3	1.2
Others	4	1.6

Monotherapy was the most frequent management strategy used across all categories of epilepsy. Phenobarbitone was the most frequently prescribed, followed by phenytoin for all seizure types (Table IV).

Table IV: Drugs prescribed to children with epilepsy on routine basis Correlated with the type of epileptic seizure, February 1-October 31, 2007, Tikur Anbessa Specialized Hospital, Addis Ababa.

Seizure type	No. of Children	N Monotherapy	PHT n (%)	PHN n (%)	CBZ n (%)	VPA n (%)	CZP n (%)
Generalized	171	142	135	63	13	7	
Tonic-clonic	141	122	118	53	7	1	n.p.
Absence	6	6	n.p.	2	2	n.p.	2
Myoclonic	10	4	5	n.p.	n.p.	3	2
Tonic	9	5	5	4	2	n.p.	n.p.
Clonic	4	3	4	n.p.	n.p.	n.p.	n.p.
Partial	39	24	21	17	15	3	n.p.
Simple partial	2	2	n.p.	1	1 .	n.p.	n.p.
Complex partial	21	14	4	5	5	n.p.	n.p.
Secondarily Generalized	16	8	4	2	2	n.p.	n.p.
Multiple seizure types	35		28	16	4	12	15
Unclassified	1	1	1				

Predictors for poor seizure remission

The outcome of the current pattern of care provided to children with epilepsy within at least 6 months after AEDs adjustment was an average remission rate of 67.9%. Poor seizure remission within at least 6 months after AED adjustment occurred in 32.1 % of the cases.

Defective care of children with epilepsy that is manifested by non compliance with AEDs was seen in 55 (22.4%) of cases. Seven variables showed significantly independent correlation with poor seizure remission and were found to increase the chances of our study children having recurrence of seizures (Table V).

Table V: Relationship of clinical and EEG features to poor seizure remission in children with epilepsy, February 1-October 31, 2007, Tikur Anbessa Specialized Hospital, Addis Ababa

Variables	Seizure remission		Adjusted OR	P
	Good	Poor	(95%CI)	
Seizure frequency				
Low	93	13	1	
High	7 2	68	6.75(3.46-13.18)	<0 .0001
Age at onset of seizures				
≤12 months	34	21	1.34(0.72-2.51)	0.348
>12 months	131	60	1	
Type of seizure				
Generalized	131	41	1	
Partial	24	15	1.76(0.82-3.76)	0 .142
Mixed seizure	20	15	6.76(3.08-14.82)	<0.0001
Management strategy				
Monotherapy	135	20	1	
Polytherapy	30	61	13.72(7.22-26.06)	<0.0001
Compliance to AED				
Yes	152	39	1	
No	42	13	12.59(6.16-25.73)	<0.0001
Associated Motor Abnormality				
Absent	142	57	1	
Present	23	24	2.60(1.35-4.97)	0.004
Cognitive abnormality				
Absent	151	54	1	
Present	14	27	4.35(2.20-8.61)	0.006
Cerebral palsy				
No	159	70	1	
Yes	6	11	0.23(0.08-0.66)	0.006
Neonatal seizure				
No	159	76	1	
Yes	6	5	1.74(0.51-5.89)	0.371
CNS infection				
No	147	73	1	
Yes	18	8	1.11(0.46-2.69)	0.805

DISCUSSION

Although the majority (75.2%) of the study children were from Addis Ababa and most (56.9%) had high rate of seizures at presentation, 63% of our patients did not receive previous AED treatment, a rate closer to that of a study in Ecuador, where only 29% had ever been treated (11).

Despite a mean duration of epilepsy of 0.81 years and accessibility of health care in the study area, 63% of our patients had not previously received AED treatment. This finding is in agreement with studies done in northwest Ethiopia (87%).There was a delay between the onset of seizure and presentation to hospital and initiation of AED management for cultural and socioeconomic reasons which is an expected scenario for health care delivery in developing countries (3,12).

In a study from South Africa, 43% of children had historic, clinical, and radiological evidence of symptomatic epilepsy (13). In this study only 47 (19.1%) of the study children had symptomatic epilepsy indicating the need for further investigation of underlying brain damage or defect. We found family history of epilepsy in only 6.1% of the cases, unlike previous reports of 22-24% (5, 8). History of peri-natal asphyxia was found in 16(6.5%), and 11(4.5%) had neonatal seizure.CNS infection was found to be the cause of epilepsy in 10.5 % of cases closer to other series from sub-Saharan African, 1-8%of cases (8, 14). Cerebral palsy was the risk in 17(6.9%) of cases compared to the 2.2% identified by Shitaye et al (5).

The dominance of the diagnostic category of seizures of generalized onset when clinical criteria alone is used is consistent with previous studies done in Ethiopia (5, 9) and a pediatric unit of a Nigerian hospital(15), but contradicts other studies performed in other countries that reported a much higher proportion of partial seizures (16,17). This could reflect a true difference between studies or clinicians' lack of familiarity with or failure to recognize or document.

Although EEG is a valuable diagnostic tool for the diagnosis and classification of epilepsy type and choosing appropriate AED, it was performed only on 61.4% of the patients because they could not afford. Based on EEG findings, 55.6% of the epileptic seizures had a generalized onset; 24.5% were partial, and 19.9% could not be classified.

This increased proportion of partial seizure when EEG data were used is consistent with previous studies from central Ethiopia (9).The higher percentage of unclassified seizures could be due to drug treatment started early before EEG is performed 18).

Sixty-three percent of the cases were on monothrapy regimen which is in agreement with the recommended optimal therapy (10, 19). Furthermore, for the majority of the patients, the choice was between phenobarbitone and phenytoin due to the fact that these drugs are cheap or are available free of charge and are the first line anticonvulsants recommended.

This study showed an average remission rate of 67.9% in all patients, a rate closer to the report from a prospective hospital based study of patients with newly diagnosed epilepsy (70-80%) after AED treatment, leaving 20-30% of the patients with chronic, intractable epilepsy (20). Several research papers, consistently, reported that high frequency of seizures, mixed/multiple seizure types, associated motor abnormality, poor cognitive development, polytherapy, and poor adherence to treatment were found to be significant predictors of poor seizure remission.

Children with multiple/mixed seizure types, associated neurodevelopmnetal deficits, and higher rate of seizures had lower remission rates in agreement with previous reports (20, 21). Polytherapy was also found to be correlated with poor remission, showing that when the first AED fails to induce remission, the chance of subsequent AEDs succeeding becomes smaller. This result is supported by the work of Kwan and Brodiei2000, Walker and Sander 1996 (22 -24).

In conclusion, the findings of this study confirmed a high rate of poor seizure remission despite anticonvulsant therapy. Therefore, we emphasize the need for more specialized neurological care of children, better organization and delivery of neurological services, as well as health education programs for the care givers of children with epilepsy to ensure compliance to treatment. Limitations, however, are that as this is a hospital based cross-sectional study, more severely ill children are likely to be included and might have biased the results. Furthermore better designed health center and community-based studies with adequate sample size are recommended.

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