

## ORIGINAL ARTICLE

## DEMOGRAPHIC AND CLINICAL FEATURES OF CHILDHOOD IDIOPATHIC EPILEPSY AT A TERTIARY CARE HOSPITAL OF PAKISTAN

Syed Sajid Hussain Shah, Bibi Aalia\*, Mohammad Ali Raza\*\*, Shahzad Najeeb\*\*, Saima Gillani\*\*, Fauzia Aitazaz\*\*\*

Department of Paediatric Nephrology, Institute of Kidney Diseases, Peshawar, \*KMU Institute of Medical Sciences Kohat, Ayub Medical College Teaching Hospital, Abbottabad, \*\*\*Department of Physiology, AJK Medical College, Muzaffarabad, Pakistan

**Background:** Recent increase in number of children diagnosed with epilepsy raised the need to find out and report the demographic and clinical features of childhood idiopathic epilepsy at a tertiary care hospital. **Methods:** Cross sectional study conducted at Ayub Teaching Hospital from July 2018 to June 2020. Patients aged 1–14 years of either gender diagnosed as idiopathic epilepsy were included from paediatric outpatients, admitted cases and private clinics. Patients with cerebral palsy, dysmorphism and microcephaly were excluded. Demographic data, birth and developmental history details, age of onset of seizures, family history of epilepsy and febrile seizures were documented. Electroencephalograms (EEGs), brain imaging (CT scans and MRIs), where available. Data was analysed at SPSS-20. **Results:** For total 83 (65% males), Mean±SD of age was 6.60±3.64 years. Majority (63.9%) were older than 5 years. Family history of epilepsy and febrile convulsions was positive in 30.1% and 14.5% respectively. Most commonly used drug for seizure control was valproic acid (84.3% patients). Brain CT scan was done in 25.3%, MRI in 16.9% patients, and EEG in 57.8%. Positive family history of febrile seizures was significantly associated with ( $p<0.05$ ) idiopathic epilepsy in males. **Conclusions:** Idiopathic epilepsy affects mostly children above 5 years of age. EEG is the most common investigation performed. When done brain imaging was normal. Valproic acid remains the most commonly used solo antiepileptic in both genders. Male patients are at higher risk of developing idiopathic epilepsy especially if family history of febrile seizures is present.

**Keywords:** Children, epilepsy, neuroimaging, EEG

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### INTRODUCTION

Globally, each year five million people are diagnosed with epilepsy. In developed countries with higher *per capita* income epilepsy is diagnosed in 49 per 100,000 people each year. In poorer countries, the number of diagnosed cases per year can reach as high as 139 per 100,000.<sup>1</sup> Estimated people in United States having epilepsy is 3.4 million with 3 million adults and 470,000 children.<sup>1</sup> According to the latest estimates, about 0.6% of children aged 0–17 years have active epilepsy.<sup>2,3</sup> This means one out of six children of school going age has epilepsy. Overall prevalence of epilepsy in Pakistan is about 9.99 per 1,000 population. Prevalence is highest in those younger than 30 years of age.<sup>4</sup>

Seizure is a manifestation of epilepsy and characterized by sudden, abnormal, hyper-synchronous discharge of cortical grey matter or neurons with temporary loss of consciousness, abnormal motor activity, autonomic dysfunction and sensory behavior.<sup>5</sup> Epilepsy and epileptic syndromes were classified as idiopathic depending upon factors such as age at seizure onset, type of seizures, electroencephalographic changes, family history, absence of an anatomic brain lesion. Idiopathic

generalized epilepsy (IGE) is a group of epileptic disorders that are believed to have a strong underlying genetic basis. Patients with an IGE subtype are typically otherwise normal and have no structural brain abnormalities.<sup>6</sup>

In children of developing countries, idiopathic epilepsy is the most common neurological disorder.<sup>7</sup> As compared to developed countries, the prevalence of epilepsy is more in developing countries due to more complications during deliveries, more chances of intracranial infections going unsuspected and delays in seeking medical help. Rural areas have a higher prevalence in comparison with urban areas, reason of which is not clear.<sup>8–10</sup> In our hospital we noted recently a surge of children with seizure disorder of various aetiologies, so we decided to conduct this study to highlight the problem in our area. Although studies for epilepsy prevalence and demography have been done elsewhere in Pakistan<sup>4</sup>, through our input we want to contribute in highlighting this important problem in paediatric population of Hazara Division.

### METHODOLOGY

This cross sectional study was done in Paediatric B unit of Ayub Teaching Hospital, Abbottabad over two years, i.e., from July 2018 to June 2020 after obtaining

approval from institutional review board. Patients from 1–14 years of age of either gender diagnosed as idiopathic epilepsy on basis of history including antenatal history, examination, normal developmental milestones and investigations including CT scan and MRI and electroencephalogram (EEG) were included in this study. Patients were enrolled from outpatients, admitted cases and patients from private clinic. Patients with cerebral palsy, dysmorphism and microcephaly were excluded from the study.

Sample size was calculated by OpenEpi sample size calculator. The prevalence of epilepsy in children was taken as 5% and estimated sample size was 73 patients. In our study we included 83 patients through non-probability, consecutive sampling after taking written informed consent. Patient’s demographic data comprising age of onset of seizures, family history of epilepsy and febrile seizures, findings on EEG, MRI and CT scan brain (where available) were recorded on the predesigned proforma.

The data was analysed using SPSS-20. Mean±SD was calculated for age of the patients. Frequencies and percentages were calculated for qualitative variables like gender of patients, type of epilepsy, family history of epilepsy and febrile convulsions, type of drugs used for seizure control and investigations done. Chi square test was applied for comparison of nominal data and results considered significant with  $p \leq 0.05$ .

**RESULTS**

In this study, total 83 patients were enrolled out of which 54 (65.1%) were males and 29 (37.9%) were females. The mean age of diagnosis of epilepsy was  $4.27 \pm 3.29$  years. Only 5 (6%) patients were less than 2 years of age, while 25 (30.1%) patients were in between 2–5 years of age (Table-1). Majority of patients 53 (63.9%) were more than 5 years of age, whereas 22 (26.5%) patients were less than 2 years, leaving 29 (34.9%) patients with ages between 2–5 years and 32 (38.6%) patients were more than 5 years of age, when they first time presented with history of seizures. Family history of epilepsy was positive in 25 (30.1%) patients while family history of febrile convulsions was present in 12 (14.5%) patients. CT scan brain was done in 21 (25.3%) patients whereas MRI brain was done in 14 (16.9%) patients. All neuroimaging including CT scan and MRI were normal. The EEG was done in 48 (57.8%) patients. Only 28 patients (25%) EEG showed epileptic activity. (Table-1)

Age of patients ranged from 1–14 years with Mean±SD of  $6.60 \pm 3.64$  years, mean for duration of illness was 4.5 years (Table-2).

Though family history of epilepsy was more in male as compare to females yet  $p=0.38$  was not significant (Table-3). There was significant relationship

between gender and family history of febrile convulsions with  $p=0.037$  as febrile convulsions with family history were more in males (Table-4).

The most common drug used for seizure control was valproic acid, which was used in 70 (84.3%) patients, leviteracetam in 5 (6%) patients, carbamazepine in 7 (8.4%) patients and lamotrigine in one (1.2%) patients. (Tables-1, 5).

Most of the male patients, i.e., up to 89% used valproic acid as sole medication followed by carbamazepine in 5.6%, in females carbamazepine use was slightly higher as up to 13% used it and majority of females, i.e., 76% used valproic acid as only medications,  $p$  was insignificant though and only a negligible 1% in both genders used combination treatment of antiepileptic (Table-5).

**Table-1: Demographics (n=83)**

Variables	Frequency	Percentage	<i>p</i>
<b>Gender</b>			
Male	54	65.1	0.500
Female	29	34.9	
<b>Age Group</b>			
≤1.99 years	5	6.0	0.070
2–4.99 years	25	30.1	
≥5.00 years	53	63.9	
<b>Family history of epilepsy</b>			
Present	25	30.1	0.096
Absent	58	69.9	
<b>Family history of febrile seizures</b>			
Present	12	14.5	0.037
Absent	71	85.5	
<b>Antiepileptic used</b>			
Valproic acid	70	84.3	0.126
Leviteracetam	3	3.6	
Valproic acid and leviteracetam	2	2.4	
Carbamazepine	7	8.4	
Valproic acid and lamotrigine	1	1.2	
<b>CT scan of brain</b>			
Done	21	25.3	0.155
Not done	62	74.7	
<b>MRI of brain</b>			
Done	14	16.9	0.300
Not done	69	83.1	
<b>EEG</b>			
Done	48	57.8	0.142
Not done	35	42.2	
Treatment completed	2	2.4	-

**Table-2: Age, weight and duration of illness (n=83)**

Variables	Min	Max	Mean	SD	SE
Age (Years)	1	14	6.60	3.63	0.399
Weight (Kg)	5.5	39	18.25	7.60	0.834
Duration of illness (Years)	4	5	4.5	0.707	0.5

**Table-3: Correlation between gender and family history of epilepsy (n=83)**

Gender	Family history of epilepsy		Total	<i>p</i>
	Yes	No		
Male	18	36	54	0.38
Female	7	22	29	
Total	25	58	83	

**Table-4: Correlation between gender and family history of febrile seizures (n=83)**

Family history of febrile seizures	Frequency	Percentage	p	
<b>Males</b>				
Present	11	20.4	0.037	
Absent	43	79.6		
<b>Total</b>	<b>54</b>	<b>100.0</b>		
<b>Females</b>				
Present	1	3.4		
Absent	28	96.6		
<b>Total</b>	<b>29</b>	<b>100.0</b>		

**Table-5: Correlation and frequencies of gender and antiepileptic used (n=83)**

Antiepileptic used	Frequency	Percentage	p	
<b>Males</b>				
Valproic acid	48	88.9	0.126	
Leviteracetam	1	1.9		
Valproic acid and leviteracetam	1	1.9		
Carbamapazine	3	5.6		
Valproic acid and lamotrigine	1	1.9		
<b>Total</b>	<b>54</b>	<b>100.0</b>		
<b>Females</b>				
Valproic acid	22	75.9		
Leviteracetam	2	6.9		
Valproic acid and leviteracetam	1	3.4		
Carbamapazine	4	13.8		
<b>Total</b>	<b>29</b>	<b>100.0</b>		

## DISCUSSION

About 50% of epilepsy cases begin in children or in adolescent age and 74% patients with epilepsy are age 18 years.<sup>11</sup> Khatri *et al*<sup>4</sup>, reported epilepsy as a common problem in Pakistan with an overall estimated prevalence of 9.99 per 1,000 population. Those younger than 30 years of age and rural population are affected more. Treatment initiation and compliance remains low and compliance is a problem in diagnosed cases. Awareness in people regarding epilepsy and its management is low.

The gender predominance in our study was slightly more as 65% males were affected. Regarding gender predominance this slight difference in generalized seizure were also noted in an Egyptian study<sup>12</sup> and by Carlson C<sup>13</sup>. Both of these studies noted that although difference between genders is only minute with only a slight male predominance in case of generalized seizures, for certain types of seizures significant difference does exist. Beghi E<sup>5</sup> in one review article gave the incidence and prevalence of epilepsy more in males.

Dragoumi *et al*<sup>14</sup>, studied the clinical courses and outcome of idiopathic epilepsy in children along with prognosis. In their study the mean age of seizure onset in children was 6.7 years while in our study mean age of onset of seizures was 4.27±3.29 years. Treatment adherence in our study remained low which is an important problem in long term management of epilepsy and affects the course and outcome of illness. Problem of non-adherence to

AEDs is also reported in other studies. Approximately three fourths of patients with epilepsy shows response to treatment but 12–67% patients relapse after withdrawal of medicine. EEG is diagnostic in about half of patients with epilepsy but literature shows that abnormal EEG done during the withdrawal of antiepileptic drug (AED) is risk factor for recurrence of epilepsy.<sup>15</sup>

Modi *et al*<sup>16</sup>, reported that early adherence interventions may actually help patients to comply with the treatment and change the course of the disease. Support groups of families can be formed and frequent follow-ups and counselling is important to enhance adherence to the AED used. In comparison to our findings an Iranian study actually reported a high compliance to AED, i.e., 72.4% patients under 18 years of age adhered to the treatment.<sup>17</sup>

Children with a positive family history of epilepsy (30.1% patients in our study) are known to be at greater risk of developing epilepsy, as there it is suggested that an underlying genetic cause may be the reason. It is also reported that children with family history of febrile seizures especially complex febrile seizures are at increased risk for IGE. Though in our study the correlation between IGE and family history was not significant but upon splitting find on gender basis males were found to be at higher risk if family history of febrile seizures is positive. Al Habbal A *et al*<sup>8</sup>, did one case control study in Syria regarding the risk factors associated with epilepsy in children. In their there was positive association between family history of epilepsy and febrile seizures.

Kozhanova TV *et al*, did one study regarding diagnosis of epilepsy in children and exome sequencing. In their study, next generation sequencing technique was used and they detected mutations in 57.7% patients.<sup>18</sup> Definitions of epilepsy clearly include that it is associated with recurrent afebrile seizures, but the fact that febrile seizures of childhood also have a genetic predisposition. Although simple febrile seizures is a benign condition but complex febrile seizures in immediate family, siblings or in the past history of patient is a risk factor for developing epilepsy. One study reported that children with febrile seizures have a six times (3%) increased risk of developing future afebrile seizures and epilepsy when compared to controls. Whereas simple febrile seizures without these risk factors have only twofold excess (1%) of developing epilepsy in future. Complex febrile seizure if, repetitive, prolonged and focal place the child at even a higher risk, i.e., 6–8%.<sup>19–22</sup>

Asghar MA *et al*, did one retrospective cohort study in tertiary care hospitals of southern

Punjab about the prescription patterns of AED.<sup>23</sup> In children it was found that valproic acid was the most common (56%) prescribed drug followed by levetiracetam (27%). In our study valproic acid was the most common prescribed drug in 84.3% patients, carbamazepine in 8.4% and levetiracetam in 6% patients. This shows that higher number of our patients are on valproic acid as compare to above mentioned study while less no. of our patients are on levetiracetam as compare to above to study.

In a retrospective study by Crevier-Sorbo G *et al*, it was found that EEG was the most common investigation done in 82% patients and neuroimaging was done in 7% patients to diagnose the epilepsy.<sup>24</sup> While in our study, EEG was done in 57.8% of patients and neuroimaging including CT scan and MRI was done in 25.3% and 16.9% patients respectively. Mwipopo EE *et al* studied the profile and clinical characterization of seizures in hospitalized children and concluded that neuroimaging studies were required mostly in children having unprovoked seizures.<sup>25</sup> In our study CT scan brain was done in 25.3% and MRI brain was done in 16.9% patients; all studies were normal. Wali A *et al*<sup>26</sup>, did a study about referral patterns at a neurophysiology centre in Quetta. They found that most of the children were referred by paediatricians for EEG and at the facility, 58% of EEG was done in children less than 18 years of age.

Another important risk factor for childhood IGE is underlying, undiagnosed, covert celiac disease. Canova C *et al*<sup>27</sup> concluded that children having celiac disease are at increased risk of epilepsy. In children when no other aetiology is found, screening for celiac disease should be considered.

## CONCLUSION

Idiopathic epilepsy is more common in children above 2 years of age; males are affected more than females. EEG was the most common investigation done for epilepsy in our study. Brain imaging of CT scan and MRI brain where available were normal. Valproic acid remained the most commonly used solo antiepileptic in both genders. A positive family history was associated with epilepsy in males.

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**Address for Correspondence:**

**Dr. Saima Gillani**, Department of Paediatrics, Ayub Medical College, Abbottabad, Pakistan. **Cell:** +92-3208512073

**Email:** drsaimagillani@gmail.com

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**SSHS:** Concept, design and data collection

**BA:** Critical review

**MAR:** Literature search

**SN:** Literature search

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**FA:** Data analysis and tabulation

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