

Surveillance of aetiologies, clinical presentation, and most common types of epilepsy among paediatric patients at a tertiary care hospital in Pakistan

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Abstract

Epilepsy is the third most common neurological disease in the world associated with a high frequency in the paediatric age group. This study aims to evaluate the prevalence, types and aetiologies of epilepsy within the Pakistani population. A retrospective review of the charts of all patients, below the age of 18 years, presenting with epilepsy to the Department of Neurology at The Children's Hospital and Institute of Child Health, Lahore, from January 2016 to December 2020, was carried out. Analysis was performed using SPSS Version 26. A *p* value of <0.05 was considered statistically significant. A total of 1,097 patients were studied, of which 644 (58.8%) were males and 451 (41.2%) females. A vast majority, i.e. 1,021 (96.1%), of the study participants, belonged to the province of Punjab. Afebrile seizures [*n*=798 (72.7%)] were more commonly reported than febrile seizures [*n*=299 (27.3%)]. Among seizure types, generalised seizures were the most common type of seizure reported in 520 (49.8%) patients. Refractory seizures were the least common type reported in 3 (0.3%) patients. Aetiology was mostly idiopathic [*n*=540 (49.2%)], followed by congenital [*n*=228 (20.8%)]. The most frequently reported duration of seizure was between one and three minutes [*n*=116 (42.3%)]. The most common ictal features seen were a combination of up-rolling of eyes and frothing from the mouth [*n*=206 (34.9%)]. Results from this study can be used by health care providers to better formulate therapeutic interventions for a timely diagnosis and effective treatment of epilepsy.

Keywords: Epilepsy, Aetiology, Paediatric, Seizures, Pakistani.

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Introduction

Epilepsy is a neurological disease characterised by an abnormally high neuronal discharge within the central nervous system.¹ It is a condition which can have long-term consequences, including neuronal death or injury, and modification of neuronal networks, depending on the type and duration of seizures.² Epilepsy affects nearly 70 million people worldwide and has a bimodal distribution with the highest reported risk in infants and the elderly.³ Two different meta-analysis reported the prevalence to be 5.18/1,000 in high income countries and 8.75/1,000 in lower income countries.^{4, 5}

Prevalence of epilepsy has also been reported in relation to aetiological factors. A meta-analysis of 222 studies noted genetic epilepsy cases to be 1.7/1,000, structural/metabolic cases to be 2.7/1,000, and cases of unknown origin to be 3.15/1,000.⁴ Epilepsy is a disorder with numerous risk factors, aetiologies, and a strong hereditary inclination rather than a single cause. Comorbidities are recognised as important prognostic markers.³

Very few studies have been conducted in Pakistan that indicate the prevalence and aetiologies of epilepsy based on evidence.^{6,7} Thus, it is of prime importance to research about epilepsy solely based on the population of the country. This study aimed to determine the prevalence, occurrence of types of epilepsies, and the aetiologies of epilepsy within the paediatric population of Pakistan.

Material and Methods

A retrospective observational study was conducted in the Department of Neurology at The Children's Hospital and Institute of Child Health, Lahore, Pakistan. Ethical approval was obtained from the ethical review board of the hospital before initiation of the study (Reference number: 208). Following the ethical approval, the study was conducted from February 15, 2021 to September 31, 2021.

The study was conducted according to the Helsinki declarations. All outpatients, below the age of 18 years,

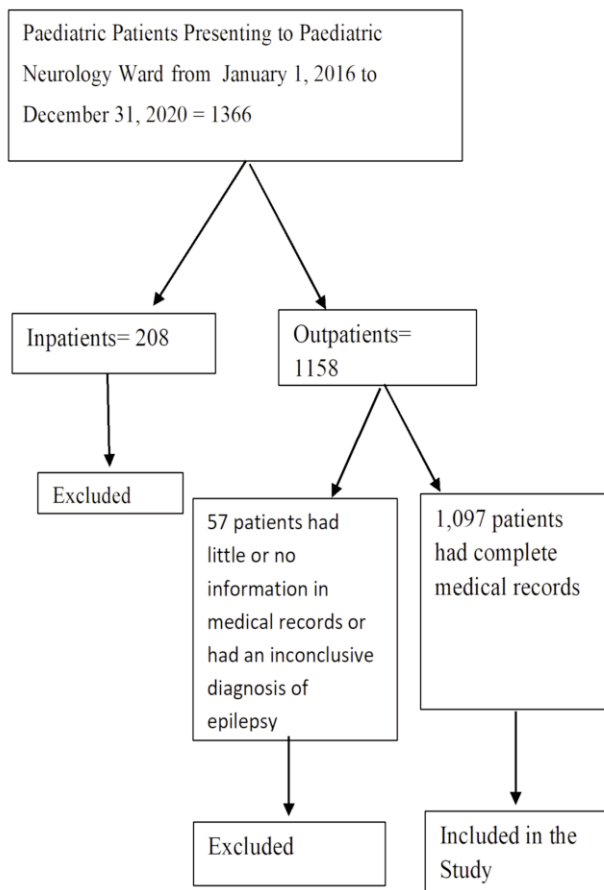


Figure-1: Case screening Flow chart.

diagnosed with epilepsy and having a follow-up in the Department of Neurology at Children's Hospital over a five-year period, from January 1, 2016 to December 31, 2020, were included in the study. Patients whose EEG reports were inconclusive and did not offer a definite diagnosis of epilepsy were excluded from the study. (Figure 1).

A minimum sample of 377 individuals was required to determine the prevalence of epilepsy assuming an anticipated prevalence of epilepsy in Pakistan to be 0.99% with 1% level of precision and 5% level of significance.^{8, 9} Sample size calculation was done using OpenEpi version 6.¹⁰ Charts of all patients were reviewed after approval from the Ethical Review Board of The Children's Hospital. Information retrieved included demographics e.g., gender, age and residence; enrolment history, i.e. detailed accounts of the seizures in chronological order, including pre-ictal, ictal, and post-ictal features; duration of seizure; precipitant, and type of seizure, etc. Furthermore, birth history, history of any trauma, family history for epilepsy, co-morbid conditions were also

noted to evaluate the possible aetiologies of epilepsy in the patient.

Types of seizures were classified as follows: Afebrile seizures (afebrile fits, astatic myoclonic seizures, infantile spasms, benign Rolandic epilepsy, benign focal epilepsy of childhood (BFEC), and generalised idiopathic epilepsy), generalised seizures (absence seizures, atonic seizures, tonic-clonic seizures, myoclonic seizures, and febrile seizures), focal partial seizures (Jacksonian epilepsy, temporal discharges, frontal lobe epilepsy, and reflex epilepsy), refractory seizures (uncontrolled fits and drug resistant epilepsy), and status epilepticus (convulsive and non-convulsive). Etiologies of epilepsy were classified as follows: idiopathic, congenital (West syndrome, ohtahara syndrome, birth asphyxia, Lennox Gastaut syndrome, microcephaly, etc.), encephalopathies (acute disseminated encephalomyelitis, early myoclonic encephalopathy, SSPE), meningitis (tuberculous meningitis, meningoencephalitis, pyomeningitis), other infections (typhoid, pneumonia, neonatal hepatitis, enteric fever, etc.), structural (tumour or trauma, hydrocephalus, choroid plexus cyst, cerebral palsy, intracranial bleeding, etc.) and other chronic conditions (nephrotic syndrome, SIADH etc.).¹¹⁻¹³

SPSS Version 26 was used for statistical analysis. Continuous data was represented as mean and standard deviation, categorical data was represented as frequencies and proportions. Associations between categorical variables were assessed using chi-square tests and Fisher's exact test. A two-sided p-value of ≤ 0.05 was considered statistically significant.

Results

A total of 1,097 patients were included in the study, of which 644 (58.8%) were males and 451 (41.2%) were females. Most of the reported epilepsy cases 1021 (96.1%) were from the province of Punjab. (Table 1).

Seizure type was classified in two different ways. The first classification was based on the presence or absence of fever (temperature of ≥ 100.4 F) at the time of seizure. If fever was present, the seizure was classified as febrile and if there was no fever, seizure was classified as afebrile. The other classification was based on ictal features. Six categories of seizures were identified as discussed in methods. Table 2 shows the frequency distribution for seizure type in the study population. A total of 798 (72.7%) patients were reported to have afebrile seizures, while the remaining 299 (27.3%) experienced febrile seizures. Generalised seizures were the most commonly reported seizure type, seen in 520 (49.8%) patients. (Table 2).

In term of aetiologies, 228(20.8%) cases were congenital, 74

Table-1: Frequency distribution table showing distribution of demographic variables.

Variable	N (%)
Age (in years)	
Less than equal to 1	380 (34.8)
Greater than 1 and less than 5	329 (30.2)
Greater than and equal to 5	382 (35.0)
Missing	6
Gender	
Male	644(58.8)
Female	451 (41.2)
Province	
Punjab	1021 (96.1)
Sindh	2 (0.2)
KPK	35 (3.3)
Kashmir	3 (0.3)
Gilgit Baltistan	1 (0.1)
Missing	35
Setting	
Rural	90 (8.5)
Urban	973 (91.5)
Missing	34

Table-2: Frequency distribution table showing distribution of the types, aetiologies, duration, and ictal features of seizures.

Variable	N (%)
Classification of seizures	
Afebrile	798 (72.7)
Febrile	299 (27.3)
Missing	0
Type of seizures	
Undiagnosed	329 (31.5)
Afebrile	45 (4.3)
Generalized	520 (49.8)
Focal partial	108 (10.3)
Refractory	3 (0.3)
Status Epilepticus	40 (3.8)
Missing	52
Etiologies of seizures	
Congenital	
Yes	228 (20.8)
No	869 (79.2)
Encephalopathy	
Yes	74 (6.7)
No	1023 (93.3)
Meningitis	
Yes	22 (2.0)
No	1075 (98.0)
Other infections	
Yes	10 (0.9)
No	1087 (99.1)
Structural, tumours and trauma	
Yes	51 (4.6)
No	1046 (95.4)

Contd. on Next...

Contd. on Previous...

Yes	56 (5.1)
No	1041 (94.9)
Unknown	
Yes	540 (49.2)
No	557 (50.8)
Patients presenting with single or multiple aetiologies	
Total patients with 1 aetiology	981 (89.4)
Total patients with 2 aetiologies	106 (9.7)
Total patients with 3 aetiologies	10 (0.9)
Duration of seizures (in minutes)	
Below 1 minute	17 (6.2)
1 - <3	116 (42.3)
3 - <5	60 (21.9)
5 - <10	53 (19.3)
10 -15	12 (4.4)
Above 15	16 (5.8)
Missing	823
Ictal Features	
Abnormal behaviour/movements	98 (16.6)
Facial twitching	13 (2.2)
Fever	7 (1.2)
Up-rolling of eyes	112 (19.0)
Up-rolling of eyes and frothing	206 (34.9)
Multiple features	152 (25.8)
None	2 (0.3)
Missing	507

(6.7%) were encephalopathies, 22 (2%) were associated with meningitis, 10 (0.9%) were due to other CNS infections, 51(4.6%) were linked to structural defects (trauma, tumours), and 56(5.1%) were due to other chronic conditions, while in 540 (49.2%) cases the aetiology was either idiopathic or unknown (Table 2). Many patients presented with multiple aetiologies; therefore, the added percentage is not 100%.

The most common duration of seizure was between 1 and 3 minutes seen in 116 (42.3%) patients. Among ictal features, up-rolling of eyes and frothing from the mouth were the most common, present in 206 (34.9%) patients. Fever was the least common ictal feature seen. Many patients, i.e. 152 (25.8%), had multiple ictal features simultaneously. (Table 2).

In majority of the patients 244 (22.2%) a precipitant for the seizure could not be identified. Among the remaining, the most common precipitant was light 184 (16.7%). In 62 (5.6%) patients, hyperventilation was also reported as the precipitant. The most common post-ictal features were attenuation and altered state of consciousness in 396 (36.1%) patients. Other notable features seen were fever, becoming paralysed, and weakness. Noteworthy conditions before seizures included vomiting, aggressive behaviour, haematemesis, black stools, and respiratory distress.

Table-3: Table showing relationship between aetiology and type of seizures.

Etiology of epilepsy	Type of seizures N (%)						p-value
	Undiagnosed	Afebrile	Generalised	Focal partial	Refractory	Non-convulsive	
Congenital	66 (20.1)	5 (11.1)	101 (19.4)	28 (25.9)	0 (0.0)	16 (40.0)	0.01
Encephalopathy	23 (7.0)	2 (4.4)	40 (7.7)	6 (5.6)	0 (0.0)	1 (2.5)	0.65
Meningitis	5 (1.5)	0 (0.0)	12 (2.3)	2 (1.9)	0 (0.0)	1 (2.5)	0.75
Other infections	2 (0.6)	0 (0.0)	6 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0.54
Structural, tumours & trauma	13 (4.0)	0 (0.0)	18 (3.5)	10 (9.3)	0 (0.0)	2 (5.0)	0.07
Other chronic conditions	15 (4.6)	3 (6.7)	33 (6.3)	1 (0.9)	1 (33.3)	0 (0.0)	0.01
Unknown	171 (52.0)	32 (71.1)	252 (48.5)	50 (46.3)	2 (66.7)	17 (42.5)	0.05

Discussion

Surveillance data on epilepsy from Pakistan is sparse and does not provide a true estimate of the prevalence of the disease in our population. Previous studies have indicated the prevalence of epilepsy in Pakistan to be 9.9 per 1,000 people.⁹ This study was conducted in one of the largest paediatric tertiary care hospitals in Punjab which caters to a mix of patients from both rural and urban areas, and ensured that the sample is a better representative of both settings. Data from this study indicates that epilepsy is twice as common in the urban population of Punjab as in rural population (24.3 per 1,000 people in urban as compared to 12.9 per 1,000 people in rural). This is in contrast from existing studies that report a reverse ratio with a two times higher prevalence in rural areas compared to urban.¹⁴ Distribution of epilepsy by gender in previous literature has reported no major difference or a higher male to female ratio of 2.4 to 3:1.¹⁵ The present study also suggests a similar distribution with a male to female ratio of 1.4:1. The age-specific estimates of prevalence of epilepsy from this study show an almost equal distribution across all three age brackets (≤ 1 , >1 - <5 , ≥ 5 years). This is consistent with the results of other studies.¹⁶

Many studies conducted globally have reported generalised seizures to be the most common type. A study conducted in India showed 78.8% of total epilepsy cases to be of generalised seizures, while another study conducted in China reported generalised seizures in 68.6% of cases.^{17, 18} Data from Pakistan also shows a similar trend.¹⁹ The results of the present study also support the global data with approximately half of the cases (49.8%) being of generalised type. Our study also reports refractory seizures to be the least common type. Afebrile and generalised seizures were more common in children less than or equal to one year of age, while focal partial and non-convulsive types were more prevalent in the age bracket of 1-5 years (P value <0.05). Research done previously in Pakistan studied epilepsy in the general population with fewer age categories in the younger population. Our study focused on epilepsy in paediatric population with three different categories within

the age bracket 0-18 years. Hence, results from our study indicating the prevalence of different types within these age brackets could provide important insights into the pattern of seizures in children.

Idiopathic aetiology has by far been the most widely reported in literature.²⁰ While 49.2% of our cases were also idiopathic, our study also showed a high prevalence of congenital causes of aetiology. Developmental delay and birth asphyxia were the most common features present in majority of epileptic patients. Some common congenital syndromes reported include benign Rolandic epilepsy, infantile spasms, and Ohtahara syndrome. Among encephalopathic aetiologies, acute disseminated encephalomyelitis was the most frequently reported cause. Amongst infectious causes, meningitis was twice as common the cause as any other infection. Majority of the meningitis cases were of tuberculous meningitis. Other infections included measles, typhoid, and neonatal hepatitis. The most common structural defect reported was hydrocephalus usually secondary to a congenital disease. Other chronic conditions leading to epilepsy that presented were hypsarrhythmia or modified hypsarrhythmia.

Patients were also assessed for the possible association between type of seizure and aetiology of epilepsy. A significant relation ($P<0.05$) with type of seizure was observed for two different etiologies: congenital and other chronic conditions. (Table 3) Patients with congenital epilepsy are more likely to present with generalised seizures compared to other types. Afebrile seizures are the least likely type to present in congenital cases of epilepsy. As for epilepsy associated with other chronic conditions, generalised seizures is seen to be the only common type of seizure to present in such cases. This association can be of value in narrowing the aetiologies of epilepsy when diagnosing patients presenting with a characteristic type of seizure. This can lead to early diagnosis and more timely treatment with better prognosis for the patient.

Limitations

The study included data from just a single tertiary care

centre within Punjab, hence a complete nationwide representation of epilepsy cases emerging in Pakistan was not possible. It is not possible to conduct multi-centre studies in Pakistan due to lack of national surveillance systems and scarcity of data registries. In addition, patients usually present at tertiary care hospitals either late or after receiving partial treatment. Therefore, it is difficult to analyse their initial status. Another limitation could be the retrospective nature of the study due to which the data that was missing or unknown in the patient files could not be traced back as the contacts of the patients had either changed or those who could be connected weren't able to recall the data when inquired about it.

Conclusion

To summarise, our study suggests the presence and prevalence of epilepsy in the paediatric population with an equal distribution across gender. Generalised seizures are the most common type of seizures in the paediatric population, while refractory seizures are the least common type. Congenital syndromes are the most common aetiology of epilepsy in this population. It is therefore recommended, that more nation-wide studies on epilepsy are needed to ascertain a true prevalence of the disease and formulate more effective interventions to reduce the burden of the disease.

Patient Consent: All data was obtained from hospital files which patients had consented to be used for research purposes upon admission to the hospital.

Disclaimer: None.

Conflict of Interest: None.

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References

1. Falco-Walter J. Epilepsy-Definition, Classification, Pathophysiology, and Epidemiology. *Semin Neurol.* 2020 ; 40:617-23. doi: 10.1055/s-0040-1718719.
2. Zimmern V, Korff C. Status Epilepticus in Children. *J Clin Neurophysiol.* 2020; 37:429-33. doi: 10.1097/WNP.0000000000000657.
3. Thijs RD, Surges R, O'Brien TJ, Sander JW. Epilepsy in adults. [Online] [Cited 2020 November 17]. Available from: URL: <http://www.thelancet.com/article/S0140673618325960/fulltext>
4. Fiest KM, Sauro KM, Wiebe S, Patten SB, Kwon CS, Dykeman J, et al. Prevalence and incidence of epilepsy: a systematic review and meta-analysis of international studies. *Neurology.* 2017; 88:296-303. doi: 10.1212/WNL.0000000000003509.
5. Beghi E. The Epidemiology of Epilepsy. *Neuroepidemiology.* 2020; 54:185-91. doi: 10.1159/000503831.
6. Ullah S, Ali N, Khan A, Ali S, Nazish HR. The Epidemiological Characteristics of Epilepsy in the Province of Khyber Pakhtunkhwa, Pakistan. *Front Neurol.* 2018; 9:845. doi: 10.3389/fneur.2018.00845.
7. Mogal Z, Aziz H. Epilepsy treatment gap and stigma reduction in Pakistan: A tested public awareness model. *Epilepsy Behav.* 2020; 102:106637. doi: 10.1016/j.yebeh.2019.106637.
8. Aziz H, Güvener A, Akhtar SW, Hasan KZ. Comparative epidemiology of epilepsy in Pakistan and Turkey: population based studies using identical protocols. *Epilepsia.* 1997; 38:716-22. doi: 10.1111/j.1528-1157.1997.tb01242.x.
9. Khatri IA, Iannaccone ST, Ilyas MS, Abdullah M, Saleem S. Epidemiology of Epilepsy in Pakistan: Review of literature. *J Pak Med Assoc.* 2003; 53:594-7.
10. Epi Info 2000 : a database, and statistics programme for public health professionals using Windows® 95, 98, NT, and 2000 computers. [Online] [Cited 2022 August 21]. Available from: URL: <https://stacks.cdc.gov/view/cdc/23208>
11. Clonic Seizures | Epilepsy Foundation. [Online] [Cited 2021 May 11]. Available from: URL: <https://www.epilepsy.com/learn/types-seizures/clonic-seizures>
12. Reflex Epilepsies | Epilepsy Foundation. [Online] [Cited 2021 June 3]. Available from: URL: <https://www.epilepsy.com/learn/types-epilepsy-syndromes/reflex-epilepsies>
13. Types of Seizures | Johns Hopkins Medicine. [Online] [Cited 2021 July 13]. Available from: URL: <https://www.hopkinsmedicine.org/health/conditions-and-diseases/epilepsy/types-of-seizures>
14. Garg D. Specific considerations for epilepsy in India. *Curr Med Issues.* 2020; 18:105-10. Doi: 10.4103/cmi.cmi_6_20.
15. Akhter N, Kamal Z, Rahman FU, Sultana P, Dhurrani Z. Awareness and Prevalence of Epilepsy; a Study in Educational Hubs at Sheringal, Khyber Pakhtunkhwa, Pakistan. *ARC J Neurosci.* 2018; 3:9-20. doi:10.20431/2456-057X.0301003.
16. Beghi E, Giussani G. Aging and the epidemiology of epilepsy. *Neuroepidemiol.* 2018; 51:216-23. doi: 10.1159/000493484.
17. Singh G, Singhal S, Sharma S, Paul BS, Bansal N, Chaudhary A, et al. Clinical characteristics of epilepsy in resource limited communities in Punjab, Northwest India. *Epilepsia Open.* 2020; 5:582-95. doi: 10.1002/epi4.12439.
18. Zheng G, Li F, Chen Y, Liu H, Wang S, Lao J, et al. An epidemiological survey of epilepsy in tropical rural areas of China. *Epilepsia Open.* 2021; 6:323-30. doi: 10.1002/epi4.12476.
19. Khan MNS, Akhter MS. Epilepsy in rural community of Pakistan: a description of one hundred patients. *J Coll Phys Surg Pak.* 2002; 12:728-30.
20. Afzal M, Shahid M. Children presenting with seizures-A hospital based study. *J Coll Phys Surg Pak.* 1999; 9:132-5.