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Epidemiology of Epilepsy among Pediatric Patients in Tabuk City

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ABSTRACT

Epilepsy is a common disease with serious health consequences. Knowledge regarding the clinical pattern of epilepsy is important for its management and prevention. The study aims to investigate the epidemiology of epilepsy among the children following King Salman Armed Forced Hospital in Tabuk city and to determine the frequency of epilepsy according to age, gender, consanguinity, and comorbidities. This is a retrospective observational study conducted among children, in King Salman Armed Forces Hospital in Tabuk, Saudi Arabia. Data from the patient's medical record was collected following its policy on data confidentiality, security, and safety. The study included 200 participants, 53.5% of them were males and 46.5% were females. 31% reported consanguinity between parents. The age of the first epileptic seizure was less than 1 year in 40.5% of patients, 2 years in 16.5%, 5 years old in 7% of patients, and 7 years old in 6.5% of patients. Epilepsy type was generalized in 81%, focal in 5.5%, and combined in 6%. The etiology of epilepsy was idiopathic in 52.5%, hypoxic-ischemic encephalopathy in 14.5%, mental insufficiency in 10%, GDD in 7.5%, ADHD in 3%, and ASD in 3%. Associated co-morbidities were reported as 4.5% infection, 5.5% genetic disorder, 26% structural disabilities, 4.5% metabolic disorder, 4% cerebral palsy, and 4% developmental delay. In conclusion, epilepsy in Tabuk City affected the young age group and was generalized in the majority, more than half were idiopathic. There is a need for further studies to examine the risk factors in greater detail.

Keywords: *Epilepsy, Seizure, Generalized epilepsy, Focal epilepsy, Saudi Arabia*

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INTRODUCTION

An epileptic seizure is a transient clinical sign and symptoms of abnormal, synchronous neuronal discharge reside in the cerebral cortex (Fisher *et al*., 2017; García, 2021; Lee *et al*., 2021; Mirghani *et al*., 2021). Epilepsy is clinically characterized by: two or more unprovoked (or reflex) seizures occurring more than 24 hours apart, or one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next ten years, or patient is already diagnosed as having epilepsy syndrome (Beretta *et al*., 2017).

According to the World Health Organization, the number of people who have epilepsy is around 50 million, given an estimated proportion between 4 and 10 per 1000 people (Scheffer *et al*., 2017).

Seizures are determined as advances in neuroimaging, molecular biology, and genomic technology. The excited International League Against Epilepsy ILAE classification system has revised in 2017. The new ILAE classification system has arranged the epilepsy into a hierarchical organization consisted of three levels, level one is seizure type (based on initial manifestation), which include focal, generalized, unknown and unclassified (Due to inadequate information or inability to place in other categories) further generalized seizure broken into motor and non-motor (absence) and focal seizure broken into either with impaired of awareness or without impaired of awareness, the clinical features during the seizure determine either the seizure motor or non-motor, Level two is epilepsy based on seizure type, which include focal (the active neuron responsible for seizure residing on one hemisphere on EEG), generalized (the active neuron responsible for seizure residing on both hemisphere on EEG), focal and generalized, combined if including both focal and generalized, and unknown if not focal or generalized, Level three is epilepsy syndrome, in which a group of signs and symptoms, Age group, EEG pattern indicate a distinctive, recognizable clinical seizure disorder. Etiology is incorporated along each level (Tabbal & Humedi, 2017; Alghamdi *et al*., 2019). The ILAE has defined six etiologic classes. These classes are: Structural, genetic, infectious, metabolic, immune, and unknown. More than one might often apply (Tabbal & Humedi,

2017).

A study was conducted in two hospitals in Tabuk city, to determine the prevalence and burden of the most commonly encountered pediatric medical disorders admitted of different age groups. A total of 325 cases were obtained from the two hospitals, the maternity and child hospital (MCH) with (222) 68% and King Khaled Hospital (KKH) with103 (31.7%) of cases, which showed 7.7% of all admitted cases, convulsions due to epilepsy or febrile convulsions were the most common neurological presentations resulting in hospitalization in children (Alghamdi *et al*., 2019).

In this study, we aimed to investigate the epidemiology of epilepsy among the children following in king Salman Armed Forced Hospital in Tabuk city and to determine the frequency of epilepsy according to age, gender, consanguinity, and comorbidities

MATERIALS AND METHODS

Study design

A retrospective observational study was carried out to investigate the epidemiology of epilepsy among children in Tabuk city, who were diagnosed and followed in King Salman Armed Forces Hospital in Tabuk, Saudi Arabia from January 2019 to December 2021.

Study area

Tabuk city in Tabuk region, Saudi Arabia.

Study setting

Medical files setting, King Salman Armed Forces Hospital, Tabuk, Saudi Arabia.

Study population

All children younger than 14 who were diagnosed and followed in King Salman Armed Forces Hospital.

Inclusion and exclusion criteria

Inclusion

- All children diagnosed with epilepsy in King Salman Armed Forces Hospital.

Exclusion

- Single or isolated seizures.
- Febrile seizures.
- Provoked seizures occur in close temporal association with an acute systemic, metabolic, or toxic insult or association with an acute central nervous system disorder, e.g., infection, trauma, or hemorrhage.
- Non-epileptic events, e.g., syncope, sleep disorders, or pseudo-seizures (behavioral disorders).
- Children older than 14 years and not restricted to the ILAE definition of epilepsy.

Sample size

Our target marginal error (confidence interval) is 5 % and the confidence level is 95% after calculations our sample size should be between 80 – 100 patients.

Sampling technique

All the records of the children in King Salman Armed Forces Hospital, Tabuk, Saudi Arabia during the stated period were approached.

Study duration

Our study was conducted over 8 months in total; 3 months of data collection will need from KSAFH's Medical files setting.

Data collection tools

Data will be gathered by paper-based files.

Data analysis plan

The data was entered by using Microsoft Excel and analyzed by using the Statistical Package for the Social Science (SPSS Inc. Chicago, IL, USA) version 23.

Ethical consideration

Approval for the research was obtained by the research ethics committee in KSAFH.

RESULTS AND DISCUSSION

The study included 200 participants, 53.5% of them were males and 46.5% were females. 31% reported consanguinity between parents. 49.5% reported a child aged 6- 12 years old, 19.5% reported an age between 12- 14 years old and 18% reported 3- 6 years old.

Table 1. Sociodemographic characteristics of participants (n=200)

Parameter		No.	%
Age	Less than one year old	11	5.5
	1–3-year-old	15	7.5
	More than 3- to 6-year-old	36	18.0
	More than 6- to 12-year-old	99	49.5
	More than 12- to 14-year-old	39	19.5
Gender	Male	107	53.5
	Female	93	46.5

In **Table 2**, the age of the first epileptic seizure was less than 1 year in 40.5% of patients, 2 years in 16.5%, 5 years old in 7% of patients, and 7 years old in 6.5% of patients. Epilepsy type was generalized in 81%, focal in 5.5%, and combined in 6%. Epilepsy was associated with epilepsy syndrome in 28.5% of participants.

As illustrated in **Table 3**, the etiology of epilepsy was idiopathic in 52.5%, hypoxic-ischemic encephalopathy in 14.5%, mental insufficiency in 10%, GDD in 7.5%, ADHD in 3%, and ASD in 3%.

Table 4 shows that 20.5% of participants reported a previous history of febrile seizure. 26% reported a family history of febrile seizure while 1.5% had a family history of a neuromuscular disorder. Associated co-morbidities were reported as 4.5% infection, 5.5% genetic disorder, 26% structural disabilities, 4.5% metabolic disorder, 4% cerebral palsy, and 4% developmental delay.

In the **Table 5**, the history of febrile seizure was significantly associated with consanguinity between parents and the age of the patient (P< 0.05).

Table 2. Age at first seizure and epilepsy type (n=200)

Parameter		No.	%
Age of patient at first seizure	less than 1	81	40.5
	1	12	6.0
	2	33	16.5
	3	12	6.0
	4	9	4.5
	5	14	7.0
	6	8	4.0
	7	13	6.5
	8	3	1.5
	9	9	4.5
	10	3	1.5
	Neonatal	3	1.5
Epilepsy type	Focal	23	11.5
	Generalized	162	81.0
	Unclassified Missed data	15	7.5

Table 3. Etiology of epilepsy among study participants (n=200)

Etiology	Infection	9	4.5
	Pre- term	18	9.0
	Genetic	11	5.5
	Structural	52	26.0
	Metabolic	9	4.5
	Neonatal encephalopathy	4	2.0
	Chromosomal	2	1.0
	Hydrocephalus	2	1.0
	mild ventricular dilatation and cerebral sulci are enlarged	2	1.0
	Cerebral palsy	8	4.0
	Developmental delay	8	4.0
	periventricular leukomalacia	8	4.0
	Missed data	103	51.5

Table 4. Co-morbid diseases and family history (n=200)

Parameter		No.	%
Associated co-morbidity	Infection	9	4.5
	Preterm	18	9.0
	Genetic	11	5.5
	Structural	52	26.0
	Metabolic	9	4.5
	Neonatal encephalopathy	4	2.0
	Chromosomal	2	1.0
	Hydrocephalus	2	1.0
	mild ventricular dilatation and cerebral sulci are enlarged	2	1.0
	Cerebral palsy	8	4.0
	Developmental delay	8	4.0
	periventricular leukomalacia	8	4.0
	Missed data	103	51.5

Table 5. Association between the history of febrile seizure with sociodemographic characters of participants (n=200)

		History of febrile seizure				Total (N=200)	P value
		Yes	No	Not associated	Not mentioned		
Age	Less than one year old	0	11	0	0	11	0.025
		0.0%	10.3%	0.0%	0.0%	5.5%	
	1–3-year-old	2	10	0	3	15	
		4.9%	9.3%	0.0%	6.0%	7.5%	
	More than 3- to 6-year-old	10	18	2	6	36	
		24.4%	16.8%	100.0%	12.0%	18.0%	
	More than 6- to 12-year-old	21	49	0	29	99	
		51.2%	45.8%	0.0%	58.0%	49.5%	
	More than 12- to 14-year-old	8	19	0	12	39	
	Less than one year old	19.5%	17.8%	0.0%	24.0%	19.5%	
Age of patient at first seizure	less than 1	14	46	2	19	81	0.027
		34.1%	43.0%	100.0%	38.0%	40.5%	
	1	1	11	0	0	12	
		2.4%	10.3%	0.0%	0.0%	6.0%	

	2	15	10	0	8	33	
		36.6%	9.3%	0.0%	16.0%	16.5%	
	3	0	6	0	6	12	
		0.0%	5.6%	0.0%	12.0%	6.0%	
	4	0	5	0	4	9	
		0.0%	4.7%	0.0%	8.0%	4.5%	
	5	4	5	0	5	14	
		9.8%	4.7%	0.0%	10.0%	7.0%	
	6	1	7	0	0	8	
		2.4%	6.5%	0.0%	0.0%	4.0%	
	7	5	7	0	1	13	
		12.2%	6.5%	0.0%	2.0%	6.5%	
	8	0	2	0	1	3	
		0.0%	1.9%	0.0%	2.0%	1.5%	
	9	0	5	0	4	9	
		0.0%	4.7%	0.0%	8.0%	4.5%	
	10	0	1	0	2	3	
		0.0%	0.9%	0.0%	4.0%	1.5%	
	Neonatal	1	2	0	0	3	
		2.4%	1.9%	0.0%	0.0%	1.5%	
Gender	Male	28	52	2	25	107	0.085
		68.3%	48.6%	100.0%	50.0%	53.5%	
	Female	13	55	0	25	93	
		31.7%	51.4%	0.0%	50.0%	46.5%	
Epilepsy classification	Combined	5	4	0	3	12	0.604
		12.2%	3.7%	0.0%	6.0%	6.0%	
	Focal	2	4	0	5	11	
		4.9%	3.7%	0.0%	10.0%	5.5%	
	Generalized	32	90	2	38	162	
		78.0%	84.1%	100.0%	76.0%	81.0%	
	Unknown	2	9	0	4	15	
		4.9%	8.4%	0.0%	8.0%	7.5%	

Epilepsy is the most common serious neurological disorder and is one of the world's most prevalent non-communicable diseases. The global prevalence of active epilepsy is around 6.38/1,000 persons. In the Arabian region, the median prevalence of active epilepsy is 4.4/per 1000 persons. In the Kingdom of Saudi Arabia (KSA), the last prevalence for active epilepsy cases was conducted in 2001 and showed an estimate of 6.5/1000 persons (Scheffer *et al*., 2017).

Onset age incidence is more commoner in early age and adolescence. This seems to be the trend worldwide (Saarinen *et al*., 2016; Farghaly *et al*., 2018; Minardi *et al*., 2019; Stephen *et al*., 2020; Alva-Díaz *et al*., 2021) and in accordance with our study results as the age of first epileptic seizure was less than 1 year in 40.5% of patients, 2 years in 16.5%, 5 years old in 7% of patients and 7 years old in 6.5% of patients. This was comparable to a previous Saudi study that reported that the most common age of patients was >6y – 12y (50 %) 110 cases then in the group aged>3y to 6y 41 cases (18.6%), there were 30 cases in the group of age 1 to 3 years (13.6 %), from birth to one year the cases were 26 (11.8%), >12y was the smallest group, with 13 cases (5.9 %) (Alva-Díaz *et al*., 2021). Another study reported that the majority of cases (83) had their first seizure in their first year of life (37.7 %), 46 cases (20.9%) in the 3y-6y age group, 45 cases (20.5%) in the >1y-3y age group, and 14 cases (18.6%) in the >6y-12y age group (Alva-Díaz *et al*., 2021). Regional research in Upper Egypt reported that the majority of the individuals evaluated (80%) claimed that their seizures began in infancy or early childhood (under 6 years) (Asnakew *et al*., 2022).

Epilepsy type was generalized in 81% of our study participants, focal in 5.5%, and combined in 6%. A previous study reported that generalized tonic/clonic accounted for (28,6%), generalized tonic (28.6%), and (4.1%) were atonic, while (10.1%) had infantile spasms, myoclonic benign myoclonus (4.1%) was discovered, progressive myoclonic myoclonus (4.1%). Absence seizures affected (4.1%). Simple partial seizures were detected in (2.7%) and complicated partial seizures in (3.6 %). Febrile convulsions were observed in (10 %). Multiple types of seizures were in (15 %) (Alva-Díaz *et al*., 2021). Another study reported that 38 patients (28%) had partial seizures, with secondary generalization in 29 of them. There were simple partials in 21 cases and complex

partials in 17. (21%) had primary generalized seizures including 4 children with absence (Srivastava *et al*., 2019). A study recorded that infancy was marked by focal seizures, whereas adulthood was marked by generalized seizures, The most prevalent seizure type among children and adolescents was generalized tonic-clonic seizures (Asnakew *et al*., 2022).

Children with epilepsy may also experience concurrent medical issues as well as cognitive and behavioral challenges, which will compound their suffering in addition to their repeated epileptic seizures. They are more likely to have academic underperformance, learning challenges, mental health issues, social isolation, and low self-esteem (Alsulami *et al*., 2022). Associated co-morbidities in our study were reported as 4.5% infection, 5.5% genetic disorder, 26% structural disabilities, 4.5% metabolic disorder, 4% cerebral palsy, and 4% developmental delay. A study reported that epilepsy was associated with infantile hemiplegia in 9 (7%) cases with or without mental retardation, and other types of cerebral palsy in 17 cases (12%). 5 other patients (4%) had microcephaly (Srivastava *et al*., 2019). Alongside isolated mental impairment, delayed motor and cognitive development occur frequently. Learning impairments were present in some patients during their school years. This is probably a result of both their underlying problems and the side effects of the antiepileptic medications they are taking. Clinical departments that care for epileptic children on anticonvulsant drugs tend to underestimate this latter effect (Alva-Díaz *et al*., 2021).

In our study, 20.5% of participants reported a previous history of febrile seizure. 26% reported a family history of febrile seizure while 1.5% had a family history of a neuromuscular disorder. This was in the line with a previous study that reported that epilepsy followed head injury in 5 cases (4%), childhood infection (probably meningoencephalitis) in 6 cases (4%), and stroke in 2 cases (Srivastava *et al*., 2019). Idiopathic epilepsy was the most common underlying cause of epilepsy (59.4%), while prenatal problems were the most common etiology for structural/metabolic epilepsy (Asnakew *et al*., 2022). Many studies have reported, Idiopathic epilepsy represents 73.5–82.6% of cases, and early childhood brain damage such as cerebral palsy, mental retardation, and congenital and hereditary diseases were the major cause of symptomatic epilepsy (Huseyinoglu *et al*., 2012; Downs *et al*., 2018). Febrile seizures, history of brain injuries, family history of epilepsy, severe maternal disease during breastfeeding, and jaundice of the newborn have had a statistically important link to the occurrence of epilepsy (Daoud *et al*., 2003).

The genetic component appears to have a substantial influence on the development of the disease, even though the origins of epilepsy are well-recognized to be complex. Numerous of the included research indicated that family history was a significant risk factor for the onset of epilepsy. For instance, a study from Jordan found that epileptic cases were 9.8 times more likely to indicate a positive family history of epilepsy than the control group (Babtain, 2013) Our study reported that, a history of febrile seizure was significantly associated with consanguinity between parents. Additionally, a study from Saudi Arabia discovered that 117 patients (27%) in a cohort of 420 epilepsy patients had a positive family history of the disorder (Chentouf *et al*., 2015). Additionally, a case-control study in Algeria found that there was a 5.37-fold increased risk of having a first-degree relative with epilepsy (Lee *et al*., 2021).

The study was limited by being retrospective and some important information including a family history of epilepsy, consanguinity between parents, and a history of febrile seizure, associated with epilepsy syndrome was missing.

CONCLUSION

In conclusion, most of the results of our studies were in accordance with similar studies from Saudi Arabia as well as international studies. There is a need for further case-control studies to examine the attributable risk in greater detail. It is necessary to address additional topics such as the incidence, risk factors, and natural histories of epilepsy. Unresolved issues imply that more community studies are necessary to gather thorough and accurate data on these problems in our environment and to plan for appropriate interventions.

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