Epilepsy in Saudi Arabia: Prevalence in Different Regions, Causes, Risk Factors, and Management: A Systematic Review

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ABSTRACT

Background: Epilepsy is the most prevalent neurological condition and is one of the most prevalent non-infectious diseases in the world. It has been reported that epilepsy is the commonest disorder encountered in most pediatric neurology clinics in the developing world. **Objective:** Is to identify prevalence in different regions, causes, risk factors, and management of epilepsy among Saudi children. **Method:** This is a systematic review including PubMed, Google Scholar, and EBSCO that by examining randomized trials, uses the following terms in different combinations: epilepsy, prevalence, causes, risk factors, and treatment of epilepsy amongst Saudi children. **Results:** The review included 9 randomized studies that identified prevalence in different regions, causes, risk factors, and treatment of epilepsy amongst Saudi children. **Conclusion:** High prevalence of epilepsy in infants and children was observed in Saudi Arabia. Family History and consanguinity among parents are well-identified risk factors in KSA.

Key Words: *Epilepsy, Prevalence, Causes, Risk factors and managing epilepsy in Saudi children.*

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INTRODUCTION

Epilepsy is a category of progressive and complicated neurological diseases characterized by epileptic seizures of an intermittent and crippling nature [1-3]. It is the most prevalent non-infectious, neurological condition in the world [4-6]. It has been reported that epilepsy is encountered in most pediatric neurology clinics, especially in the developing world [7].

The prime reason for epilepsy is unidentified in about 60% of all cases [8]. Genetic and inherited conditions, such as severe brain damage, stroke, and complications arising from prior illnesses, may result in epilepsy, with the involvement of both triggers in many cases [9]. Epilepsy etiology is categorized as systemic, hereditary, and unknown according to the 2010 International League against Epilepsy (ILAE) study [10].

Estimates for epilepsy in childhood are approximately 0.5% [11]. The latest findings have indicated that the highest occurrence appears in infants aged less than one year and 1 to 12 years as well at a rate of 102/100,000 cases per year, in children aged 11 to 17 years, the occurrence reported as 21–24/100,000 cases [12]. In developed nations, an average of around 50 per 100 000 children experiences epilepsy per year [13].

Epileptic attacks of convulsions can differ considerably between patients. An epileptic seizure is a temporary condition of manifestations attributed to irregular, excessive, synchronous neural activation in the brain [14]. Some of them take little seconds and even go unnoticed;

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others only affect one arm or one leg, while others affect the entire body [15]. Epileptic seizures typically do not last for long. If convulsions last more than five minutes, it is referred to as "status epilepticus." The utmost category of epileptic convulsions arising in infancy and childhood, though, is the feverish convulsions. Febrile seizures are sporadic seizures triggered by fever; they do not specify the existence of epilepsy, even if frequently repeated [16]. Epileptic seizures may cause physical harm mostly if the child has generalized seizures as the whole body convulses uncontrollably [17]. Fear of experiencing seizure is very distressing, particularly if they occur recurrently. Children with epilepsy have substantial contests because epilepsy could be severe and restrict their capability to study and learn. Shame and deficient of public awareness about the disorder can undesirably affect the communal and emotional utility of children [18].

Children are managed by pediatric neurologists. As with many medical disorders, history taking is the key to the evaluation of epilepsy [19]. Key historical points include the history of seizures, medication use history, past medical history, and history of alcohol or illegal drug use. History of immunosuppression or cancer is also important [20]. Electroencephalography (EEG) is a biomarker for epilepsy diagnosis [21]. Electrolytes should also be obtained and in patients with fever; lumbar puncture should be addressed [22]. Imaging is recommended if an acute intracranial phase is suspected in cases with a history of acute head trauma, history of malignancy, immunocompromising, fever, chronic headache, anticoagulation, patients older than 40 years, or in case of focal seizures [23].

Many drugs may be effective in the management of epilepsy as first-line or adjunctive medications. The choice can be influenced by side effects and may be performed in conjunction with a neurologist [24]. Drugs for epilepsy can be classified according to their mode of action, they comprise sodium channel blockers (carbamazepine, oxcarbazepine, eslicarbazepine, phenytoin, fosphenytoin, lamotrigine, lacosamide, and zonisamide), and GABA receptor agonists (benzodiazepine and barbiturates). Other medications with related mechanisms comprise GABA reuptake hinders (tiagabine), hinders of GABA-transaminase (vigabatrin), glutamate adversaries (topiramate, felbamate, perampanel), medicines with bonding to synaptic vesicle 2A protein (levetiracetam, brivaracetam), in addition to medications with various mechanisms (gabapentin, pregabalin, valproic acid) [25]. The chief line of management is benzodiazepine like diazepam, midazolam, or lorazepam. Phenobarbital and Phenytoin are considered second-class epilepsy medications and are typically used when benzodiazepines fail [26].

The study objective is to identify prevalence in different regions, causes, risk factors, and management of epilepsy among Saudi children.

METHODOLOGY:

A systematic review was carried out, including PubMed, Google Scholar, and EBSCO using the following terms in different combinations: epilepsy in children, childhood epilepsy, epilepsy in Saudi children, and epidemiology of childhood epilepsy. We included all full texts [randomized controlled trials, observational, and experimental studies which to identify prevalence in different regions, causes, risk factors, and management of epilepsy among Saudi children. As it is clear in Figure (1), the authors extracted the data, and then the author's names, year, and region of publication, the study type, period of study, and the result were reported (Table 1).

Statistical Analysis:

No software has been utilized to analyze the data. The data was extracted based on a specific form that contains (Author's name, publication year, country, methodology, and results). These data were reviewed by the group members to determine the initial findings, and identify prevalence in different regions, causes, risk factors, and management of epilepsy among Saudi children. A double revision of each member's outcomes was applied to ensure the accuracy of the work.

RESULTS:

The search of the mentioned databases returned a total of 90 studies that were included for title screening. Forty-six of them were included for abstract screening, which leads to the exclusion of 21 articles. The remaining 25 publications full-texts were reviewed. The full-text revision leads to the exclusion of 16 studies, and 9 were enrolled for final data extraction (Table 1).

The included studies had different study designs.

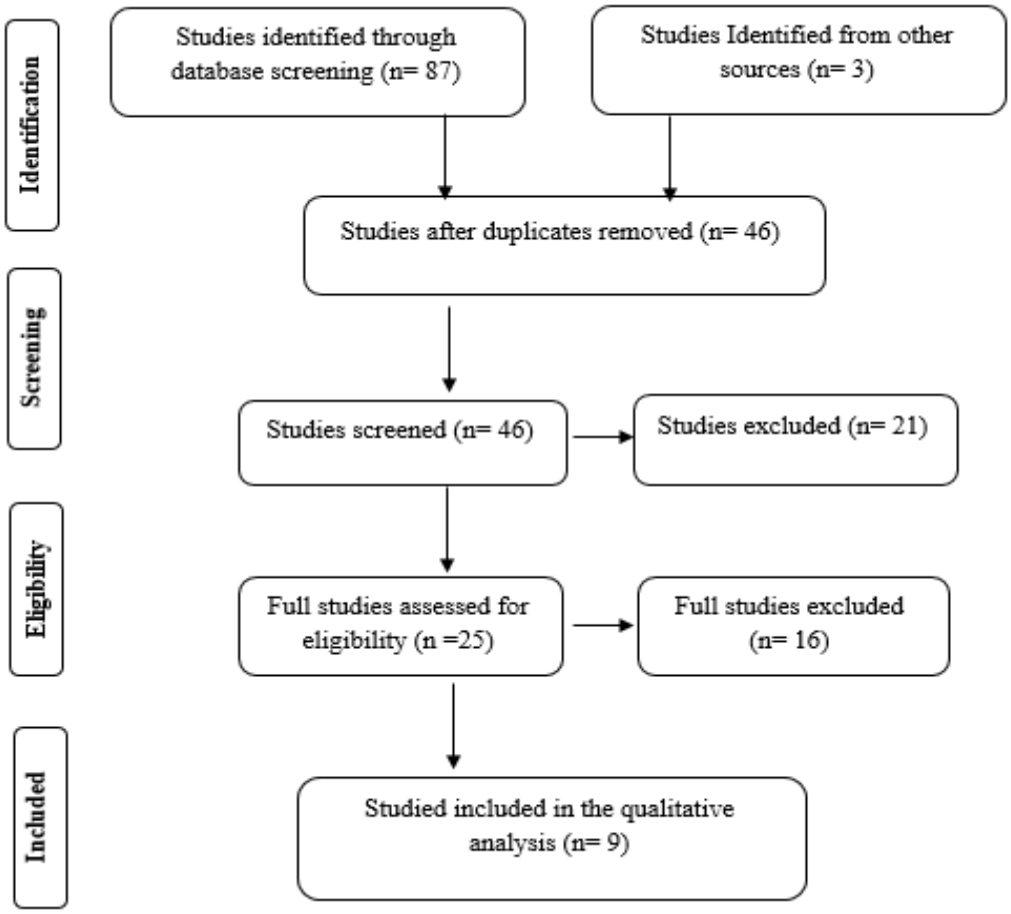

Figure 1: Flow chart representing the process of data extraction for the study

Table 1: Author, Country, Year of publication, Methodology, and Results

Author, Year, Country	Objective, Methods	Results
Alsharif, Mahmoud Mohammed et al. [27] 2017 Turaif city, Saudi Arabia	A community-based, descriptive, cross-sectional study was carried out in Turaif city, from July 2016 to January 2017 to measure the prevalence rate of epilepsy and its associated risk factors in children and adolescents attending schools.	The prevalence rate of epilepsy was reported as (5.5%); 68.2% of the cases were males. Consanguinity between parents was 59.1% (p=0.000). Family history was reported in 68.2% of cases (p=0.000).
Hamdy, Nermin A et al. [28] 2014 Al Qassim, Saudi Arabia	In a case-control epidemiological study, we examined the hospital files of epilepsy cases, in the period between October 2011 and April 2012 to define the most common seizure type, etiologies, and progress of cases in King Fahad Specialist Hospital- Al-Qassim.	The study showed that (76.2%) bulk of cases had generalized tonic-clonic seizures; followed by (7.6%) complex partial seizures. 73% of our patients suffered from epilepsy without apparent cause. Cerebro Vascular injuries and Skull trauma were the most common causes of epilepsy. Hemiplegia, intellectual delay, and psychiatric disease were the most associated comorbidity. No significant relation between controlled seizure and duration of illness or hospitalization or EEG changes was observed.

Yasir Alanazi et al. [29] 2018 North region of Saudi Arabia	A cross-sectional descriptive study was carried out to measure the prevalence rate of epilepsy in children and adolescents of schools (6-18 years) in the Northerly region of Saudi Arabia and consanguinity among mothers and fathers in the educational time 2016-2017.	The study reported that; 59.1% of epilepsy cases had mothers and fathers who were cousins and consanguinity in mothers and fathers was considerably concomitant with the presence of epilepsy. 68.2% had epilepsy cases in their families, this was statistically related to its occurrence (p=0.000).
Subki AH, et al. [30] 2018 Jeddah, Saudi Arabia	A Multicenter Cross-Sectional Study was conducted to measure to how extent epilepsy affects the quality of life of the affected children and their relatives using a self-reported translated form of the "Impact of Pediatric Epilepsy Scale" (IPES) survey tool (questionnaire) completed by the mamas of kids with epilepsy, enlisted in three hospices in Jeddah, Saudi Arabia	The study concluded that childhood epilepsy may have a great influence on the lives of children and families. Non-Saudi children and children with severe seizures had poorer quality of life. These groups need more help in handling the effects of epilepsy on their day-to-day functioning and quality of life. Family income, migrant status, cause, and frequency of seizures are all significant factors affecting the lives of children with epilepsy.
Alonazi, Noufa A et al. [9] 2018 Alkhobar, Saudi Arabia	A retrospective chart review study was carried out between January 2010 and December 2011 at a tertiary center in Saudi Arabia to appraise the reasons for epilepsy in the included 212 children suffering during their first 2 years of age through the International League Against Epilepsy classification released in 2010.	The most frequent seizure type was tonic-clonic at 106 (56 percent), followed by clonic at 29 (15.3 percent), myoclonic at 22 (11.6 percent), and tonic at 16 (8.4 percent). Pyramidal symptoms, global developmental delay, hypotonia, micro/macrocephaly, and pathological computed tomography and/or magnetic resonance imaging of the brain were more frequent in the structural/metabolic community ($p < 0.05$). Electroencephalography was irregular in 136 (72 per cent) patients, especially in the structural / metabolic community ($p = 0.011$).
Bahkali MA, et al. [31] 2019 Riyadh, Saudi Arabia	A descriptive, cross-sectional study conducted to assess the quality of life issues among children participated in the study using a self-administered questionnaire on 100 mothers having an epileptic child younger than 12 years during the period from November to December 2012.	The study reported that 40% of the mothers sensed that their epileptic child may hurt themselves throughout epileptic crises, 58% watch their children for the terror of damage or injury, and only 50% of mothers like to know how to act during an epileptic attack.
Saeed M, et al. [32] 2014 Taif, KSA.	A descriptive, Cross-Sectional study was conducted over 4 years to investigate the prevalence rate of associated behavioral problems and prognosis with Benign Childhood Epilepsy with Centro Temporal Spikes including thirty-two children.	The study found that the prevalence of BRE is (7.44%). Six patients (18.8%) specified a household history of BRE. While 28 cases suffer from right side centrotemporal releases and 4 cases had two-sided discharges.
H. Alghamdi AA et al. [33] 2019 Abha City, Aseer Region, KSA	A retrospective study on epileptic children in Maternity and Children Hospital, Abha, Saudi Arabia for the period from Oct2015-March2016 to assess characteristics of affected	Sixty percent of seizures were generalized tonic/clonic. Many comorbidities were defined in affected cases. The most affected age group was 50% (6 years – 12 years).

	children and the pattern of their seizure disorders	
Rabie Faten M. et al. [34] 2016 Abha and Khamis Mushait, KSA	A retrospective study carried in schools to investigate the prevalence rate and risk influences of epilepsy in Abha and Khamis Mushait, KSA using a special simplified questionnaire representing all possible forms of epilepsy.	Twenty out of 2500 students had epilepsy. The reported causes of epilepsy were cerebral trauma and febrile convulsions. Family history of epilepsy and the consanguinity between parents were risk factors.
Hommady Raid H. et al. [35] 2017 Riyadh, KSA	A retrospective chart review study conducted in a tertiary center, Riyadh, KSA to investigate predictors of SE outcome among all diagnosed children (≤ 14 years old) of SE admitted to the inpatient department be-tween January 2005 and December 2015.	The average status epilepticus SE-related mortality rate was 2.6%. Four patients had an SE period greater than 24 hours. Age, ethnicity, SE length, and EEG results were not predictors of negative outcomes. Pediatric SE is linked with neural disease.

DISCUSSION:

Epilepsy is distressing > 50 million persons worldwide (85% of them in developing countries). Many previous kinds of research have argued epilepsy in school-age kids. The worldwide incidence of childhood epilepsy is estimated to be 4-8/1000 inhabitants [36]. In Turkey, a study found that 22 children among 1,625 school students were diagnosed as epileptic. The prevalence rate of active epilepsy was 4.9/1000 in males and 12.4/1000 in females with a total of 8.6/1000 [37]. In Kayseri's study [38], the reported prevalence rate of epilepsy, in boys was 9/1000, while it was 6/1000 in females with a total 8/1000. A Bahkali MA, et al. study in KSA discussed above reported 6.5/1000 as the prevalence of epilepsy as the highest in Arab countries [31]. Another study reported an overall prevalence rate of 6.54/1000 for active epilepsy similar to the results of other studies from developed and developing countries [39]. The average incidence rate in 32 previous types of research around the world has been estimated at 5.16/1000 [40]. Prevalence in Pakistan was reported as 9.8/1000 [41], Ecuador 6.7–8/1000 [42], USA 5.7–6.8/1000 [43], Nigeria 5.3/1000 [44], China 4.8/1000 [45], India 4.8/1000 [46] and Tunisia 3.6/1000 [47].

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 [37]. In another study, premature birth increased the risk of epilepsy 2.6 times, and reduced family salary, augmented 3.3, and 1.6, respectively [38]. Consanguinity between parents was also significantly associated with epilepsy ($P<0.05$) [29].

Regarding mortality rate, a systematic review reported that studies with high quality showed a lower incidence of mortality, between 2.7% to 5.2%, and morbidity of less than 15% [47]. Moghaddasi observed that epilepsy patients had higher death rates than people without epilepsy [48].

Acute characteristics and fever causes are found to be the commonest reasons for SE, agreeing with another study reported that they only account for 8.6% and 14.7%, correspondingly [49, 50]. On the other hand, Kroczka et al. [51] reported that physical/metabolic epilepsy which is a result of brain illnesses that lead to retarded developmental, neural diseases, and atypical EEG communal in children attending the hospitals with convulsions [52]. The study also reported different causes of epilepsy with adjustable rates as intracranial infection cerebral malformation, degenerative brain disease, and perinatal brain damage. In a study discussed in the Table above, perinatal insults like hypoxic-ischemic encephalopathy were the most frequent causes of structural/metabolic epilepsy, followed by metabolic disorders, infections, and trauma [9]. Strokes were reported to be the cause of epilepsy in 49% of patients included in a study in England [53] and 46% in Sweden [54]. High consanguinity rates between parents in Saudi Arabia were also identified as a risk factor as mentioned above with a percentage of 59% [55].

New research in Saudi Arabia found a high prevalence of brain CT abnormalities (42.7%) in children who had their first obvious seizure [44]. Another research revealed irregular EEG results in the majority of patients in the structural/metabolic community compared with the other groups which can be explained by the fact that the etiology of brain insult in the structural/metabolic group tends to be more pertinent and, therefore, likely to show abnormal EEG findings [9, 53].

CONCLUSION:

High incidence rates of childhood epilepsy were observed in Saudi Arabia. Family History and consanguinity

between parents are well-identified risk factors in KSA. Recommendations for taking appropriate measures to minimize the risk factors of the disease. We also recommend the health system to encourage well-planned health awareness campaigns and conferences to increase the public awareness about causes and risk factors of the disease and to increase the knowledge of parents about immediate seizure management in their children.

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