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Pediatric Epilepsy and its Health Conditions in UAE: A Review Article

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ABSTRACT

Epilepsy is one of the major public health concerns in Arab countries, as it contains a total of 80% of cases worldwide. There are two age peaks for onset: childhood and adulthood, but children experience the highest burden. Epilepsy in childhood can have an impact on educational performance as well as psychological and social interaction. Epileptic patients are also susceptible to a wide range of other frequent health issues. The co-morbidities often cause more burdens and difficulties than the seizures themselves. Pathologically, epilepsy is of three types: acquired, idiopathic, and developmental or genetic origin. The disease is based on glutamate and GABA excitation and inhibition, respectively. EEG, MRI, PET, SPECT, and CT scan are among the main diagnostic procedures available for the treatment. This review covered all the research studies published in peer-reviewed journals on Web of Science between 2014 and 2024. It focused on seeking a better understanding of epilepsy, its kinds, accessible therapies, and co-morbidities by providing significant insights that can benefit the UAE's healthcare system. EEG and MRI are the two effective techniques used for epilepsy treatment. The UAE healthcare system should focus on adopting the genetic basis of the disease for a precise and targeted treatment.

INTRODUCTION

Epilepsy is known as a brief recurrence of symptoms and indicators brought on by erratic, synchronous, or excessive neuronal activity in the human brain (Hussein *et al.*, 2018; Naseer, 2022). Several uncontrollable body movements, either the whole body or a specific body part, can cause epilepsy. Extreme or unusual electrical charge disruptions in the various parts of the brain cause epileptic seizures ranging from brief attention spans to protracted spasms (Panebianco *et al.*, 2016). Undesirable clinical features can generally follow epileptic seizures. Patients experience neurological, behavioural, and emotional consequences from these seizures, particularly if they recur frequently (Swanson *et al.*, 2024). Even though epilepsy is one of the oldest known conditions in the world, dating back to 4000 BC in written records, the general public's perspective of the condition has not changed much over time. It is still dominated by myths and incorrect notions (Kaculini *et al.*, 2021). Epileptic patients face prejudice and social stigma, misunderstandings, and unfavourable views about the condition in general, which may avert these people from getting treatment and living self-assured lives (Anwar *et al.*, 2020).

Epilepsy is defined as a chronic, non-communicable brain disorder characterized by neurobiological, cognitive, psychological, and social implications, as well as seizure recurrences by abnormal electrical activity of the brain (Beghi, 2020; Tenney, 2020). Pediatric epilepsy, the term used to describe the disease when it appears in the pediatric population, is a complex neurological disorder that covers a diverse range of seizure types. Seizures can be apparent as staring spells, convulsions, subtle facial twitches, or short lapses in consciousness. An epileptic seizure is a brief episode of signs and symptoms brought on by abnormally high or synchronized brain neuronal activity based on guidelines of the International League Against Epilepsy (Fisher *et al.*, 2014), according to pediatric research that uses the International Classification of Epileptic Seizures, (Perucca *et al.*, 2018; Schubert-Bast *et al.*, 2023).

To understand pediatric epilepsy, a thorough knowledge of age-specific parameters must be required because seizures can appear in various ways depending on the age of the child. Infants may show modest symptoms like cyclic eye movements, while older kids may have more apparent convulsions (Manokaran *et al.*, 2024). Besides clinical issues, children with pediatric epilepsy may have significant challenges to their social, cognitive, and emotional development (Naseer, 2022). Seizures can affect a child's learning, memory, and focus, adversely affecting academic performance and general quality of life. Moreover, social isolation and psychological issues for the children and their families might be intensified by the stigma attached to epilepsy (Clifford *et al.*, 2023). The present study aimed to enhance the understanding of epilepsy, its types, available treatments, and co-morbidities by contributing valuable insights that can improve the UAE's healthcare system.

LITERATURE REVIEW

Types of Epilepsy

Generalized Seizure Epilepsy: Generalized seizure epilepsy is caused by a widespread, excessive electrical discharge that simultaneously affects both the brain hemispheres. When the entire brain is involved, there may be a rhythmic, whole body jerking with stiff limbs, loose muscle tone, and blink-and-stare symptoms. Generalized seizure epilepsy is divided into (Guerrini *et al.*, 2019):

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Idiopathic Generalized Epilepsy

Idiopathic generalized epilepsy, the most prevalent type of epilepsies in children and teenagers, is characterized by distinct seizure patterns, onset age, and distinctive electroencephalogram (EEG) abnormalities. About 15-20% of all epilepsies are classified as idiopathic generalized epilepsies (IGEs), and a majority of them are also known as genetic generalized epilepsies (GGEs).

Cryptogenic Generalized Epilepsy

Cryptogenic generalized epilepsy is defined as seizures whose genesis is unclear but thought to be symptomatic. Almost 40% of all adult-onset cases have cryptogenic epilepsy, with a small percentage in the pediatric age group (Chow & Poon, 2022). Anti-epileptic medications are generally used for the treatment of many epilepsy cases, and 50% of patients can live a seizure-free life after the treatment. However, the prognosis of cryptogenic epilepsy is unclear, and despite intensive therapy, seizures return frequently. The likelihood of recurrence is 48% after two years for cryptogenic seizures with an abnormal EEG.

Symptomatic Generalized Epilepsy

Symptomatic epilepsies are focal or diffuse brain abnormalities and are classified by numerous etiological classifications, including structural, genetic, metabolic, immunological, infectious, and unknown.

Focal Seizure Epilepsy

Focal seizures are triggered by an aberrant electrical discharge in any brain hemisphere. These seizures are further divided based on how they affect the child's memory, consciousness, and memory. Partial seizure is another name for focal seizure epilepsy. According to population-based studies, up to 60% of all seizures (Specchio *et al.*, 2022). It is crucial to characterize the symptoms and indications of focal seizures. Brain trauma, infections, strokes, and tumours are the leading causes of focal seizures and epilepsy. Only a small portion of the brain is affected, so a child is fully conscious during a seizure. The common types of focal seizure epilepsies are:

Gelastic Epilepsy

Gelastic epilepsy is characterized by rare epileptic symptoms represented by fits of stereotyped laughing or smiles that last for less than a minute. These laughs are unprovoked and not triggered by external factors. The primary aetiology of gelastic epilepsy is its well-established correlation with hypothalamic hamartoma in children. The seizures of gelastic epilepsy are started with high frequency in childhood, early puberty, and general cognitive impairment (Mirandola *et al.*, 2023).

Temporal Epilepsy

The majority of focal seizures started in the temporal lobe region of the brain fall under the category of temporal epilepsy. These seizures are divided into mesial and neocortical or lateral temporal epilepsy based on involved neural circuity (Maizuliana *et al.*, 2020). Seizures with mesial temporal epilepsy originate from the amygdala, entorhinal cortex, parahippocampal gyrus, and hippocampal regions. The temporal neocortex, parietal and occipital junctions, and the associative sensory areas (language, hearing, and vision) are the brain regions implicated with neocortical temporal epilepsy. Apart from neurological aspects, psychological co-morbidities such as anxiety, inter-ictal dysphoria, and depression with cognitive, behavioural, and learning impairment are frequently observed in temporal epilepsy, especially in the pediatric population (Vinti *et al.*, 2021).

Mechanism of Epilepsy

Epilepsy, the most prevalent neurological condition, is characterized by recurring seizures. Long-term recurrent seizures may result in mental illnesses and cognitive impairment, which can negatively impact the ability to social engagement and work opportunities of an epileptic patient (Chen *et al.*, 2020). Although the exact mechanism of epilepsy is still unknown, it is generally considered a self-facilitated pathological process brought on by brain injury that eventually causes dysfunction of ionic pathway, nerve damage, inflammation, mossin fibrosis, and synaptic plasticity (Gan & Südhof, 2020). Many researchers have demonstrated that over-excitation of N-methyl-D-aspartate receptors (NMDARs) results in neuronal death by increasing the levels of aspartate and glutamate in various neurological conditions such as epilepsy, Alzheimer's disease, stroke and Parkinson's disease (Chen *et al.*, 2022; Essiz *et al.*, 2021; Fricker *et al.*, 2018; Singh & Panda, 2024). In central nervous system, NMDAR is the primary excitatory receptor involved in the synapses of glutamatergic neurons and GABAergic interneurons (Chen *et al.*, 2022; Hanada, 2020). NMDARs are hetero-tetramers found in the brain that are generally made up of two GluN1 subunits and four different subunits of GluN2 (GluN2A-D), or a combination of GluN2 and two different GluN3 (GluN3A and 3B) subunits.

Recent findings indicate a strong connection between the NMDAR subunit encoding genes and epilepsy. Human epilepsy may result from the genetic abnormalities of NMDAR involving the GRIN1, GRIN2A, and GRIN2B mutations with language and minor speech delay and cognitive impairment (Lemke *et al.*, 2013; Sivakumar *et al.*, 2022; Xu *et al.*, 2019; Xu & Luo, 2018). The mutations in GRIN1 encode the subunit GluN1, significantly altering the neuronal activity and leading to various epileptic disorders in adults and children (Fry *et al.*, 2018; Wyllie *et al.*, 2013). The gene GRIN2A, which encodes GluN2A subunits, is considered epileptogenic and responsible for Landau-Kleffner syndrome, benign epilepsy, and atypical partial epilepsy (Elmasri *et al.*, 2022). Over 30% of GRIN2B variations have epilepsy, while 70% of GRIN2A variations lead to epilepsy development (Myers *et al.*, 2019).

Prevalence & Incidence of Pediatric Epilepsy

About 50 million people of any age, gender, ethnicity, or social background are affected by epilepsy worldwide, according to a recent report by WHO on Global Disease Burden (Gotlieb *et al*., 2023). In the general population at any given moment, between 4 and 10 out of every 1000 persons are thought to have active epilepsy (Trinka *et al*., 2023). Approximately 5 million individuals receive an epilepsy diagnosis each year worldwide. The variations in the prevalence of epilepsy are not attributed to the particular contents but rather to the economic condition of nations and the corresponding healthcare system standards. The incidence of epilepsy is twice as high in low and middle-income countries as it is in high-income nations. Each year, 49 out of every 100,000 individuals are diagnosed with epilepsy in high-income nations, and the number may reach 139 per 100,000 in nations with low and moderate income (J. S. Miller *et al*., 2024; Vergonjeanne *et al*., 2021). The difference in the incidence is primarily because different etiologies, such as infections, prenatal insults, and head trauma, have other effects. Epilepsy is the most prevalent chronic neurological illness that ruins people's lives, especially when seizures are severe and occur uncontrollably (J. S. Miller *et al*., 2024; Perucca *et al*., 2014).

With the prevalence rates ranging from 12% to 41%, epilepsy has been associated with a higher risk of mental illness. The most common mental co-morbidity in epilepsy patients is mood disorders, with the incidences of depression and recurrent seizures reported to be 11% and 60% (Alsaadi *et al*., 2015). According to an estimate from 2010, 724,500 people in Arab countries have epilepsy, with the incidence rates of 0.9 in Saudi Arabia, 6.5 in Iran, and 12 in Sudan per 1000 (Al Habbal *et al*., 2021; Spiciarich *et al*., 2019).

METHODS AND MATERIALS

Search Strategy

This review article included recent research studies and reviews of publications and articles relating to epilepsy in pediatric patients. The main focus of this review was on what is pediatric epilepsy, available diagnostic treatments in UAE, and the associated health problems like ADHD and other co-morbidities. Data was acquired from online databases such as Google Scholar, PubMed, Science Direct, IEE, Web of Science, NCBI, Hindawi, BioMEd, Research Gate, MEDLINE, and EMBASE.

A literature search was conducted to find papers on the incidence, causes, therapies, and risks of epilepsy in children and adolescents for this study. Studies including keywords like "epilepsy," "pediatric epilepsy," "types of epilepsy," "prevalence of epilepsy in UAE," "diagnosis of epilepsy," "pharmacological and non-pharmacological treatments," "epidemiological factors of epilepsy," "co-morbidities or impact on epilepsy management," "effectiveness of treatments" were included from last 10 years between 2014 and 2024. The boolean (AND, OR) and proximity (NEAR, NEXT, WITHIN) operators were used to combine the search terms.

At first, databases were searched for relevant publications, and then text words were analyzed and included in the title, abstract, and index keywords of articles. A second search was performed using all the found keywords, index terms, and MeSH terms for MEDLINE across the online databases. Recent studies were discovered by looking through the reference list of studies, papers, and publications using PubMed, Google Scholar, and Google to find the relevant data. The search terms were looked up from fully accessible articles in the titles, abstracts, and whole texts. This is a review article; therefore, not all the data regarding pediatric epilepsy management and prevention has been provided entirely. Thus, emphasis was given to including the most important and relevant studies in this review.

Inclusion Criteria

After considering the relevant research, the titles were filtered using the inclusion and exclusion criteria. Only those studies already published in peer-reviewed journals and conference papers were included. These studies were focused on improving the understanding of the research criteria.

- All the research articles published in peer-reviewed journals in the English language were included.
- Research studies discussing epilepsy, pediatric epilepsy, and its types were considered part of this study.
- Research studies discussing the prevalence, incidence, and risks of epilepsy were included.
- Review studies conducted in epilepsy focusing on the UAE and Arab nations were considered.
- Studies evaluating the diagnostic criteria were focused.
- Research focused on pharmacological and non-pharmacological treatments were also included.
- This study included data from a literature review, review articles, research studies, overview studies, and case studies on UAE.

Exclusion Criteria

Studies that fulfil any given conditions were excluded from this review;

- Papers written in languages other than English were excluded.
- Research with no supporting evidence for predetermined findings
- Studies whose goal had nothing to do with pediatric epilepsy.
- Duplicated studies were not considered.
- Studies containing data outside the Arab nations were also not considered
- The study did not include review articles with study-related titles but unrelated material.
- Papers that did not discuss the prevalence and risk factors of pediatric epilepsy in the UAE were also excluded.

DISCUSSION

Diagnosis of Epilepsy

Most epileptic patients can lead normal and healthy lives with proper care and diagnosis, but some suffer from severe mental problems. Therefore, regular healthcare may be required (Asnakew *et al.*, 2022). Early diagnosis may help improve patients' medical condition, but 75% of patients still do not receive the proper care in low-income nations compared to 10% in developed countries (Tana *et al.*, 2024). Various diagnostic methods are used, including electroencephalogram (EEG), magnetic resonance imaging (MRI), computed tomography (CT) scan, positron emission tomography (PET), single photon emission computed tomography (SPECT) and genetic testing (Acharya *et al.*, 2015; Elger & Hoppe, 2018; Lemoine *et al.*, 2023). Blood testing is also used to describe the etiology of toxic and metabolic encephalopathies, and other methods are also used to identify the false negative results and helpful in diagnostic confirmations.

EEG is considered the most effective method for diagnosing epilepsy as it helps to identify focal or generalized seizures and rule out epilepsy syndrome (Benbadis *et al.*, 2020). However, CT scans have a detection rate of 30% for focal seizures. Neuroimaging is critically important in evaluating epilepsy, with progress in MRI technology and acquisition protocols improving the accuracy of identifying epileptogenic lesions (Goodman & Szaflarski, 2021). Structural MRI is also important for identifying epileptogenic lesions, but there are chances of false negatives in 15-30% of patients with refractory focal epilepsy (Bernasconi & Bernasconi, 2022).

PET and SPECT are used for functional imaging that helps identify epileptogenic zones and allow pre-surgical evaluation (Juhász & John, 2020). Genetic testing is essential to find the cause of some epilepsy types, but it has limitations of high cost and lack of availability (Striano & Minassian, 2020). PET and SPECT imaging helps in localizing the area of the cortex responsible for the initiation of seizures, especially in patients with focal epilepsy who have a normal MRI, multiple abnormalities, or inconsistencies between MRI and EEG (Brinkmann *et al.*, 2021).

Treatments

Non Pharmacological Treatments

First aid

First aid treatment refers to the assistance of someone to the patient in managing the circumstances at the time of epileptic seizure. The stigma and unfavourable attitude towards those who have epilepsy is more challenging than the disease itself. People seem scared when they see someone experiencing an epileptic seizure due to the associated misconception. The most crucial thing is to remain composed and assist the sufferer because it is proven from the studies that with the right instructions and training, patients and their families can easily control or manage epileptic seizures (Cross *et al.*, 2022). There is no need to call an ambulance in epileptic seizures because it is not an emergency. Therefore, self-management training is the most beneficial for patients in managing their seizures independently and will also increase their confidence (Wiles *et al.*, 2023). It is seen that cyanosis can be caused in some patients due to respiratory muscle paralysis, but it is a momentary condition and returns to normal once the seizure stops. Therefore, the patient's heart rate, blood glucose level, and respiration must be assessed when the seizure duration is over (Anwar *et al.*, 2020). It is advisable to keep the patient relaxed and calm after the seizure. The patient may sleep for hours or even a day following the seizure due to the restlessness of the seizure attack (Sman, 2023).

Ketogenic Diet

A ketogenic diet is rich in fats, low in carbohydrates, and sufficient protein. Ketone bodies, such as beta hydroxyl butyrate and acetoacetate, are produced from the metabolism of high fats in the body. As a non-pharmacological therapy, ketone bodies show promising results even when tested compared to new anti-epileptic medications (Chan *et al.*, 2023). It is mostly utilized as a treatment for patients with drug-resistant epilepsy or for those who are unable to have a surgical operation. Ketone diet therapy is not successful for patients having problems with fatty acid metabolism and oxidation; therefore, a complete examination must be carried out for all these problems (Anwar *et al.*, 2020). Several researchers prove that the ketone diet reduces the frequency of epileptic seizures in about 30-40% of children due to its anticonvulsive properties, affecting both the neurotransmitters and neuronal membrane (Cicek & Sanlier, 2023; El-Rashidy *et al.*, 2023). In neuronal membranes, the ketogenic diet modifies the vesicular glutamate transporters that are chloride ion-dependent and work by filling presynaptic vesicles. These chloride ion channels are competitively inhibited by acetoacetate, a ketone molecule, which ultimately decreases the excitatory neurotransmitter (glutamate) and increases the inhibitory neurotransmitter (GABA) (Giourou *et al.*, 2015).

Lifestyle Modifications

traumatic brain injuries resulting from accidents and traumas are also avoided to reduce the seizure chances in epileptic patients. A wholesome and clean diet is essential to prevent epilepsy. Reducing stress and tension is also helpful in protecting epileptic individuals from seizures. Additionally, an epileptic patient must take their medication properly as directed by the physician to reduce the chances of seizures in epileptic patients (Akram *et al.*, 2022).

Epilepsy Surgery

surgical interventions are only recommended when the patient does not respond to non-invasive therapies and medications. Focal resection for non-critical brain areas, such as temporal lobe epilepsy and lesionectomy for brain tissue aberrations, are included in surgical intervention.

Tumors are high-risk causative agents for epilepsy and can lead to seizure removal with surgical interventions. Neuro-stimulation devices can also be used for cases ill-suited for resection or ablation, but they provide palliative treatment due to low seizure removal rates (Anwar *et al*., 2020).

Pharmacological Treatments

Anti-Epileptic Drugs (AEDs)

Anti-epileptic drugs or anticonvulsive pharmaceuticals are considered the most essential treatment choice for epileptic seizures (Gopalan & P, 2023). There are many AEDs available, but the choice is influenced by epilepsy type, the patient's general health and age, and the existence of other medical disorders. About 65% of children are completely cured by AEDs when administered at the early stage of the disease. Particular care must be exercised when taking AEDs to prevent interactions with potentially dangerous medications. Patients should administered only those AEDs which are prescribed after the complete examination of the drug interaction mechanism, potential side effects, and appropriate dose (Eze *et al*., 2015; Mir *et al*., 2023). When analyzing an AED profile for epileptic seizure, its safety, effectiveness, and tolerability are crucial factors to be considered. Most AEDs are inhibitors of sodium or calcium ion channels or the GABA neurotransmitter, and these medications have different actions (Rana *et al*., 2023; Zhao *et al*., 2017). Bumetanide, felbamate, ganxolone, regtibine, parampanel and carbamazepine are common effective AEDs. Still, new AEDs are also being developed for treating those seizures in which the traditional AEDs are ineffective. New AEDs are mostly used for the treatment of drug-resistant epilepsy. AEDs may negatively impact the body's systems, compromising their effectiveness and functionality. The frequently occurring side effects are headaches, behavioural abnormalities, ataxia, and some allergic reactions.

Co-morbidities of Epilepsy

Attention Deficit Hyperactivity Disorder (ADHD)

The Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) classifies ADHD as a neurodevelopmental disorder with four subtypes: inattentive, hyperactive or impulsive, combined, and unspecified. In children, the prevalence of ADHD is estimated to be 5%, while in adults it is 2.5% (D. J. Miller *et al*., 2024). There is no particular evidence present whether the occurrence of ADHD and epilepsy indicated a comorbid psychiatric condition or the transient effects of epilepsy. Therefore, it is crucial to carry out a comprehensive evaluation before starting treatment for ADHD in children. EEG monitoring is very helpful for identifying unreported seizures, particularly if inattention is a primary illness symptom (Ahmed *et al*., 2022).

Cognitive & Developmental Issues

The hippocampus is the primary target of recurrent epileptic seizures, which can lead to impairments in brain plasticity. These impairments mainly affect the academic performance of children. A systematic study conducted by Wo *et al.* (2017) examined the frequency of academic challenges in epileptic children and concluded that about 70% of children have lower academic performance as compared to the normal (Wo *et al*., 2017). These cognitive issues often show after epileptic surgery; therefore, cognitive rehabilitation has been suggested as a treatment modality.

Social Challenges

Approximately 1.1 million children with epilepsy grow up to be adults every year, according to the reports of WHO in 2022 (Fiest *et al*., 2017; WHO, 2022). Adolescence is a critical time for both physical and psychological growth for anybody, but individuals with epilepsy are more likely to experience additional challenges such as social stigma, mental health and neurodevelopmental disorders, loneliness, and a sense of not being independent (Goselink *et al*., 2022; Healy *et al*., 2020). Numerous epidemiological studies have also demonstrated that people with epilepsies are highly vulnerable to adverse outcomes related to work, social contacts, family relationships, and experiential activities; all of these are essential predictors of quality of life (Gauffin *et al*., 2022; Steiger & Jokeit, 2017). Social challenges associated with epilepsy are not only limited to adulthood, but children with epilepsy have also been shown to have poorer social skills than children without epilepsy, even in their early years.

People who have epilepsy as children are frequently found to have quite high rates of social issues as adults, which leads to challenges in maintaining a job, engaging in family, community and cultural life, and developing interactions with others. Therefore, it is necessary to prioritize social functioning to improve the life quality of people with epilepsy (Asadi-Pooya *et al*., 2021; Goselink *et al*., 2022; Steiger & Jokeit, 2017). It is questionable to what extent social competency issues are caused by psychosocial issues or underlying deficiencies brought on by brain injuries associated with epilepsy. From a psychological point of view, social participation and the capacity to implement parental overprotectiveness and seizure fear.

RECOMMENDATIONS

This study found that genetics, demography and co-morbidities all contribute to the development of epilepsy. The aetiology of epilepsy is multifaceted; therefore, a multidisciplinary and integrated strategy should be used to treat epilepsy in children and adolescents.

More studies should also be conducted in the UAE population to estimate the prognosis and diagnosis of the disease and the effectiveness of available treatment, including brain imaging, scanning and other biological markers. Genomic sequencing and analysis should also be given significant importance as they have clinical implications and would be helpful for the precise management of epilepsy types.

CONCLUSION

UAE should raise awareness among the people to remove the myths related to epilepsy through media campaigns and school-based health education. It is also important to undertake initiatives aimed at increasing epilepsy knowledge, eliminating stigma, and improving early access to healthcare services. Neonates and children should give extra attention to prevent difficulties that could harm their development. Additional research should be carried out in the UAE to identify the actual risk factors for epilepsy among children. There is also a need to implement new techniques for the treatment of epilepsy.

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