## Comorbid neurodevelopmental disorders in children with epilepsy: A single-center observational study

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#### Abstract

**Introduction**: Neurodevelopmental disorders are a group of conditions that occur before school age and affect development. They can cause learning, communication, social interaction, or behavior difficulties. The objective of the present study was to identify the neurodevelopmental disorders present in children with a diagnosis of epilepsy who attended a public reference hospital in Venezuela.

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**Methods:** The present cross-sectional observational study included children diagnosed with epilepsy who attended a neuropediatric consultation at the University Hospital of Maracaibo in Venezuela between March 2022 and March 2023. The presence of neurodevelopmental disorders was established according to the doctor's criteria, who evaluated each patient in the controlled trials. The chi-square test was used to analyze the categorical variables.

# **Results**: A total of 110 patients were analyzed; 66 men (60.0%) were aged 7.3 $\pm$ 6.2 years, and generalized epilepsy predominated (76.4%). A total of 56 patients presented with neurodevelopmental disorders: 19 with intellectual development disorders (33.9%), 9 with attention deficit hyperactivity disorder (16.0%), 14.2%, 7 with autism spectrum disorders (12.5%), 7 with language disorders (12.5%), and 6 with motor disorders (10.9%).

**Conclusions**: In the present investigation, it was observed that patients diagnosed with epilepsy had a high incidence of comorbid neurodevelopmental disorders, which included cognitive and behavioral alterations. Therefore, every professional needs to recognize the clinical signs of these disorders to provide timely multidisciplinary care that improves the quality of life of these patients and their families.

#### Keywords:

MeSH: Learning Disabilities; Epilepsy; Language Disorders; Child.

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## Introduction

According to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), neurodevelopmental disorders are a group of conditions that begin in the developmental period, often present before the child starts school, and are characterized by a developmental deficit that leads to deficiencies in personal, social, academic or occupational functioning. Epilepsy is a chronic neurological disorder characterized by recurrent unprovoked seizures of cerebral origin with motor, sensory, or autonomic disturbances with or without loss of consciousness that can occur regardless of age, sex, or race [1]. It has an incidence of 61.44 per 100,000 person-years and a lifetime prevalence of 7.60 per 1,000 people in many countries. The prevalence of NAFLD in the pediatric population is approximately 3.9 per 1,000 inhabitants [2]. A broad spectrum of comorbid conditions coexist at the time of presentation in a child with epilepsy or develop later, and many of these comorbidities can sometimes be even more disabling than epilepsy itself; therefore, identifying the neurodevelopmental disorders that are part of this range of conditions that these patients can present is essential  $[\underline{3}, \underline{4}]$ . The most common neurodevelopmental disorders related to epilepsy are intellectual development disorder (IDD), attention deficit hyperactivity disorder (ADHD), specific learning disorder, and autism spectrum disorders (ASDs). Communication disorders include the following: language disorders, phonological disorders, childhood-onset fluency disorders (stuttering), social communication disorders (pragmatic), and other specified and unspecified communication disorders. Motor disorders include coordination disorders, stereotyped movement disorders, and tic disorders.

The objective of the present study was to identify the presence of neurodevelopmental disorders in children with a diagnosis of epilepsy who attended the Neuropediatric Consultation of the Autonomous Service of the University Hospital of Maracaibo (SAHUM).

## Materials and methods

#### Type of study

The present study was observational and descriptive and involved longitudinal observation. The source was retrospective.

#### Scenery

The present study was conducted during the Neuropediatrics consultation of the Autonomous Service Hospital Universitario de Maracaibo (SAHUM). The study period was from March 1, 2022, to March 31, 2023.

#### Universe and sample

The Universe included all patients admitted to the Neuropedinology Unit of the institution. The sampling procedure was nonprobabilistic.

#### Inclusion criteria

Patients aged 0 to 14 years, with a diagnosis of epilepsy, and with a follow-up of at least one year were included. Patients for whom follow-up data were unavailable for one year were excluded.

#### Information collection procedure

Once the research was accepted at the hospital and approved by the Human Research Ethics Committee of the Faculty of Medicine, Universidad del Zulia, Maracaibo, Venezuela, the information recorded in the computer system of each digital medical history of the children in the study period was requested from the management of each hospital.

Anonymized data were obtained from the medical history of those who met the inclusion criteria. These data were recorded in a data collection database; the anonymized information was organized according to a unique code assigned to each patient.

#### Variables

The following study variables were recorded:

- 1. Age.
- 2. Sex.
- 3. Type of epilepsy.

4. Neurodevelopmental kind of disorder.

#### Biases

The leading researcher always maintained the data with a guide and records approved in the research protocol to avoid possible interviewer, information, and memory biases. Observation and selection bias were avoided by applying participant selection criteria. All clinical variables during the study period were recorded. Two researchers independently analyzed each record in duplicate, and the variables were registered in the database once their agreement was verified.

#### Statistical analysis

A non-inferential analysis was performed. Frequencies and percentages are presented for categorical variables. The 95% confidence intervals for the proportions are presented. The SPSS V23 program (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) was used for the analysis.

## Results

#### Participants

A total of 110 patients were included in the study.

#### General characteristics of the population

A total of 110 patients with a diagnosis of epilepsy were registered; 60.0% (66/110) were men, with an average age of 7.3 ± 6.2 years, and generalized epilepsy predominated (76.4%) (Table 1).

Table 1. Characteristics of sociodemographic and clinical pa-
tient participants of the study.

Characteristics	Frequency	(%)
Sex	N=110	
Women	44	40.0
Man	66	60.0
Age (Years)		
< 1	15	13.6
1 to 2	15	13.6
3 to 5	14	12.9
6 to 11	46	41.8
12 to 14	20	18.1

#### Neurodevelopmental disorders

Table 2 identified 56 patients with epilepsy complicated with neurodevelopmental disorders (50.9%), for a 95% confidence interval ranging from 41.51% to 60.29%. The table shows that IDD (33.9%), followed by ADHD (16.0%), Learning Disorder (14.2%), ASD and Language Disorder (12.5%) had the third highest prevalence, followed by Motor Disorder (Stereotypies) (10.9%).

Table 2.	Distribution according to neurodevelopmental dis-
orders.	

Disorder	<b>Frequency</b> n=110	(%)
No disorder	54	49.1
Intellectual development disorder	19	17.3
Attention and hyperactivity disorder	9	8.2
Specific learning disorder	8	7.3
Autism spectrum disorder	7	6.4
Language disorder	7	6.4
Motor disorders (stereotypies)	6	5.5

## Discussion

In the Khanam 2023 study, in which the authors identified the neurodevelopment comorbidities of children with epilepsy, 31.4% of the patients were between 1 and 2 years old, with an average age of 4.7  $\pm$  2.8 years, differing from the findings of this research [5]. Similarly, another study by Kirsten M. 2016 carried out to determine the distribution and risk characteristics of comorbid neurodevelopment and mental health comorbidities among children and adolescents (6 to 18 years) with epilepsy showed that 54.5% were women [6]. The findings of this study are compared with epilepsy statistics, which indicate that these findings do not differ according to age group or sex [7].

In this regard, Wagner and Cols in 2015 evaluated the association between epilepsy, mental health, and neurodevelopmental comorbidities in children and adolescents aged 6 to 18 years and reported. They reported patients with epilepsy presented comorbid developmental disorders, highlighting that ADHD, ASD, and intellectual disability differ from the findings of the present investigation  $[\underline{Z}]$ .

The Neurodevelopmental Disorders Working Group 2017 conducted a study to investigate the prevalence, risk factors, clinical characteristics, and neurobehavioral comorbidities of epilepsy and acute symptomatic seizures in school-age children in Kilifi, Kenya. Among their results, neurobehavioral and neurological comorbidities were more frequent in those with epilepsy (54%) than in children without epilepsy (3%, P <0.0001). Among children with epilepsy, the most evident associations were extensive for ASD [odds ratio (OR)=36.83; 95% confidence interval (CI)=7.97-170.14], ADHD (OR=14.55; 95% CI=7.54-28.06), cognition (OR=14.55; CI=3.52-60.14), and motor impairments [8]. Similar findings were obtained in the present investigation regarding the prevalence of neurodevelopmental disorders in 50.9% of epileptic patients; however, the findings differed from those of the present study regarding the higher incidence of intellectual development disorder (33.9%) and other comorbidities.

Wagner and Cols (2015) reported the prevalence of comorbid neurodevelopmental disorders in adolescents during the process of puberty, during which adolescents with epilepsy may experience neuropathological changes and psychosocial factors that are more influential (isolation, social, and independence with self-control), increasing vulnerability to increased epileptic activity and mental health comorbidities [7]. Similarly, cognitive and behavioral comorbidities are often observed in children with epilepsy and are more common and severe in refractory epilepsy. These comorbidities are associated with poorer quality of life, greater behavioral and language problems, and poorer social skills, negatively affecting long-term psychosocial functioning. To enable early intervention and therapy, children and adolescents with epilepsy should undergo regular testing for cognitive comorbidities [9].

Finally, comorbid conditions, including cognitive impairment, neuropsychiatric problems, and social difficulties, are common in children with epilepsy and are often more disabling than the disease itself. Biological factors associated with an increased risk of comorbidity in patients with epilepsy include younger age at seizure onset and cognitive impairment [10].

## Conclusions

In the present study, it was observed that patients diagnosed with epilepsy had a high incidence of comorbid neurodevelopmental disorders, which included cognitive and behavioral alterations. Therefore, every professional needs to recognize the clinical signs of these disorders to provide timely multidisciplinary care that improves the quality of life of these patients and their families.

#### Abbreviations

IDD: Intellectual development disorder. ADHD: Attention Deficit Hyperactivity Disorder. ASD: Autism spectrum disorder.

#### Supplementary information

No supplementary materials are declared.

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Not declared.

#### Author contributions

Oscar Meza: Conceptualization, data curation, formal analysis, funding acquisition, research, writing - original draft. All the authors read and approved the final version of the manuscript.

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#### Availability of data and materials

The data were collected from medical archives and are not publicly available due to patient confidentiality but are available through the corresponding author upon reasonable academic request.

#### Statements

#### Ethics committee approval and consent to participate

This study was approved by the Human Research Ethics Committee of the Faculty of Medicine, Universidad del Zulia, Maracaibo, Venezuela. The participants' guardians signed the consent to participate.

#### **Publication consent**

Patient-specific images, X-rays, and studies were not available for publication.

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#### **Conflicts of interest**

The authors declare that they have no conflicts of interest.

#### Author information

Not declared.

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