REVISTA ECUATORIANA DE PEDIATRÍA
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ORIGINAL ARTICLE

Relationship between autism spectrum disorder and epilepsy in a pediatric population in Quito-Ecuador

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Received: May 2, 2021
Accepted: November 19, 2021
Published: December 13, 2021
Editor: Dr. Paúl Astudillo Silva.

Bibliographic letterhead:

Astudillo A, Garzón E, Erazo P. Relationship between autism spectrum disorder and epilepsy in a pediatric population in Quito-Ecuador. Revista Ecuatoriana de Pediatría 2021;22(3):Article 21:1-6 doi: https://doi.org/10.52011/121

Abstract

Introduction: Compared to the general population, there is a higher prevalence of epilepsy in children with autism spectrum disorder (ASD), with an indecency of approximately 20%. There is no plausible mechanism for ASD as a cause of epilepsy; however, its cooccurrence is surely the result of predisposing factors for both conditions, including genetic and environmental factors. The objective of this study was to establish the prevalence of epilepsy in patients with ASD and find a correlation with other factors, such as sex, etiology, type of seizure or epileptic syndrome, age of onset of epilepsy, EEG abnormalities, and therapeutic response.

Methods: A retrospective longitudinal study was carried out based on the clinical records of the Center for Neurological and Nutritional Diseases in Children and Adolescents (CENNA) of 81 patients (3-19 years) with a diagnosis of ASD, where patients coexisted with epilepsy for a period of 6 years, and the different variables in this group.

Results: Eighty-one patients with a diagnosis of ASD were identified, of whom 12 patients (15%) had coexisting epilepsy. When analyzing the degree of ASD, it was evidenced that comorbidity in both entities is more common in ASD grade 3 (58.33%). The age of onset of epilepsy ranged between 5 and 10 years (42%). Twenty-five percent of patients had a family history of epilepsy, while only 8% had a family history of ASD. All types of epileptic seizures occurred in patients with ASD, but the most common were focal-type seizures (58%), specifically motor seizures with altered consciousness (33%). In addition, there was a 100% improvement in autistic behavior in the patients who received their antiepileptic treatment, and only 8% had difficult-to-control epilepsy.

Conclusion: The study showed a significant prevalence of epilepsy in the population diagnosed with ASD. The study managed to observe the distribution of the population with comorbidities of ASD and epilepsy to find a common variable between both pathologies in the future. To our knowledge, this is the first retrospective study in Ecuador that analyzes the comorbidity of ASD and epilepsy in the Ecuadorian population.

Keywords:

MESH: Epilepsy; Autistic Disorder; autism; /genetics; Environment; Child Behavior.

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Introduction

Autism spectrum disorder (ASD) is a prevalent entity with an incidence of approximately 1 in 100 people [1]. Patients with ASD who present comorbidities present a lower quality of life [2]. In Ecuador, in the population under 5 years of age, the prevalence of ASD was 0.28% (0.18% - 0.41%), and in the population aged 5 to 14 years, the prevalence was 1.7% (1.29 - 2.15%) [3]. The prevalence of epilepsy in Ecuador is 7 to 12 per 1000 inhabitants, of which 20% are refractory to pharmacological treatment. The mortality of these patients is 6 times higher than that of the Ecuadorian population in general [3].

Compared with the general population, there is a higher prevalence of epilepsy in children with ASD. The reported frequency of epilepsy with ASD is 5–40%, compared to the general population (0.5–1%) [4]. Finding a relationship between the two conditions can have a direct effect on the treatment of patients; if there was a specific identified risk factor for developing epilepsy in patients with ASD, perhaps epilepsy could be prevented or at the same time less recognized early for the initiation of adequate treatment. Epilepsy is not a contraindication to treating ASD with adequate medication, but it is important to take into account possible pharmacokinetic interactions [5]. The comorbidity of ASD and epilepsy has been widely discussed in the literature; however, regardless of many possible explanations, the association between these two conditions is still unclear, and further research and comprehensive analyses are needed to find the right possible common pathophysiological mechanism [5, 6].

The aim of this study was to establish the prevalence of epilepsy in a patient with ASD to define the type of seizure or epileptic syndrome, the age of onset of epilepsy, abnormalities in the electroencephalogram, and the therapeutic response and to find a correlation between epilepsy and other factors, such as sex and etiology.

Population and methods

Study design

The design is a retrospective longitudinal study based on the analysis of medical records over a period of 6 years.

Stage

The study was carried out at the Pediatric Neurology Service of the Center for Neurological and Nutritional Diseases in Children and Adolescents (CENNA) of the City of Quito, Ecuador. The study period was established between June 1, 2015, and June 30, 2021.

Participants

A database search of the clinical histories of patients diagnosed with ASD was carried out. The diagnosis of ASD was based on the DSM-5 diagnostic criteria performed by a comprehensive assessment of neurology, psychology and pediatrics of the CENNA center, and within the variables, the coexistence of epilepsy in the same group was evaluated. Patients with complete clinical history data were selected. All patients included in the study were evaluated with a complete medical history and physical and neurological examination, and an additional head magnetic resonance imaging study was performed in all patients. The clinical history of the patients with epilepsy included information on the characteristics of the seizures, frequency, number of antiepileptic drugs and response to treatment.

Variables

The variables were descriptive demographic and clinical variables. All patients with ASD and seizures underwent EEG; the types of seizures and epileptic syndromes were classified according to the ILAE 2017 classification by a pediatric neurologist. The EEGs were interpreted by an epilepsy specialist, and the abnormalities were classified as normal baseline activity, frontal focal activity, central temporal focal activity, multifocal epileptiform activity, generalized epileptiform activity, frontotemporal focal epileptiform pattern, and outbreak suppression. According to the etiology of the seizures, the patients were classified into three groups: symptomatic or syndromic (with proven etiology), probably syndromic (with high suspicion, but there is no proven etiology because no additional vesting at the request of legal guardians) and of unknown/idiopathic cause (lack of clinical or laboratory evidence of a possible syndrome).

Data sources

For each variable, institutional software for recording clinical records was used as a data source, electronic clinical records were consulted, and physical records

were also consulted. The data were compiled in an electronic sheet to later be transferred to the statistical software.

Control of sources of bias

Medical records whose data were not complete were excluded, and the imputation of lost or excluded data was avoided. The data were double-checked by independent sources.

Study size

The sample was nonprobabilistic, in which all potentially eligible cases from the Center for Neurological and Nutritional Diseases in Children and Adolescents (CENNA) were included.

Management of quantitative variables

Nominal quantitative variables are presented as frequencies and percentages. Due to the great variability of numerical data in the data analyzed in the clinical histories, the data were grouped into ranges and became categorical variables.

Statistical Methods

The independent variable was patients with a diagnosis of ASD, and the dependent variable was patients with epilepsy comorbidity. These data were obtained by the evaluation of specialists registered in the clinical history of each patient. Descriptive statistics are used. The categorical variables allowed a statistical description of the data distribution in the studied sample, and the statistical package used was STATA 16.1.

Results

Participants

The study identified a total of 81 patients with a diagnosis of ASD, of whom 12 patients (15%) had coexistence epilepsy. The cases not included in the study are presented in Figure 1.

Characteristics of the studied population

There were 12 cases, of which 12 cases (50%) were women and 6 cases (50%) were men. The age of the patients ranged from 3 to 19 year.

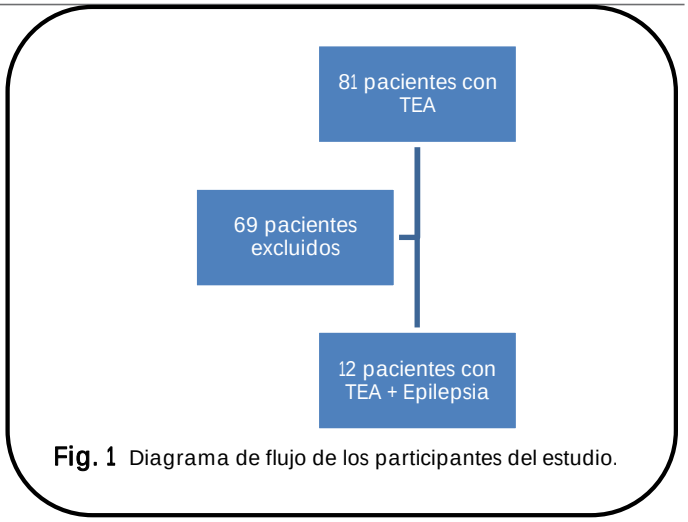

Fig. 1 Diagrama de flujo de los participantes del estudio.

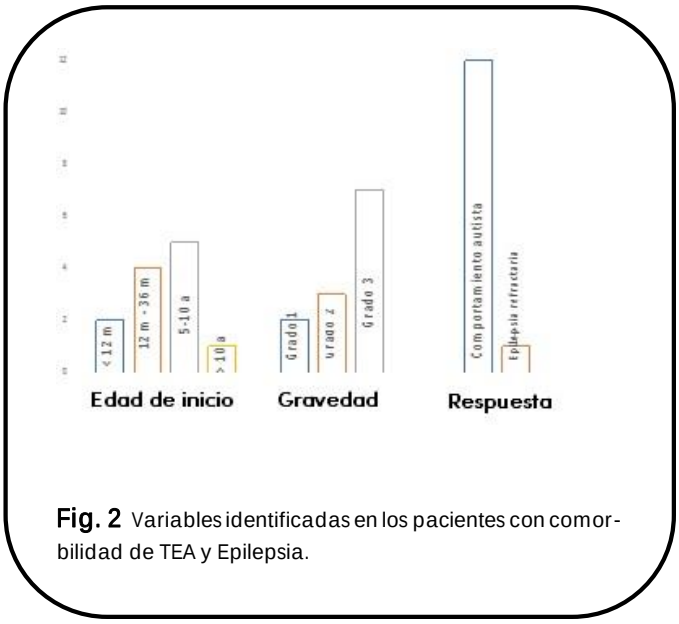

Fig. 2 Variables identificadas en los pacientes con comorbilidad de TEA y Epilepsia.

Main results

Of the 12 patients identified, analyzing the degree of ASD according to the diagnostic criteria of the DSM-V revealed that comorbidity in both entities was more common in ASD grade 3 (58.33%) (Figure 2). The age of onset of epilepsy was between 12 months and 10 years (Figure 2), but most of them were in the range between 10 and 19 years (42%). Regarding the risk factors, 58.33% did not present any direct family member with any of the comorbidities. In addition, 25% of patients have a family history (APF) of epilepsy, while only 8% have a family history of ASD. The patient with a family history of ASD did not present a risk factor for epilepsy. There were no differences between the pre-

valence of epilepsy in the different etiologies (92% unknown origins and 8% structural origin), probably due to the high prevalence of epilepsies of genetic origin not studied due to the high cost of these tests in our setting. The types of seizures found in the patients studied are presented in Table 1. All types of seizures occurred in patients with ASD, but the most common were focal-type seizures (58%), specifically motor seizures with altered consciousness (33%). The most prevalent EEG finding was focal epileptiform activity (41.7%), among which a predominance of frontal focal activity (25%) was observed, and the distribution of EEG patterns is shown.

Regarding the therapeutic response, there was a 100% improvement in autistic behavior in the patients who received their antiepileptic treatment. Only 8% of the patients with both comorbidities had refractory or difficult-to-control epilepsies (Figure 2).

Table 1 Types of epileptic seizures in patients with comorbidities of ASD and epilepsy

Type of seizure	n= 12	%
Focal	7	58.33
FMC without impaired consciousness	3	25
FMC with impaired consciousness	4	33.33
Generalized	5	41.66
Generalized tonic-clonic seizures	4	33.33
Generalized myoclonic seizures	1	8.33

FMC: Focal motor crisis

Discussion

Main Findings of the Study

The study showed a significant prevalence of epilepsy in the population diagnosed with ASD.

Importance of the findings

The study managed to observe the distribution of the population with comorbidities of ASD and epilepsy to find a common variable between both pathologies in the future. The study managed to observe the distribution of the variables in the study population. Finding a relationship between the two conditions may have a direct effect on the treatment of patients. If there was a specific identified risk factor for developing epilepsy in patients with ASD, epilepsy could be prevented or at least recognized early to the initiation of adequate treatment.

Studies with related findings

The comorbidity of epilepsy and ASD has been described in the literature, and the prevalence of both entities is between 5-40% [7]. In a meta-analysis of all the articles published from 1963 to 2006, it was shown that epilepsy occurs more commonly in patients with syndromic ASD, female patients, and patients with intellectual deficiency [8]. The frequency of epilepsy in our population with a diagnosis of ASD was 15%. This is a relatively high percentage compared to the prevalence of ASD in Ecuador, with a prevalence of 1.7% [9].

Clinical relevance of the findings

To our knowledge, this is the first retrospective study in Ecuador that analyzes the comorbidity of ASD and epilepsy in the Ecuadorian population.

Study limitations

One of the limitations of the study is the size of the sample, which compared to the current literature could be considered a nonsignificant sample. In addition, the information analyzed was taken from an outpatient and nonhospital center, where it would be expected that patients with both comorbidities they attend for decompensation more frequently.

Future investigations

Many studies have identified IQ as a factor that directly influences this association [10,-12]., In the study group, there was no measurement of the IQ because most validated instruments for intellectual assessment include the assessment of language, and one of the bases for the diagnosis of ASD is the lack of language; therefore, the IQ may be undervalued in these patients. The database would determine in the future that IQ is measured in the reevaluation process because it is a factor that can improve with therapeutic interventions.

Recommendations

To investigate the coexistence of epilepsy in patients with a diagnosis of ASD early, association studies should be established in the future to identify significant risk factors between both comorbidities.

Conclusions

There is a significant prevalence of epilepsy in the population diagnosed with ASD. The study was able to observe the distribution of the population variables with comorbidities of ASD and epilepsy to find a common variable between both pathologies in the future.

Abbreviations

ASD: Autism Spectrum Disorder. EGG: Electroencephalogram.

Supplementary information

Supplementary materials are not declared.

Acknowledgments

The work of the staff of the Center for Neurological and Nutritional Diseases in Children and Adolescents (CENNA) is recognized.

Authors' contributions

Álvaro Nicolay Astudillo: Conceptualization, Data preservation, Fund acquisition, Research, Resources, Software, Writing - original draft, Writing: revision and editing.
Elizabeth Nicole Garzón: Conceptualization, Data Conservation, Fund Acquisition, Research, Resources.
Patricia Cecilia Erazo: Methodology, Formal Analysis, Project Management, Supervision, Validation, Visualization.

Financing

The authors financed the expenses incurred in the production of this research.

Availability of data and materials

The data sets generated and/or analyzed during the current study are not publicly available due to the confidentiality of the participants but are available through the corresponding author upon reasonable academic request.

Declarations

Ethics committee approval and consent to participate

Not required for descriptive observational studies.

Publication consent

It does not apply to studies that do not publish MRI/CT/Rx images or physical examination photographs.

Conflicts of interest

The authors declare no conflicts of interest.

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