Ghana Alternative Medicine Journal (GAMJ)
Abbreviated Key Title: Gha alt Med Jrnl
ISSN 2756-7176 (Print) Open Access
Journal homepage: https://saspublishers.com/journal/gamj/home

OPEN ACCESS

Comorbidity ASD and Epilepsy

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DOI: 10.36347/gamj.2023.v04i04.001 | **Received:** 03.09.2023 | **Accepted:** 09.10.2023 | **Published:** 14.10.2023

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Abstract **Original Research Article**

Autism spectrum disorder is a category of neurodevelopmental disorders characterized by early and persistent deficits in communication and social interaction, as well as the presence of repetitive or restricted patterns of behaviour and interests. The comorbidity between epilepsy and ASD is well described in the scientific literature, its prevalence is estimated between 5 and 44.4% [3]. This comorbidity represents a major challenge for researchers, raising many questions about the nature of their association, and the best approaches for effective management. A retrospective and descriptive study was carried out at the Child Psychiatry Department of the Ibn Nafis Hospital, Mohammed VI University Hospital, spread over a period of one year: January 2022 to January 2023, based on the exploitation of files. Inclusion criteria: patients under 18 years of age, who meet the DSM V diagnostic criteria for ASD and have comorbid epilepsy. Sixteen patients were included in this study, for socio-demographic parameters, there is a male predominance with a frequency of 56.25%, the mean age of patients: 8.12 years with extremes of 3 and 13 years with a predominance in the age group of 6 to 12 years (56.25%). Most studies report a male predominance that can be explained by the higher frequency of ASD in male subjects in the general population. Several studies indicate that women with autism have a higher risk of developing epilepsy compared to men (Elia *et al*., 1995; Danielsson *et al*., 2005; Hughes & Melyn, 2005). Clark *et al*., report a greater risk of ASD in cases of seizures occurring before the age of 2 years. An onset of seizures in the first year of life is particularly associated with autism. In a study of 246 children with autism aged 4 to 15 years, 16 children had epilepsy. Future research will continue to inform our understanding of this interconnection between epilepsy and ASD highlights the complexity of disorders covering both genetic and neurobiological aspects, which are needed to further clarify the underlying mechanisms of this association.

Keywords: Epilepsy, ASD, Comorbidity.

INTRODUCTION

Autism spectrum disorder is a category of neurodevelopmental disorders characterized by early and persistent deficits in communication and social interactions as well as the presence of repetitive or restricted patterns of behavior and interests, its prevalence is estimated at: 0.75-1% (US 2017: 1/59 children; 1/49 G; 1/189 F).

Epilepsy is a lasting predisposition to generate seizures, it is a chronic neurological condition that is characterized by the recurrent and sudden occurrence of epileptic seizures [1, 2].

However, there is an intriguing intersection where these two conditions come together, creating an ever-changing field of study: the comorbidity between epilepsy and ASD is well described in the scientific literature, its prevalence is estimated between 5 and 44.4% [3].

This comorbidity represents a major challenge for researchers, raising many questions about the nature of their association, and the best approaches for effective management. In this article, we will dive into this complex intersection between epilepsy and ASD, exploring the key elements that define this comorbidity.

The aim of this work is to identify, through a case study and a literature review, the epidemiological and clinical characteristics of ASD comorbidity - epilepsy.

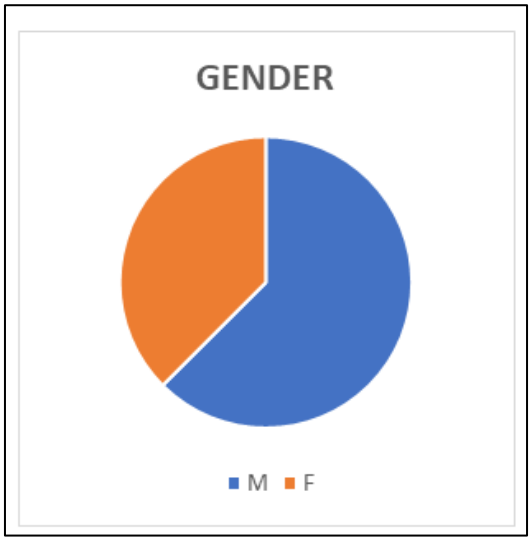
MATERIAL AND METHOD

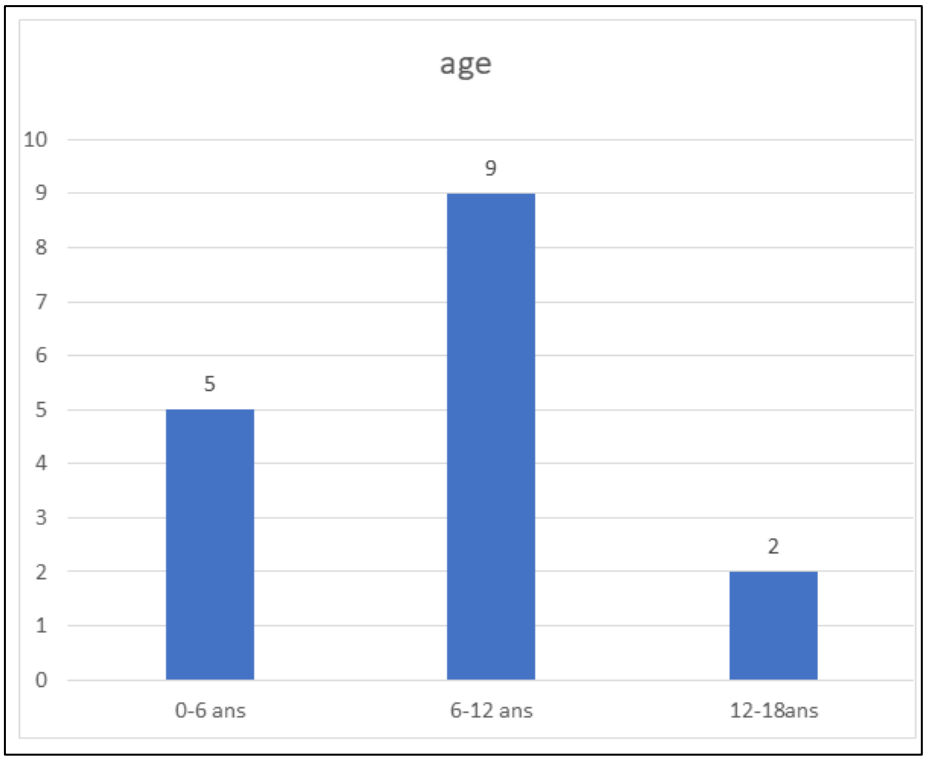
A retrospective and descriptive study was carried out at the Child Psychiatry Department of the Ibn Nafis Hospital, Mohammed VI University Hospital, spread over a period of one year: January 2022 to January 2023, based on the exploitation of files.

Inclusion criteria: patients under 18 years of age, who meet the DSM V diagnostic criteria for ASD and have comorbid epilepsy.

RESULTS

Sixteen patients were included in this study, for socio-demographic parameters, there is a male predominance with a frequency of 56.25%, the mean age of patients: 8.12 years with extremes of 3 and 13 years with a predominance in the age group of 6 to 12 years (56.25%).





For anamnestic parameters: there is a normal course of pregnancy and childbirth in 10 patients, perinatal asphyxia in 5 cases.

12 patients had delayed psychomotor development and language and 4 patients had language delay without motor delay, 2 patients had a family history of epilepsy.

Average age of diagnosis of ASD: 6.6 years, average ASD in 56.25% of cases and severe in 43.75%, comorbidity with intellectual disability was observed in 12 patients or 75% of cases, 5 patients were on prescription medication for behavioral disorders, and the main molecule prescribed: risperidone with an average dose of 0, 75 mg / day, all patients benefited from psychomotor and speech therapy rehabilitation as well as parental guidance work.

Average age of epilepsy diagnosis: 2.6 years, all patients had generalized tonic-clonic seizures with two cases of developmental regression after the first seizure.

Nine patients underwent brain imaging with no abnormalities and EEG performed in all patients

13 patients were on monotherapy: sodium valproate or carbamazepine with epilepsy stabilisation in 87.5% of cases.

The diagnosis of epilepsy (pediatrician) preceded that of ASD in 13 patients or 81.25% of cases and the diagnosis of ASD (child psychiatrist) preceded that of epilepsy in 3 patients or 18.75%.

DISCUSSION

❖ **Epidemiology:**

1/Prevalence of epilepsy in patients with ASD

Table 1: The co-occurrence of epilepsy and autism: A systematic review [4]

author	Country	Number of patients	Age range	Prevalence
Icasiano *et al*., (2004)	Australia	177	2-17	6,2
Liu *et al*., (2006)	USA	167	2,4-18,2	11
Oslejskova *et al*., (2007)	Rep tcheque	205	5-15	31,1
Hussin *et al*., (2011)	Egypt	143	2-15	16,1

Pavone *et al*., Report a 55% higher frequency for syndromic ASD compared to ASD Idiopathic (7.4%).

2/Prevalence of ASD in patients with epilepsy:

Table 2: Prevalence and risk factors for autism spectrum disorder in epilepsy [5]

Author	Country	Number of patients	Prevalence
Reily *et al*., (2015)	UK	85	21
Matuso *et al*., (2010)	Japon	519	5
Clarke *et al*., (2005)	USA	97	32
Su *et al*., 2016	Taiwan	3755	2,4

❖ **Gender:**

Most studies report a male predominance that can be explained by the higher frequency of ASD in male subjects in the general population. Several studies indicate that women with autism have a higher risk of developing epilepsy compared to men (Elia *et al*., 1995; Danielsson *et al*., 2005; Hughes & Melyn, 2005).

A meta-analysis of 14 studies found that the prevalence of epilepsy was 34.5% in women, compared to 18.5% in men (Amiet *et al*., 2008). However, this correlation between sex and epilepsy could be influenced by the presence of more severe mental retardation in women with autism, as demonstrated by Gillberg *et al*., In a prospective study of 55 participants: the higher the level of mental retardation, the lower the male/female ratio (Gillberg *et al*., 1991).

❖ **Age**

Two peaks in the age of seizure onset are described: one before age 5, the other in adolescence after age 10 (Volkmar & Nelson, 1990). Clark *et al*., report a greater risk of ASD in cases of seizures occurring before the age of 2 years. An onset of seizures in the first year of life is particularly associated with autism. In a study of 246 children with autism aged 4 to 15 years, 16 children had epilepsy.

In 80% of them, seizures began within the first year of life (Wong, 1993). In the studies of Matsuo *et al*., and Berg *et al*., the diagnosis of epilepsy preceded that of ASD in 36, 7 and 85.7% of cases, respectively.

Table 3: Prevalence and risk factors for autism spectrum disorder in epilepsy [6]

Authors	diagnosis Epilepsy before ASD	diagnosis ASD before epilepsy
Matsuo *et al*.,	36,7%	25,3%
Berg *et al*.,	85,7%	14,3%

Symptoms of ASD may be present before diagnosis, which is usually between the ages of 3 and 5.

❖ **Intellectual disability:**

Table 4: Prevalence of epilepsy in patients with ASD with or without epilepsy

Authors	ASD and ID	ASD without ID
Amiet *et al*., (2008)	21,4%	8%
Bolton *et al*., (2011)	23,7 %	1,8%

The presence of intellectual disability is associated with a high risk of ASD and epilepsy. Recent research data in the field of epilepsy and ASD have shown that epilepsy, ASD and ID could result from the same neurological injury [7].

Several studies suggest that nearly half of children diagnosed with ASD have an associated intellectual disability [8, 9].

❖ **Type of epilepsy:**

Some studies report a predominance of complex parietal seizures with or without secondary generalization, Jokiranta *et al*., find a frequency of 70% compared to generalized seizures from the outset whose frequency was 27% [10]. A high prevalence of ASD has been observed in some epileptic syndromes: infantile spasm syndrome and Dravet syndrome [11, 12]. Regarding the severity of epilepsy in ASD patients, a High frequency (34%) of refractory epilepsy was observed in the study by Sansa *et al*.,

In the majority of reported cases, encephalogram records show focal epileptiform abnormalities, with frequency of frontal or temporal/centrotemporal discharges with a predominance of occipital tips was observed by Nass *et al*., as well as the presence of EEG epileptiform discharges in the absence of a history of seizures have also been observed in children with ASD.

❖ **Pathophysiological significance**

In some cases, given the high prevalence of epilepsy in the general population, it is not excluded that a fortuitous coexistence of autism and epilepsy may occur [13].

However, the relationship between autism and epilepsy is complex and the pathophysiological significance of their association remains unclear.

A range of different seizures and seizure syndromes have been identified in relation to autism. Electroencephalograms (EEGs) of autistic people often reveal epileptic abnormalities, even in the absence of seizures, which may suggest the presence of increased sensitivity to seizures. The study by Casanova *et al*., puts forward the hypothesis that an alteration in the internal organization of microcolumns in the cortex of autistic subjects could be associated with a defect in the local inhibition of projection circuits [14]. A possible association between an abnormality in GABA-ergic fibers and increased seizure frequency in individuals with autism has been identified [15].

It is also conceivable that autism and epilepsy share genetic and neurodevelopmental origins, particularly in the case of syndromic autism. Additionally, it has been suggested that epilepsy may contribute to the onset of autism-related symptoms [16].

Two examples can be found:

a) When epilepsy originates in a specific area of the brain, usually located in the temporo-frontal region, this can lead to a regression of autism-related skills. However, it is possible to observe significant improvement through medical or even surgical treatment [17].
b) Various epileptic encephalopathies are related to mental retardation and/or autistic features, presumably due to a particular developmental influence, as is the case with West Syndrome, for example [18].

The combination of epilepsy and ASD is a complex tandem because several studies have found that people with ASD have an increased risk of developing epilepsy compared to the general population. This prevalence varies depending on the severity of ASD, but is statistically significant [19].

In some people, epilepsy may occur even before ASD symptoms become apparent. This raises questions about the role of epilepsy in the subsequent development of ASD, although the underlying mechanisms remain unclear.

Diagnosing epilepsy in people with ASD can be complicated by difficulties with communication and social understanding. Seizures can also be misinterpreted as autistic behaviors.

The various studies have advanced as etiopathogenetic hypotheses of this comorbidity of genetic factors: Certain genes related to epilepsy may also be involved in the development of ASD. Genetic mutations may therefore be a common factor for both conditions. Some brain abnormalities associated with ASD and epilepsy are, suggesting that structural alterations in the brain could contribute to their comorbidity.

CONCLUSION

The comorbidity between epilepsy and autism spectrum disorders is an ever-evolving area of research.

Although the underlying mechanisms are not yet fully understood, it is essential to recognize the existence of this comorbidity for adequate management of those affected. Future research will continue to inform our understanding of this interconnection between epilepsy and ASD highlights the complexity of neurodevelopmental disorders and highlights the importance of ongoing research to better understand these conditions as extensive longitudinal studies, covering both genetic and neurobiological aspects, are needed to further clarify the underlying mechanisms of this association.

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