

## Epilepsy in children with autism spectrum disorders in Albania

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### Abstract

**Aim:** Epilepsy is quite common in autism spectrum disorders (ASD) and represents a challenge for its treatment. We aimed to assess the prevalence of epilepsy in children diagnosed with ASD in Tirana, the capital of Albania.

**Methods:** This is a cross-sectional study including 128 children diagnosed with autism spectrum disorder showing up at the National Center of Child Welfare, Development and Rehabilitation in Tirana during the period 2012-2013. Electroencephalographic (EEG) recordings were obtained for all subjects. In addition, all children underwent a psychiatric examination. Two independent child neurologists examined ASD children and diagnosed and classified epilepsy according to agreed criteria.

**Results:** The mean age of children was 4.2±1.6 years (range: 0-7 years). Prevalence of epilepsy among ASD children was 21.1% during the study period. According to age-group, seizures occurred in 15.6% of the children aged ≤3 years and 29.4% of those aged 4-7 years. Among epileptic ASD children, the most common type of epilepsy was the psychomotor epilepsy, present in 59% of cases, alone or combined with other types of epilepsy. Around 22% of epileptic ASD children had epilepsies that caused a great deal of complications in the child's daily life and that proved to be therapy resistant.

**Conclusion:** Epilepsy in ASD children in Albania is quite common. Therefore, ASD children must be carefully examined in order to detect the existence of co-existing epilepsy and adapt the treatment to this scenario. Clearly, treating epilepsy and ASD poses considerable challenges to the individual, family and the health system in Albania.

**Keywords:** autism spectrum disorder, children, epilepsy.

## Introduction

The prevalence of epilepsy is considerably higher among individuals with autism compared to the general population. However, the association of epilepsy with autism is largely unknown. Children experiencing forms of epilepsy that do not respond to common medication often suffer from various forms of neurodevelopmental disorders and autism (1,2). An association of infantile autism with epilepsy was observed in Kanner's first published article describing 11 autistic children in whom two (18%) developed epilepsy before reaching adult age. Other authors found that more than one in four of some 60 autistic children had had epilepsy by the time they reached early adult age and a "two-tops" peak distribution of onset of epilepsy in autism, one peak being in infancy and the other in adolescence (3,4). Despite its frequent association with autism, epilepsy in children with autism has never been systematically studied. Several authors have noted that all types of epilepsy occur in autism but the relative frequency of various types of seizure disorders in autism is unknown (5,6).

Autism spectrum disorder (ASD) is characterized by impaired social interaction skills and limitation of various activities and interests. Aggression and hyperactivity and/or inattention are frequently associated with ASD. At present, little is known about differences in the autism phenotype between children with and without epilepsy. International literature suggests that ASD is associated with female gender (7,8), impaired cognitive skills (9,10) and developmental regression (11,12).

Despite the available evidence, there is still insufficient information about epilepsy and ASD. There are suggestions that epilepsy seizures might affect children with ASD and therefore the establishment of such association might ameliorate patients' care (13,14).

In Albania there is little information about the association of epilepsy and ASD. Therefore, our objective was to estimate the prevalence of epilepsy in children suffering from ASD in this Balkan country.

## Methods

### *Study design*

This is a cross-sectional study including 128 children diagnosed with autism spectrum disorder and presenting at the National Centre of Child Welfare Development and Rehabilitation in Tirana, Albania, over the period 2012-2013.

### *Data collection and analysis*

For every participant we collected information regarding the occurrence of epilepsy and its type and age of onset. Systematic inquiry into the problem of epilepsy occurrence, type, frequency, and age of onset was accomplished in all cases. When epilepsy was detected, it was classified into grand mal, petit mal, psychomotor, infantile spasms, and other types of seizures.

Electroencephalographic (EEG) recordings were obtained for all subjects and, in most cases, several EEGs were carried out. Some of these included recordings performed only in the waking state, whereas others included recordings using various types of activation. In all cases under study, an assessment of cognitive functions was also carried out.

The research protocols and medical records were carefully assessed by two child neurologists who extracted all relevant information to epilepsy and made comprehensive assessments and diagnoses. The intelligence quotient was also measured for each child under study.

Data were analyzed using SPSS software. Chi-squared test was used to compare the differences between categorical variables. Student's t-test was used to compare continuous variables according to several study groups. A P value  $\leq 0.05$  was considered as statistically significant.

## Results

In total, 128 children were included in the study (43.8% girls). The mean age of children was 4.2 ( $\pm 1.6$ ) years, range 0 to 7 years.

Prevalence of epilepsy among ASD children was

21.1% (27/128). Epileptic cases had had two or more epileptic seizures during the study period. The characteristics of ASD children with epilepsy are presented in Table 1. Among epileptic children with ASD 41% of them were boys. The age of onset was most often in the first year of life. ASD children with epilepsy presented with abnormal EEG recordings in 92.6% of cases whereas 3 (11%) epileptic children had bilaterally synchronous

irregular spike and wave activity only (Table 1). In addition, 2 (7%) ASD children with epilepsy had had typical and 1 (3.7%) had had atypical hypsarrhythmia in infancy. Around 26% of ASD children with epilepsy had a dominance of abnormalities in temporal recordings. When clearly lateralized, these were as often right as left sided. Altogether 12 (44%) of ASD children with epilepsy had a major abnormality seen on the EEG (Table 1).

**Table 1. Characteristics of ASD children with epilepsy**

Variable	ASD children with epilepsy (n=27)	
	Absolute number	Percentage
<b>Gender: Boy</b>	11	40.7%
<b>Abnormal EEG recording</b>	25	92.6%
<b>Bilaterally synchronous irregular spike and wave activity only</b>	2	7.4%
<b>Dominance of abnormalities in temporal recordings</b>	7	25.9%
<b>Typical hypsarrhythmia in infancy</b>	2	7.4%
<b>Atypical hypsarrhythmia in infancy</b>	1	3.7%
<b>Major abnormality on EEG</b>	12	44.4%

Several different types of epilepsy were detected in the 27 epileptic cases under study (Table 2). Six children had had infantile spasms (IS), all of whom now have other types of seizures. At the time of the study, psychomotor epilepsy (PSM) was the

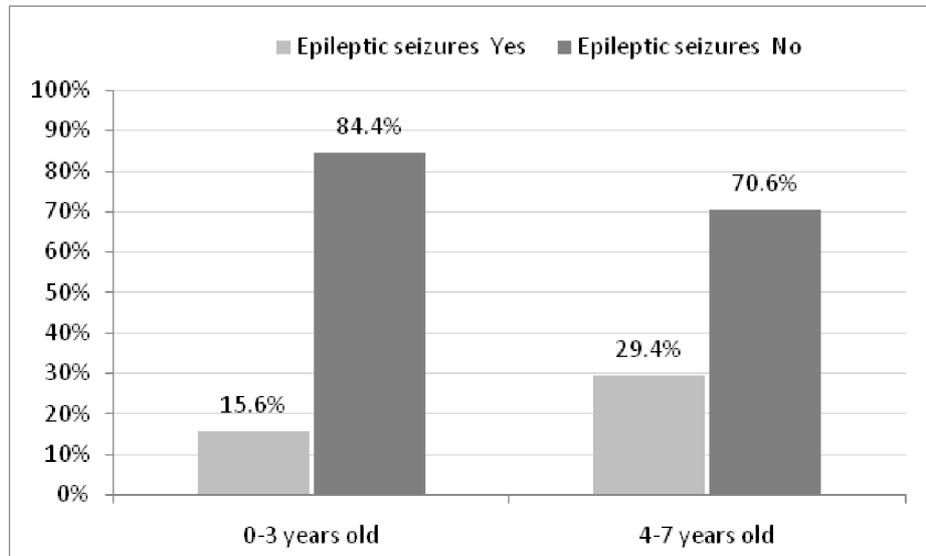
most common type diagnosed (Table 2). Grand mal (GM) and minor motor seizures (MM) occurred in several cases also, but were less common compared to PSM and IS (Table 2).

**Table 2. Type of epilepsy among ASD children**

Type of epilepsy	Absolute number	Percentage
<b>Minor Motor Seizures (MM)</b>	2	7.4%
<b>Grand Mal (GM)</b>	2	7.4%
<b>GM and MM</b>	2	7.4%
<b>Psychomotor Epilepsy (PSM)</b>	4	14.8%
<b>PSM &amp; GM</b>	6	22.2%
<b>PSM &amp; GM &amp; MM</b>	4	14.8%
<b>PSM &amp; GM &amp; PM</b>	2	7.4%
<b>Infantile Spasms (IS)</b>	6	22.2%
<b>Total</b>	27	100%

According to age-group, epileptic seizures occurred in 12 (15.6%) out of 77 children  $\leq 3$  years old and in 15 (29.4%) children out of 51 children 4-7 years

(Figure 1). This difference was not statistically significant ( $P=0.09$ ).

**Figure 1. Frequency of seizures among all children under study, by age-group**

*Correlation with IQ:* There was no clear-cut trend regarding IQ in the epileptic group cases when compared with the non-epileptic group.

*Severity of Seizure Disorder:* Of the 27 children, six (22.2%) had epilepsies that caused a great deal of complications in the child's daily life and that proved to be therapy resistant. These children also generally reacted with behavioral deterioration after receiving recommended doses of anticonvulsant medication. Almost all of the commonly used drugs had been used singly and in various combinations in these cases. Some children felt much better regarding the seizure disorder and the behavioral problems when receiving low or no doses of antiepileptic treatment.

## Discussion

This study is amongst the few studies reporting on the prevalence of epilepsy among a relatively large sample of children diagnosed with autism spectrum disorder in Albania. The prevalence of epilepsy in this sample of ASD children was 21.1%. A variety of seizure types occurred, but psychomotor epilepsy was, by far, the most frequent, occurring in 59% of all epilepsy cases in this study. A mixture of psychomotor epilepsy and other types was very

common as well.

This finding is in line with previous studies that report the association with epilepsy during childhood, adolescence and early adult life. Many of the cases of epilepsy in those studies had their onset in early adolescence (14). Therefore, the indications suggest that the prevalence of epilepsy will probably rise considerably in our country in the next ten years.

The EEG abnormalities detected seemed to stem from temporal regions and phylogenetically older parts of the brain in a majority of the cases (12,15). Infantile spasms were also fairly common and had affected 6% of the autistic children. International literature suggests that more than one in ten children experiencing infantile spasms will develop autism and other autism related characteristics (6,16). There is an association between tuberous sclerosis and infantile spasms and an association between autism and tuberous sclerosis (6,16) and one girl in our study had the combination of all three in addition to severe mental retardation.

There are still doubts about the temporal relationship between epilepsy and autism even though some studies have found that epilepsy might cause autism (5,17) since epilepsy often developed before the appearance of autistic symptoms in these cases.

However, because of the very limited scientific

evidence available, it is almost impossible to definitively conclude that epilepsy might cause autism (18). Epilepsy in autism is often considered to be specifically associated with severe mental retardation, but this was not the case in our study. The numbers are too small for general conclusions, but it is relatively clear that epilepsy can occur in autism in the absence of mental retardation (3,19).

## Conclusion

Because of the doubts surrounding the association of epilepsy and autism, this area continues to attract considerable research interest. Indications suggest

that epilepsy should be carefully monitored in children with autism. Identification of children with increased risk for epilepsy has important implication for the prognosis and treatment of the disease (2,5,20). Adequate treatment of children experiencing simultaneously autism and epilepsy poses a major challenge to the health system and the family partly because of insufficient knowledge about the associations and interactions between these two conditions, as elaborated earlier in our discussion. Therefore, future research is needed in order to shed light upon this combination of health conditions and the most appropriate ways to address them.

**Conflicts of interest:** None declared.

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