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Original Article (Pages: 18037-18043)

Abnormal EEG in Autistic Patients without Any History of Clinical Seizures

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Abstract

Background: There is insufficient information regarding whether epileptic manifestations, in the absence of seizures, contribute to the development of autism symptoms. Electroencephalography (EEG) is the most widely used tool for diagnosing epileptic brain activity. Despite the possibility of the simultaneous manifestation of epilepsy with autism, it cannot be accurately said that epileptic activity, in the absence of seizures, contributes to the emergence of autism symptoms. Therefore, it is important to investigate the prevalence of epileptic activity in non-epileptic people with autism. The purpose of this research was to examine the EEG of autistic patients without a history of clinical seizures to determine anomalies.

Method: The studied population consisted of children between 1 and 18 years of age with autism who had referred to the neurology clinic of the hospital and the neurology office in 2022. Cases with a history of clinical seizures were excluded from the study.

Results: A total of 50 children were studied. The results of 64% of EEG cases showed anomalies. A significant relationship was found between birth type and EEG result. As, in natural delivery, 77% of the results of EEG had anomalies (p=0.048). EEG results showed anomalies in 61% of people who did not have problems at birth and 71.4% of those who had problems at birth.

Conclusion: This study showed that a significant percentage of children with autism spectrum disorder and no history of clinical seizures have abnormal EEGs that should be investigated in terms of manifestations related to epilepsy.

Key Words: Autism, Clinical seizures, EEG.

* Please cite this article as: Golmakani H, Heydarian F, Khademian M, Mahdavikia S. Abnormal EEG in Autistic Patients without Any History of Clinical Seizures. Int J Pediatr 2023; 11 (07):18037-18043. DOI: **10.22038/ijp.2023.71097.5219**

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Received date: Mar.07,2023; Accepted date: Jul.29,2023

1- INTRODUCTION

Autism was first recognized in 1930 as a neurodevelopmental disorder characterized by qualitative defects in social interactions and communication skills, and restricted and repetitive interests and behavioral patterns (1).

Patients with autism spectrum disorder include a heterogeneous group of people whose onset of deficits in social interaction and language development can be seen in early childhood. Behavior often worsens and cognitive decline may also be observed. At least some children with autism are apparently healthy before the onset of the disorder. In some of these children, the onset of deterioration may be in late childhood (2).

The prevalence of autism has increased significantly in recent decades (1). Currently, the prevalence of autism is 1 in every 68 births (3). The prevalence of this disease is 4 to 5 times higher in boys than in girls. But the disorder in girls is associated with severe mental retardation; Autistic spectrum disorders have a strong genetic component (4).

Factors involved in the occurrence of autism include maternal viral infections, use of valproic acid and thalidomide, diabetes, maternal blood pressure and obesity during pregnancy, age of parents at the time of pregnancy, intervals between pregnancies, along with some environmental factors such as contact with mercury, radioactive substances and insecticides (5).

Despite much research on the biological factors that contribute to the development of autism, the set of factors necessary for the syndrome to occur is unclear. Evidence of neural involvement in autism syndromes is accumulating. Conner's (1943) initial report, in which he described 11 children with autism, provided important insights into the neurological component of the syndrome (2).

Epilepsy is the most common chronic and recurrent disease of the nervous system in childhood with a prevalence of 8 per 1000 people (6).

Autism spectrum disorder and epilepsy are common neurodevelopmental disorders that make up a large part of the burden of neurological diseases in children and adults with comorbidities up to 30% or more. Some researchers have suggested that the degree of clinical overlap between autism and epilepsy results from a common neurodevelopmental dysfunction. The heterogeneous spectrum of symptoms that characterize both disorders makes it difficult to study the commonalities and differences between these disorders. There is evidence of abnormal epileptiform abnormalities in children with epilepsy even in the absence of clinical seizures, but little is known about the clinical or therapeutic implications of this disease (7).

The prevalence of epilepsy in patients with autism spectrum disorders is higher than in the general population. In addition, in autism patients, the incidence of epileptic activity in EEG ranges from 23.6% to 60.8% (8).

The main method used to record and describe the paroxysmal epileptic activity that often occurs in autism is the EEG. EEG recordings may also be used to examine functional connectivity in different brain regions over time through EEG coherence, which is a quantitative assessment of the correlation between the frequency spectra of two EEG signals (9).

This useful feature could help to better understand the disrupted connections in brain regions revealed by functional MRI studies in patients with autism (10).

Therefore, in the current study, EEG was used to determine the presence or absence of epileptic abnormalities in autistic children without any history of clinical seizures.

2- METHODOLOGY

2-1. Design and Population

This descriptive-analytical study was conducted on children with autism referred to the neurology clinic in the children's hospital and a children's neurology clinic in the northeast of Iran in 2022.

2-1.1. Inclusion and Exclusion Criteria

The criterion for entering the study included all under-18-year-old autistic children with the absence of previous seizure history, and if a seizure occurred upon entry or during the study, the person was excluded from the study.

2-2. Data Analysis

In this study, demographic information, the types of birth and disorders at birth were recorded; and their relationships with the EEG results were investigated. Tables and graphs were used to describe the data, and chi-square test of independence was used in SPSS version 25 to analyze the data.

2- RESULTS

In this study, a total of 50 children with autism were investigated; 39 (78%) of whom were boys and 11 (22%) were girls. In terms of age distribution, 30% of children were between 1 and 3 years old and 32% were between 3 and 5 years old. Moreover, 22 percent of children were between 5 and 7 years old, 8 percent were between 7 and 10 years old, and 8 percent were more than 10 years old (**Fig. 1**). Regarding the type of delivery, (48%) 24 people were born by cesarean section and (52%) 26 people were born naturally. Problems related to the birth time did not exist in (72%) 36 people and were reported in (28%) 14. Out of the total of 50 children studied, 18 (36%) had normal EEG and 32 (64%) had abnormal EEG.

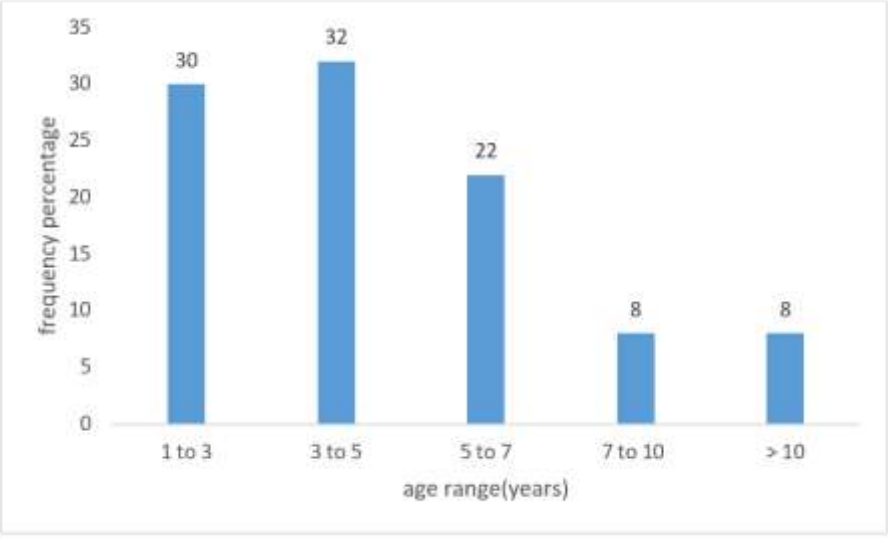

Fig. 1: Age distribution of studied children with autism

To investigate the relationship between birth type and EEG results, a chi-square test of independence was used, the results of which are shown in **Table 1**. Accordingly, out of 24 cases of cesarean section delivery, the EEG results of 12 individuals were normal and 12 cases were abnormal. While, out of 26 cases of natural delivery, the EEG results of 20 cases were abnormal.

Table-1: Analysis of the EEG results based on the type of birth

Variable			EEG		Total
			Abnormal	Normal	
Type of delivery	CS	Count	12	12	24
		%	50	50	100
		%EEG	37.5	66.7	18
		% From total	24	24	48
	N	Count	20	6	26
		%	76.9	23.1	100
		%EEG	62.5	33.3	52
		% From total	40	12	52
	Total	Count	32	18	50
		%	64	36	100
		%EEG	100	100	100
		% From total	64	36	100

Table 2 shows the results of the chi-square test of independence. The significance value in **Table 2** was less than 0.05. Therefore, at the 95% confidence level, birth type and EEG results were not independent from each other and had a significant relationship.

Table-2: Chi-square test results (type of birth and EEG results)

Test	Value	Degrees of freedom	Significance coefficient
Pearson's chi-square *	3.926	1	0.048

*: Number=50

The effect size findings between type of birth and EEG results are presented in **Table 3**. The value of the effect size of birth type and EEG results was determined based on Cramer's V index.

Table-3: Effect size results between type of birth and EEG results

Test	Value	Significance coefficient
Cramer's V *	0.28	0.048

*: Number=50

The value obtained for Cramer's V index was 0.28, which indicated a moderate effect size between type of birth and EEG results.

Chi-square test of independence was also used to investigate the relationship between problems at birth and EEG results (**Table 4**).

Accordingly, in the group of people without any problems at birth, 22 cases had abnormal results and 14 cases were normal. Furthermore, among children with birth problems, 10 cases were abnormal and 4 were normal. The value of significance in **Table 5** was greater than 0.05. Therefore, at the 95% confidence level, birth problems and EEG results were independent of each other and had no significant relationship. The magnitude of the effect size of birth problems and EEG results based on Cramer's V was very weak (**Table 6**).

Table-4: Analysis of the EEG results based on the problems related to the time of birth

Variable			EEG		Total
			Abnormal	Normal	
Problems revealed at birth time	No	Count	22	14	36
		%	61.1	38.9	100
		%EEG	68.8	77.8	72
		% From total	44	28	72
	Yes	Count	10	4	14
		%	71.4	28.6	100
		%EEG	31.3	22.2	28
		% From total	20	8	28
	Total	Count	32	18	50
		%	64	36	100
		%EEG	100	100	100
		% From total	64	36	100

Table-5: Chi-square test results (problems at birth and EEG results)

Test	Value	Degrees of freedom	Significance coefficient
Pearson's chi-square	0.466	1	0.495

*: Number=50

Table-6: Effect size results between at-birth problems and EEG results

Test	Value	Significance coefficient
Cramer's V	0.097	0.495

3- DISCUSSION

In a retrospective study by Santarone et al., out of 292 children younger than 6 years who received an initial multidisciplinary diagnosis of autism spectrum disorder, 78% of cases had abnormal EEG results (11). The amount of abnormal EEG cases in this study was 14% higher than that in the current study, which could be due to the difference in age groups, since the current study included children up to 18 years old.

Sharma et al., carried out a study to determine the prevalence of epilepsy and EEG abnormalities in autistic children aged between 3 and 14 years. Out of a total of 100 epileptic children studied, epilepsy was recorded in 23% and subclinical EEG abnormalities were reported in 8%. There was a significant association between adverse perinatal events and epilepsy and adverse perinatal events were found to be independent predictors of epilepsy (12). In contrast to the above study, in the present study, problems related to the time of birth were not significantly related to EEG abnormalities.

Chez et al., examined EEGs of a large number of children with autism to determine the extent and nature of EEG abnormalities in children with symptoms of autism who had no identifiable seizures or genetic problems. From a total of 1268 children with autism who were examined between 1996 and 2005, children with identified genetic disorders, tuberous sclerosis, or a history of seizures were excluded from the study. EEG abnormalities were found in 60.7% of the remaining 889 children without any

previous evidence of epilepsy (13). In the current study, the rate of abnormal EEG results was 64%, which is close to that reported in the above study.

In a study conducted by Parmeggiani et al., on 345 patients with autism, autistic regression was not correlated with seizures and EEG paroxysmal abnormalities (14). However, in the study by Hrdlicka et al., it was stated that autistic regression occurs more frequently in patients with epilepsy ($p < 0.01$) (15). Parmeggiani et al. showed that while EEG paroxysmal abnormalities occur mainly in childhood, epilepsy tends to occur ($p < 0.001$) as age increases. In this study, two peaks were determined for the age of seizure onset: between 0 and 5 and between 10 and 15 years, while there was no difference between idiopathic and symptomatic cases (14). Although, in the above study, the age range of 0-5 years was one of the age ranges for the onset of seizures, in the current study, where people with a history of clinical seizures were left out, a significant part of the studied population (62%) were cases with less than 5 years of age. According to Hrdlicka et al., abnormal neurodevelopmental events occurring during the first year of life are significantly correlated with epileptiform EEG abnormalities ($p < 0.05$) (15).

In another study by Ekinci et al., on children with autistic spectrum disorder, the prevalence of epilepsy was found to be 14.2% and the frequency of interictal epileptiform EEG abnormalities was 24.6%. Interictal epileptiform EEG abnormalities were associated with a diagnosis of epilepsy ($P= 0.0001$) (16). In the study by Lee et al., conducted on thirty patients diagnosed with autism spectrum disorder, although all patients suffered clinical seizure events, the EEG results were variable and 23 out of 30 patients (76.6%) showed epileptiform EEG abnormalities (17). Alaimo et al., retrospectively studied 400 consecutive patients with autism and epilepsy in which seizures were captured in 45 patients. This study provided clinical-EEG correlates of seizures in autism spectrum disorder patients (18).

4- CONCLUSION

This study showed that despite the absence of clinical seizures, a significant percentage of children with autism have epileptic abnormalities and EEG can help in early diagnosis.

5- ETHICAL CONSIDERATIONS

The parents were aware of the archiving of medical records and test results, and confidentiality of the patients' personal information was carefully considered by the researchers.

6- ACKNOWLEDGMENT

The researchers are grateful to the parents of the children participating in the study.

7- CONFLICT OF INTEREST

None.

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