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**ORIGINAL ARTICLE****Electroencephalogram Changes in Autism Spectrum Disorder Patients at Zagazig University Pediatric Neurology Outpatient Clinic**Angi Alsharif<sup>1</sup>; Ahmed Siam<sup>2</sup>; mohammed Arafa<sup>2</sup><sup>1</sup>Pediatrics Department, Alahrar teaching hospital, Zagazig, Egypt<sup>2</sup>Pediatrics departement, Faculty of Medicine ,Zagazig University, Zagazig, Egypt**Corresponding author**

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**ABSTRACT**

**Background:** Electroencephalogram (EEG) changes have been recorded in Autism Spectrum Disorder (ASD) patients among hundreds of studies all over the world. Some may have stated EEG as a necessity in the ASD investigations. This study was done in order to determine whether there is a link between the severity of the clinical picture of ASD and the changes seen on the electroencephalogram

**Methods:** The study took place at Zagazig University outpatient pediatrics neurology clinic, in the duration between January 2018 and February 2019. A case control study that included 42 children between 3 and 7 years in each group. The control group included children visiting the clinics for minor illnesses. The case group included ASD diagnosed patients with severity assessed using Childhood Autism Rating Scale (CARS). Both groups were video recorded while having an electroencephalogram done

**Results:** EEG changes were more prevalent in autistic children (40.5% compared to 7.2%) and despite the high prevalence compared to non-autistic children, they had no effect on the severity of symptoms ( $p < 0.001$ ).

**Conclusions:** EEG changes had no significant effect on the severity of Autism symptoms despite being more prevalent in ASD patients than healthy children.

**Keywords:** EEG, Autism, CARS, ASD, non-epileptic.

**INTRODUCTION**

Autism, also referred to as autism spectrum disorder (ASD), constitutes a neurodevelopmental disorder characterized by impairment in communication, including language and social skills, along with restricted repertoire of interests and behaviors and by atypical sensory reactivity [1]. ASD signs mostly appear before 3 years of age. In some cases, it can be diagnosed as early as 18 months. The incidence of autism has increased over the past years; owing that to the raised awareness of the disease and the development of accurate diagnostic modalities [2]. Subsequently, an increase in research of the pathophysiology of this disease, including conditions that are associated or lead to it. Relatively little is known about autism clinical correlations and comorbidities in Middle Eastern and Arab countries. Recently, there has been some developing research in the area of autism in the Middle East. The prevalence of ASD among

children with developmental disorders in Egypt was documented as 33.6% [3]

Interictal epileptiform discharges (IED) were found in multiple groups of people with no previous history of seizures [4] There are a lot of reports of interictal EEG changes in ASD children. As these abnormalities may occur in individuals without seizures, they are more likely to indicate the presence of brain dysfunction. Searching more about what causes these changes may lead to more reasonable theories about the etiology of ASD hoping that one day a complete map will be drawn featuring all the details of this disease.

The relationship between epilepsy and ASD was always under study. Many studies proved the ASD plays an important factor that increases the incidence of seizures, and vice versa. That means that epilepsy increases the risk of Autism. This makes us accept the two as co morbidities [5]. A large percentage of ASD patients with epileptic changes on EEG showed no evidence of symptoms, although improvement was seen in their behavioral symptoms after taking antiepileptic

drugs [6]. This study aimed to detect the relationship between the EEG abnormalities and the severity of symptoms of autism measured by childhood autism rating scale (CARS).

### METHODS

This case control study was conducted at Pediatrics Neurology Unit, Faculty of Medicine, Zagazig University Hospitals during the period from July 2018 to February 2019. A total sample of 84 children, 42 in each group.

**Case group: Inclusion criteria:** Patients from 3-7 years old, from both genders and all socioeconomic groups diagnosed with ASD according to Diagnostic and Statistical Manual of Mental Disorders – 5<sup>th</sup> edition (DSM-V-TR), the Childhood Autism Rating Scale (CARS) [7].

**Exclusion criteria:** Patients with any disorder that would have explained the autistic features (e.g., Rett syndrome, Tuberous sclerosis, Fragile X syndrome, Landau Kleffner syndrome) and epileptic patients and patients with history of head trauma, neurological disorders, metabolic disorders, head trauma or presence of other psychiatric disorders or mental disorder were all excluded along with patients aged less than 3 years or more than 7 years.

A Control group of healthy children attending the outpatient clinics for minor illnesses, of age and sex matching to the case group. Children having serious illnesses or neurodevelopmental disorders were excluded.

A Structured interview was done to both groups. Using a predesigned questionnaire for parents including child's age, sex and developmental history and to exclude any neurological or psychiatric diseases from the patient's history. Medical and Neurological examination was also done to exclude any neurological, metabolic disorders and head trauma. DSM-V-TR criteria were used in the diagnosis of ASD under the supervision of a pediatric neurology staff member. CARS criteria were used to assess the severity of the diagnosed cases. Electroencephalography (EEG) was done for all patients using the Stellate Harmonie system, which has a standard number of 28 channels arranged according to the 10-20 system. EEG was recorded for an hour along with continuous video observation. Both were displayed at the same time, which allowed comparison of the EEG changes and the recorded events. The EEG tracing was analyzed regarding: background activity, generalized slowing or spike wave, focal slowing or spike wave and focal with secondary generalization. All EEG were carried out under normal standard conditions i.e. the child is lying

supine completely relaxed and asleep in a quiet room.

### Ethical Declaration:

A written informed consent was taken from all parents of children participating in the study, and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of The World Medical Association (Declaration of Helsinki) for studies involving humans.

**Statistical Analysis:** Data were coded, entered, checked and analyzed using SPSS version 25.0 (Statistical Package for the Social Sciences). Data were presented as Mean  $\pm$  Standard deviation (SD) for quantitative variables, numbers and percentage for categorical variables. T test was used for independent samples. Chi square test ( $\chi^2$ ) when appropriate.

The results were considered:

- Significant when the probability of error is less than 5% ( $p < 0.05$ ).
- Non-significant when the probability of error is more than 5% ( $p > 0.05$ ).
- Highly significant when the probability of error is less than 0.1% ( $p < 0.01$ ) [8]

### RESULTS

Demographic data of both case and control groups were presented in table (1). Statistical differences between the two groups regarding sex or age distribution were insignificant ( $p > .05$ ).

There was a noticeable statistically significant difference between the autistic group and the control group regarding the EEG abnormalities ( $p < 0.001$ ), 40.5% of the autistic patients had abnormal EEG, 21.4% had generalized EEG changes, 7.1% had focal EEG abnormalities, 7.1% having focal changes with secondary generalization and nearly 4.8% showed slowing EEG wave. Whereas the control group had only 7.1% generalized EEG changes as presented in table (2).

Mild Autism was prevalent among 16.7% of children in the case group, 73.8% had moderate autism and 9.5% had severe autism as seen in table (3). There was no statistical significance difference between mild, moderate and severe cases in regards to EEG change ( $p > .05$ ). There was no statistical significance difference between male and female cases in EEG changes.

In this study male children showed higher rates of (ASD) diagnosis than female children (61.9% males)

**Table 1: Demographic data of two studied groups.**

Variable	Cases (n=42)		Control (n=42)		t	P
<b>Age (years)</b>						
Mean ± SD	3.75 ± .5		3.75 ± .5		0.22	0.83
Range	3 – 5.2		3 - 5			NS
<b>variable</b>	<b>No</b>	<b>%</b>	<b>No</b>	<b>%</b>	<b>χ<sup>2</sup></b>	<b>P</b>
<b>Sex:</b>						
Female	16	38.1	18	42.9	0.20	0.66
Male	26	61.9	24	57.1		NS

SD: Standard deviation t: independent t test χ<sup>2</sup>: Chi square test NS: Non significant (P>0.05)

**Table 2: EEG Changes among the two studied groups.**

Variable	Cases (n=42)		Control (n=42)		χ <sup>2</sup>	P
	No	%	No	%		
<b>EEG:</b>						
No change	25	59.5	39	92.9	<b>12.86</b>	<b>&lt;0.001</b> **
Change	17	40.5	3	7.1		
<b>Change type:</b>						
Generalized	9	21.4	3	7.1		
Focal	3	7.1	0	0		
Focal with 2ry generalization	3	7.1	0	0		
Slowing	2	4.8	0	0		

χ<sup>2</sup>: Chi square test \*\*: Highly significant (P<0.01)

**Table 3: Relation between severity of Autism and EEG changes among the cases group.**

Variable	Mild (n=7)		Moderate (n=31)		Severe (n=4)		χ <sup>2</sup>	P
	No	%	No	%	No	%		
<b>EEG:</b>								
No change	5	71.4	18	58.1	2	50	0.59	0.75 NS
Change	2	28.6	13	41.9	2	50		
<b>Change type:</b>								
Generalized	1	14.3	7	22.6	1	25		
Focal	0	0	2	6.5	1	25		
Focal with secondary	1	14.3	2	6.5	0	0		
Slowing	0	0	2	6.5	0	0		

χ<sup>2</sup>: Chi square test NS: Non significant (P>0.05)

**DISCUSSION**

Autism Spectrum Disorder is a neurodevelopmental scope of disorders which differ in severity, with common impairments including social interaction and individual verbal and non-verbal communication with others, that is associated with restricted repertoire of stereotyped behaviors and by abnormal sensory reactivity, all together limit everyday performance [1]. There are a lot of reports of interictal EEG changes in ASD children. As these abnormalities may occur in

individuals without seizures, they are more likely to indicate the presence of brain dysfunction, that’s why searching more about what causes these changes may lead to more reasonable theories about the etiology of ASD.

In this study, there was statistically significant difference between the autistic and the control groups regarding the EEG abnormalities as there was high rate of subclinical epileptiform abnormalities among the autistic group (40%) compared to (7%) at the control group .These

results agree with a study done by Yasuhara who found that abnormal EEG discharges occurs in 85.8% (870/1014) [9], it also agrees with a study done by Tando in 2012 which showed changes in 52.4% of a group of autistic children aged between 3 and 6 years [10].

A retrospective study of 24-hour ambulatory digital EEG results was conducted between years 1996 and 2005 and took place in Chicago, data was obtained from 889 autistic individuals (with no brain malformations, prior medications, or clinical seizures). This consecutive study showed that 60.7% of the patients had abnormal EEG activity during their sleep [11].

The exclusion of both severely retarded individuals, those who have clinical seizures and those with any evidence of other neurodevelopmental disorders removes the bias of some previous studies that may have increased the percentages of abnormal EEG activity [12].

These high rates of EEG abnormalities among ASD children suggest that this activity may be a factor in the pathology of cognitive impairment, behavioral problems, language dysfunction, and increase the possibility of development of clinical seizures later [13]. Although a lot of studies stated that even though EEG abnormalities may predict future evident epileptic activity, these changes showed no significant effect on the cognitive development and autistic features of the ASD patients whatsoever [11].

In this study male children showed higher rate of (ASD) diagnosis than female children (61.9% males aged between 3 -7 years). The majority of boys was also and always noted in all studies on ASD [14]. Autism spectrum disorder is approximately 4 times more prevalent in boys than girls [15]. Our data is consistent with a 18 years long Swedish study published in year 2006, it was performed on all individuals born during this period of time, this wide study showed a male prevalence with a ratio of 3.8 boy for each girl [16]. The incidence of generalized EEG abnormalities was only 14.3% in children with mild autism, 22.6% in those with moderate autism and 25% in severely autistic children. As regards to focal changes, in mild cases no one showed focal changes, while 6.5% of moderate cases and 25% of the severe group showed focal changes on their EEG, all these results showed no significant relation between the EEG changes and the severity of autism. These results were in agreement with a study conducted by Oslejskova in year 2008 proved that low IQ and reduced functionality significantly correlate rather with epileptic seizures than just sub-clinical epileptiform abnormality on EEG [17]. Another study which is in concordance

with our results, is a study done on 57 children with ASD in year 2009 and showed no significant relation between severity of autism symptoms and presence of IEDs [18].

#### LIMITATIONS OF THE STUDY

The small sample size was a strong limitation, given the low return rate. No other sources of behavioral data, such as direct observation or school reports were used to corroborate parent reports of adaptive and maladaptive behaviors. Methodological difference (differences in the type of EEG recording, routine awake EEG in other studies and in the present study sedation and inducing sleep was used).

#### CONCLUSION

EEG abnormalities are frequently recorded in patients with autism despite the absence of seizures, this strongly helps in proving that ASD has a neurological basis. Proving that there are EEG changes would not be of any clinical benefit as any early intervention is not needed until seizures are really manifested. This study also showed that there is no significant relation between the severity of autistic symptoms and EEG changes, and although this field is rich in data and needs a lot of research and studied to understand its aspects more thoroughly, it would be of no value to make EEG a routine in the evaluation of patients with ASD.

#### RECCOMENDATIONS

A larger sample size should be used as a small number of studied cases reduces the power of statistical analysis done. More research should be done in this field in order to study the relationship between the electroencephalogram changes found in ASD patients and the autistic symptoms.

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