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Original Research Article

Association of autism spectrum disorder with epilepsy and abnormal electroencephalogram in children

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ABSTRACT

Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by various brain abnormalities, although its exact cause remains unknown. Epilepsy is commonly associated with ASD, and children with ASD often exhibit paroxysmal EEG abnormalities, even without clinical seizures. Both ASD and epilepsy have a significant impact on a child's well-being and contribute to the burden on the family. This study aimed to assess the association of autism spectrum disorder with epilepsy and abnormal electroencephalogram in children.
Methods: This comparative cross-sectional study was conducted in the outpatient Department of Pediatric Neurology, National Institute of Neurosciences (NINS), Dhaka, Bangladesh from January 2021 to July 2022. The study included a total of 60 children aged 31 months to 14 years diagnosed with autism spectrum disorder (ASD) at the pediatric outpatient department (OPD) in NINS, selected purposively. Data analysis was performed using the SPSS version 25.0 program.
Results: In the ASD with epilepsy group, 50% of children had moderate ASD, and 50% had high ASD. In the ASD with abnormal EEG group, 66.67% had high ASD, and 33.33% had moderate ASD. In the ASD-only group, 81.25% had moderate ASD, 12.5% had high ASD, and 6.25% had low ASD. When comparing these groups with their corresponding comparison groups, the ASD with abnormal EEG group exhibited significantly more severe autism than children with ASD and normal EEG ($p<0.001$). Conversely, the ASD-only group had less severe autism than children with ASD and epilepsy/abnormal EEG ($p<0.001$).
Conclusion: Children with ASD and abnormal EEG had a higher severity of autism, with 66.67% categorized as high severity. In contrast, children with ASD only experienced less severe autism, with 81.25% categorized as moderate. This indicates that ASD-only children tend to have a milder presentation of autism compared to those with ASD and comorbid epilepsy or abnormal EEG.

Keywords: Autism spectrum disorder, ASD, Epilepsy and abnormal electroencephalogram, Anxiety, Depression, Specific phobia

INTRODUCTION

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by enduring challenges in social interaction and communication, alongside the presence of restricted and repetitive behaviors.[1] The diagnostic and statistical manual of mental disorders, fifth edition (DSM-5), defines autism as a spectrum disorder with two primary domains, (a) persistent deficits in social communication and interaction, and (b) restricted, repetitive patterns of behaviors, interests, or activities.[2] Common features of

autism include difficulties in social interaction, communication, repetitive behaviors and interests, sensory sensitivities, and occasionally cognitive delays.[3] The prevalence of autism spectrum disorder (ASD) is approximately 1% worldwide.[4]

According to the community report on autism by the ADDM network, the prevalence of autism was 1 in 44 (2.3%) among 8-year-old children in 2018, which increased from 1 in 54 in 2016.[5] In Bangladesh, the prevalence of ASD ranges from 0.15% to 0.8%.[6] The nationwide survey on young children with autism spectrum disorder in Bangladesh in 2017 reported that 17 children out of every 10,000 are affected by ASD.[7]

Epilepsy is a neurological condition characterized by either two unprovoked seizures occurring more than 24 hours apart, one unprovoked seizure with a high likelihood of recurrence, or a diagnosis of epilepsy syndrome.[8] Epilepsy is more prevalent among individuals with autism spectrum disorder (ASD), with reported rates ranging from 5% to 46%, significantly higher than the general population prevalence of 0.5% to 1%.[9,10]

Importantly, electroencephalographic abnormalities can occur in individuals with ASD even in the absence of clinical seizures. A significant proportion of individuals with autism spectrum disorder (ASD), ranging from 6.7% to 65%, exhibit interictal epileptiform discharges on routine EEG studies.[11,12] These EEG abnormalities vary from nonspecific changes to epileptiform patterns and may increase the risk of epilepsy development or impact cognition, social communication, and behavior.[13]

The association between ASD and epilepsy dates back to the earliest description of autism by Kanner et al, yet the influence of epilepsy on autistic symptoms remains less understood.[14] Nonetheless, several studies suggest that individuals with ASD and coexisting epilepsy often present with heightened autism symptoms.[15]

Traditionally, the severity of autism spectrum disorder (ASD) is assessed based on the degree of impairment in three main domains, general intelligence, language performance, and ASD-specific core symptoms. This includes the magnitude of social-communicative deficits and restricted/repetitive behaviors unique to ASD.[16]

Direct measures used to estimate the severity of core ASD features include the autism diagnostic observation schedule (ADOS), autism diagnostic interview-revised (ADI-R), social responsiveness scale (SRS), and childhood autism rating scale (CARS).

Among these, ADOS is considered the gold standard for diagnosing autism, with its classification often used as an additional indicator of autism severity by researchers.[17] The objective of this study was to assess the association of autism spectrum disorder with epilepsy and abnormal electroencephalogram in children.

METHODS

Study type

This was a comparative cross-sectional study that was conducted in the outpatient Department of Pediatric Neurology, National Institute of Neurosciences (NINS), Dhaka, Bangladesh.

Study duration

Study duration was from January 2021 to July 2022.

Sample size

For this study, 60 children aged 31 months to 14 years diagnosed with autism spectrum disorder (ASD) at the pediatric outpatient department (OPD) in NINS were included using a purposive sampling technique. Approval for the study was obtained from the hospital's ethical committee, and written consent was obtained from all participants before data collection.

Inclusion criteria

Inclusion criteria required patients to meet the diagnostic and statistical manual of mental disorders, 5th Edition (DSM-5) criteria for ASD.

exclusion criteria

The exclusion criteria for this study included patients with ASD caused by genetic or syndromic factors, progressive neurodegenerative disorders, and epileptic encephalopathy as indicated by history and EEG findings.

Statistical analysis

In this study, the associations of autism spectrum disorder (ASD) with epilepsy and abnormal electroencephalogram (EEG) were analyzed and disseminated based on three groups: 'ASD with and without epilepsy,' 'ASD with normal and abnormal EEG,' and 'ASD with epilepsy or abnormal EEG compared to ASD only.' Data were processed and analyzed using the SPSS version 25.0 program as required. In statistical analysis, a p value of less than 0.05 was considered indicative of significance.

RESULTS

The mean age of our participants was 5.97±3.29 in the ASD with epilepsy group, 4.65±2.10 in the ASD with abnormal EEG group, and 5.88±2.55 years in the ASD-only group. Across all three groups, there was a male predominance, with 66.67% in the ASD with epilepsy, 62.50% in the ASD with abnormal EEG, and 78% in the ASD-only group. However, when comparing each group with its respective comparison group, there was no statistically significant difference in age or gender distribution.

We found the most common antecedent event was a wide parental age gap (10 years and more). Other antecedents included low birth weight, maternal diabetes, single parenthood, and twin pregnancy. The most prevalent co-morbidity in all three groups was attention-deficit/hyperactivity disorder (ADHD), with rates of 75% in the ASD with epilepsy, 62.50% in the ASD with abnormal EEG, and 67.74% in the ASD-only group. However, when comparing each group with its respective comparison group, encopresis was found to be significantly higher in the ASD-only group (p=0.026).

Our findings revealed that speech delay/regression was the most common core symptom, present in 91.67% of both the ASD with epilepsy and the ASD with abnormal EEG group, and in 100% of the ASD-only group. Regarding core features, unusual sensory interests were significantly more prevalent in the ASD with abnormal EEG (p=0.041) and less prevalent in the ASD-only group (p=0.31). Among children with ASD and epilepsy, 50% were classified as having moderate ASD, and the other 50% were classified as having high ASD.

In the ASD group with abnormal EEG, 66.67% scored high on the ADOS comparison score. However, in the ASD-only group, the majority (81.25%) scored moderate. When comparing each group with its corresponding comparison group, the ASD group with abnormal EEG exhibited significantly more severe autism (p≤0.001), while the ASD-only group demonstrated less severe autism (p≤0.001).

Table 1: Demographic characteristics of the participants (n=60).

Indicators	ASD with epilepsy	ASD without epilepsy	P value	ASD with abnormal EEG	ASD with normal EEG	P value	ASD-only	ASD with epilepsy /abnormal EEG	P value
	(n=12)	(n=48)		(n=24)	(n=36)		(n=32)	(n=28)	
	% (N)	% (N)		% (N)	% (N)		% (N)	% (N)	
Age in years									
Mean (SD)	5.97 (±3.29)	5.3 (±2.35)	0.422	4.65 (±2.10)	5.95 (±2.71)	0.052	5.88 (±2.55)	4.93 (±2.50)	0.153
Gender									
Male	66.67 (8)	72.92 (35)	0.667	62.5 (15)	77.78 (28)	0.198	78.13 (25)	64.29 (18)	0.235
Female	33.33 (4)	27.08 (13)		37.5 (9)	22.22 (8)		21.88 (7)	35.71 (10)	
Male:Female	2:01	2.7:1	--	1.6:1	3.5:1	--	3.6:1	1.8:1	--

Table 2: Antecedent events among the participants.

Indicators	ASD with epilepsy	ASD without epilepsy	P value	ASD with abnormal EEG	ASD with normal EEG	P value	ASD-only	ASD with clinical seizure/ abnormal EEG	P value
	(n=12)	(n=48)		(n=24)	(n=36)		(n=32)	(n=28)	
	% (N)	% (N)		% (N)	% (N)		% (N)	% (N)	
Low birth weight	8.33 (1)	4.17 (2)	0.554	4.17 (1)	5.56 (2)	0.809	6.25 (2)	3.57 (1)	0.635
Maternal diabetes	8.33 (1)	4.17 (2)	0.554	8.33 (2)	2.78 (1)	0.333	3.13 (1)	7.14 (2)	0.476
Twin pregnancy	0.00 (0)	4.17 (2)	0.472	0.00 (0)	5.56 (2)	0.24	6.25 (2)	0.00 (0)	0.178
Wide parental age gap (≥10 years)	58.33 (7)	29.17 (14)	0.058	37.5 (9)	33.33 (12)	0.74	28.13 (9)	42.86 (12)	0.233
Single parents	8.33 (1)	4.17 (2)	0.554	0.00 (0)	8.33 (3)	0.147	6.25 (2)	3.5 (1)	0.635

Table 3: Comorbid conditions associated with ASD among participants.

Indicators	ASD with epilepsy	ASD without epilepsy	P value	ASD with abnormal EEG	ASD with normal EEG	P value	ASD only	ASD with clinical seizure/ abnormal EEG	P value
	(n=12)	(n=47)		(n=24)	(n=35)		(n=31)	(n=28)	
	% (N)	% (N)		% (N)	% (N)		% (N)	% (N)	
ADHD	75.00 (9)	63.83 (30)	0.466	62.50 (15)	68.57 (24)	0.628	67.74 (21)	64.29 (18)	0.779
Anxiety	8.33 (1)	2.13 (1)	0.289	4.17 (1)	2.86 (1)	0.785	3.23 (1)	3.57 (1)	0.942
Depression	8.33 (1)	2.13 (1)	0.289	4.17 (1)	2.86 (1)	0.785	3.23 (1)	3.57 (1)	0.942
Specific phobia	8.33 (1)	25.53 (12)	0.2	12.50 (3)	28.57 (10)	0.143	29.03 (9)	14.29 (4)	0.172
Self-injury	33.33 (4)	21.28 (10)	0.381	25.00 (6)	22.86 (8)	0.849	22.58 (7)	25.00 (7)	0.827
Feeding problems	25.00 (3)	8.51 (4)	0.115	8.33 (2)	14.29 (5)	0.487	9.68 (3)	14.29 (4)	0.585
Sleep problem	41.67 (5)	31.91 (15)	0.524	29.17 (7)	37.14 (13)	0.525	35.48 (11)	32.14 (9)	0.787
Enuresis	0.00 (0)	6.38 (3)	0.369	0.00 (0)	8.57 (3)	0.141	9.68 (3)	0.00 (0)	0.091
Encopresis	0.00 (0)	10.64 (5)	0.238	0.00 (0)	14.29 (5)	0.053	16.13 (5)	0.00 (0)	0.026
Constipation	16.67 (2)	27.66 (13)	0.435	16.67 (4)	31.43 (10)	0.201	32.26 (10)	17.86 (5)	0.205

ADHD: Attention-deficit/hyperactivity disorder

Table 4: Core ASD symptoms comparison in the three groups.

Indicators	ASD with epilepsy	ASD without epilepsy	P value	ASD with abnormal EEG	ASD with normal EEG	P value	ASD-only	ASD with clinical seizure/ abnormal EEG	P value
	(n=12)	(n=48)		(n=24)	(n=36)		(n=31)	(n=28)	
	% (N)	% (N)		% (N)	% (N)		% (N)	% (N)	
Speech delay or regression	91.67 (11)	97.92 (47)	0.281	91.67 (22)	100.00 (36)	0.078	100.00 (32)	92.86 (26)	0.124
Stereotype speech/behaviour	50 (6)	66.67 (32)	0.284	62.50 (15)	63.89 (23)	0.913	68.75 (22)	57.14 (16)	0.352
Abnormal eye contact	41.67 (5)	39.58 (19)	0.895	37.5 (9)	41.67 (15)	0.747	37.50 (12)	42.86 (12)	0.673
Joint attention	25 (3)	29.17 (14)	0.774	20.83 (5)	33.33 (12)	0.293	31.25 (10)	25 (7)	0.592
Unusual sensory interests	83.33 (10)	64.58 (31)	0.212	83.33 (20)	58.33 (21)	0.041	56.25 (18)	82.14 (23)	0.031
Abnormal hand mannerisms	33.33 (4)	31.25 (15)	0.89	41.67 (10)	25.00 (9)	0.174	25 (8)	31.67 (19)	0.235
Self-injurious behavior	0.00 (0)	2.08 (1)	0.614	0.00 (0)	2.78 (1)	0.41	3.13 (1)	0.00 (0)	0.346
Temper tantrum	25.00 (3)	10.42 (5)	0.184	8.33 (2)	16.67 (6)	0.352	12.50 (4)	14.29 (4)	0.839
Echolalia	8.33 (1)	18.75 (9)	0.386	12.50 (3)	19.44 (7)	0.48	21.88 (7)	10.71 (3)	0.247

Table 5: Comparison of severity of ASD among three study groups.

Indicators	ASD with epilepsy	ASD without epilepsy	P value	ASD with abnormal EEG	ASD with normal EEG	P value	ASD-only	ASD with clinical seizure/ abnormal EEG	P value
	(n=12)	(n=48)		(n=24)	(n=36)		(n=31)	(n=28)	
	% (N)	% (N)		% (N)	% (N)		% (N)	% (N)	
ADOS (Autism Diagnostic Observation Schedule) interpretation									
Borderline/ Low	0.00 (0)	4.17 (2)	0.408	0.00 (0)	5.56 (2)	<0.001	6.25 (2)	0.00 (0)	<0.001
Moderate	50.00 (6)	31.25 (31)		33.33 (8)	80.56 (29)		81.25 (26)	39.29 (11)	
High	50.00 (6)	64.58 (11)		66.67 (16)	13.89 (5)		12.50 (4)	60.71 (17)	

DISCUSSION

In this study, the mean age of participants was 5.97±3.29 years in the epilepsy group, 4.65±2.10 years in the abnormal EEG group, and 5.88±2.55 years in the ASD-only group. Upon comparison with their respective comparison groups, there was no statistically significant difference observed. Capal et al, conducted a similar study at Cincinnati Children's Hospital Medical Center in the USA and found that the age of ASD diagnosis was younger in the group with normal EEG results than in the group with abnormal EEG results (p=0.02) and in the group with epilepsy (p=0.03).[18] The age of participants in the ASD-only group was similar to that of the ASD with epilepsy group in a study conducted by Ko C, et al., but there was no abnormal EEG group in their study.[15]

There was a male predominance observed in all three study groups, consistent with findings from other studies on ASD.[15,18] This aligns with the DSM-5 statement indicating that for every female diagnosed with autism, there are four males on the autism spectrum. A meta-analysis of prevalence studies conducted by Loomes R. et al. also supports our finding.[19] Among the 12 patients in our ASD with epilepsy group, 4 had a normal EEG, and 8 had abnormal EEG discharges. Among them, the majority (58.33%) exhibited focal epileptiform discharges, while only 1 patient (8.33%) showed non-specific findings in the form of slow background activity. Among non-epileptic patients, 32 had a normal EEG, while 16 had abnormal EEG discharges. Among the 16 patients with abnormal EEG discharges in the non-epileptic group, 13 exhibited focal (81.25%) and 3 (18.75%) non-specific findings. Thus, the most frequent EEG abnormality observed in both groups was the presence of focal epileptiform discharge. Similar findings were reported by Capal et al.[18] In this study, the most frequent antecedent event associated with ASD was a parental age gap of 10 years or more. Although there is an association between advancing parental age and autism, it is noteworthy that in this study, no mother was older than 40 years, and all fathers were younger than 45 years.[20] Sandin et al, supported our findings, indicating an increased risk of ASD associated with a moderate-to-large difference in parental ages of 10 years or more.[21] Additionally, the other study aligns with our findings, as they also identified language impairment as a primary presenting feature of ASD, followed by social withdrawal and stereotypies.[22]

In our study, ADHD emerged as the most frequent associated comorbidity of autism across all three groups, consistent with findings from other studies. Other common associations included sleep difficulty, anxiety, depression, specific phobia, self-injurious behavior, feeding problems, enuresis, encopresis, and constipation. While some studies, such as the one by Bougeard et al, reported similar comorbidities, they also noted additional participants with tics, sight and hearing impairment.[23]

However, in our study, no statistically significant differences were found when comparing these comorbidities across the groups. The findings from our study regarding the severity of ASD align with those of Yousufa et al, who also found a statistically significant relationship between EEG abnormalities and the severity of autism.[24] Additionally, the study by Touchman et al, in Florida supports our findings, indicating that regression was associated with epilepsy and epileptiform EEG.[25] The lack of significant difference between the ASD with epilepsy group and the ASD without epilepsy group in our study contrasts with the findings of Chanyoung Ko et al, who reported significant impairments in social functioning among ASD participants with epilepsy compared to those without epilepsy.[15] This discrepancy may stem from differences in sample characteristics, assessment measures, or other factors influencing the study outcomes. Further research may be needed to explore these discrepancies and better understand the relationship between epilepsy, ASD severity, and social functioning.

Limitations

This study's limitations include its single-center design with a small sample size and a short duration of data

collection. Consequently, the findings may not fully represent the broader scenario across the entire country, and caution should be exercised when generalizing the results.

CONCLUSION

Children diagnosed with autism spectrum disorder (ASD) and abnormal EEG exhibited a higher severity of autism (66.67%) compared to children with ASD alone, among whom a lower percentage (81.25%) experienced moderate autism severity

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