A neuroimaging study in childhood autism

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Abstract:

Background: Childhood autism is now widely viewed as being of developmental neurological origin. Abnormality in neuroimaging is reported in autism. **Objectives:** To delineate the proportion of structural magnetic resonance imaging (MRI) and electro encephalography (EEG) abnormality among the children with Autism and to assess any association of MRI and EEG changes with co morbid mental illness. **Methods:** It was a cross sectional descriptive study done at a child and adolescent consultation centre, Dhaka. The study was carried out from January 2009 to December 2009.Both boys and girls were included in the study. A total of 42 children with childhood autism aged between two and 12 years participated in this study. Diagnosis of autism was based on ICD-10(DCR) criteria. **Results:** Abnormalities were found to be 35.7% in MRI and 42.9% in EEG. EEG abnormalities were found in the form of defuse slow waves activities, generalized faster activities, epileptogenic discharge and mixed discharge. The abnormalities in MRI was found in the form of diffuse cortical atrophic changes, focal cortical atrophy in frontal and temporal cortex with widening of major sulci, prominent ventricles, periventricular degeneration and abnormal basal ganglia. EEG changes were significantly associated with increased number of co-morbid illness (mental retardation, epilepsy and others). **Conclusion:** A number of abnormalities that observed in the present study indicative of relations between structural and physiological dysfunctions and childhood autism. Further exploratory and in-depth researches are certainly required in this field. Intervention of autism needs to address co morbidities for better outcome.

Key words: Autism, Neuroimaging, Co morbidity

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Introduction :

Autism, also referred to as autism spectrum disorder (ASD), constitutes neurodevelopmental disorder characterized by impairment in communication, including language , social skills and comportment often involving rigidity of interests and repetitive, stereotypical behaviors.[1] The prevalence of autism is estimated at 2-5per10, 000 with number expanding to 10-20 per 10,000 if broader definitions are used.[2,3]The male: female ratio is about 3:1.[4] In Bangladesh, first exploratory study in 2005 on child psychiatric disorders in rural, urban and slum areas reported the prevalence of autism is 0.2% (ranged up to 0.9%).[5] The incidence of autism appears to be increasing. In 2011, Manning *et al.* using birth certificate and Early Intervention data reported that in the Commonwealth of Massachusetts between 2001 and 2005 the incidence of ASD diagnosed by 36 months of age increased from 56 to 93 infants per 10,000. Whether this increased incidence reflects better reporting and/or diagnosis or whether other factors are involved remains to be determined. None-the-less, such an increase in incidence is alarming.[6] ASD is considered by leading researchers to be a genetically determined disorder in three representative twin studies.[7-9] Estimated heritability is about 90%.[10] Sibling concordance varies from about 3 to 14%; linkage studies are consistent with a polygenic mode of transmission.[11] Analysis of several studies revealed that there was a link between autism, seizures, signs of neurological impairment and mental retardation which provided evidence that autism is a pervasive devel-

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opmental disorder with a neurological basis.[12] During typical development, the brain undergoes a highly dynamic process of dendritic branching, synaptic pruning, and myelination, which continues into adolescence and adulthood.[13-17] In contrast, the brains of at least some autistic children are hypothesized to undergo accelerated brain growth before age two followed by a premature slowing of growth.[18,19] Aberrant growth rates in brain regions implicated in social impairment, communication deficits and repetitive behaviors in autism, suggesting that growth rate abnormalities persist into adolescence.[20] No focal defect has been demonstrated in structural MRI. Important findings, so far, include increased brain volume, structural abnormality in frontal lobe and corpus callosum in a proportion of Autistic individuals.[21] From a public health perspective, ASDs are an important cause of morbidity high service utilization because of their early onset, lifelong persistence, high level of associated impairment, and absence of effective treatment for the core problems.[22] Less well-investigated cause of impairment may be psychiatric co morbidities. For other psychiatric disorders, co morbidity is common, although the cause are often not well understood .[23-25] Delineating psychiatric co morbidity may identify targets for specific intervention that could reduce overall impairment and improve quality of life.[26,27]

It is evident from representative studies that neuroanatomical and neurophysiological abnormalities as well as significant co morbid mental illness exist among the children with autism. Sharing clinical experience with related professionals, we also developed the similar impressions and intended to explore these issues in Bangladesh. Therefore, this study was aimed to delineate the proportion of structural magnetic resonance imaging (MRI) and electro encephalography (EEG) abnormality among the children with Autism and to assess any possible association of MRI and EEG changes with co morbid mental illness.

Methods :

It was a cross sectional, descriptive study. The study was done at Child and Adolescent consultation centre, Dhaka. The study was carried out from January 2009 to December 2009.Both boys and girls within age ranges 2-12 years were included in the study. A selection criterion for the study was the ICD-10 DCR criteria for Childhood Autism. The study place was selected by convenient sampling technique. A total 42 sample were taken consecutively who fulfilled the inclusion criteria and consent given by the guardian. All the ethical issues have been considered in the study. A structured questionnaire designed by the researcher to collect information related to socio-demographic data of the children and guardians. Informations that included in this questionnaire were child age, sex, education status, habitat and social status. ICD-10 DCR is the 10th revision of International Classification of Diseases by the World Health Organization which was used for diagnosis of autism and other co-morbid psychiatric disorders.[28] Clinical assessment of low IQ was confirmed by applying psychometric test by using The Wechsler Intelligence Scale for Children (WISC-R) to assign Mental retardation according to ICD-10 DCR. It was developed by David Wechsler, is an individually administered intelligence test for children between the ages of 6 and 16 inclusive that can be completed without reading or writing. The WISC takes 65-80 minutes to administer and generates an IQ score which represents a child's general cognitive ability. The current version, the WISC-IV was produced in 2003 followed the UK version in 2004. WISC has proven validity and reliability. WISC-R (1974)[29] has been translated and adopted in Bangla for using this scale among Bangladeshi children. The scale is also usable in the children of 1-2 years of age. This Bangla WISC-R was used in this study. The subjects were only categorized as mentally retarded, but no other subgroups of mental retardation were considered. Information provided by the guardian and referring physicians regarding seizure disorder and diagnosis of seizure were recorded accordingly. In Bangladesh, best possible and sizable clinical neuromiaging are EEG and structural MRI that were used in this study. For each subject, 24 channeled EEG recording was performed. The electrodes were placed according to the 10 /20 international system. Restless or anxious patients were pre-medicated by a low dose of diazepam. The EEG assessment was performed by one experienced neurologist. The rater was blind to psychopathology of the patients. The EEG record was divided into three groups: normal EEGs, EEG with non-epileptiform abnormality of background activity, abnormal EEG with epileptiform discharges. The patients

have also under gone MRI scanning to detect structural abnormality of brain. The statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS, version 17.0). Descriptive statistics and Chi-Square test were used for the analysis of the relationship between co-morbidities with EEG and MRI findings.

Results:

Among 42 participants male and female representations were 33(78.6%) and 9(21.4%) respectively. Mean age was 6.24years (ranges 2y 4m to 12y).Socioeconomic status categorizes as high16 (38.1%), middle 25(59.5%) and low1(2.4%).Table –I revels that most of the participants were not attending to any school, only two were attending special and three in main stream school but with low academic performance. Figure-1 shows the comorbidity with Childhood autism.

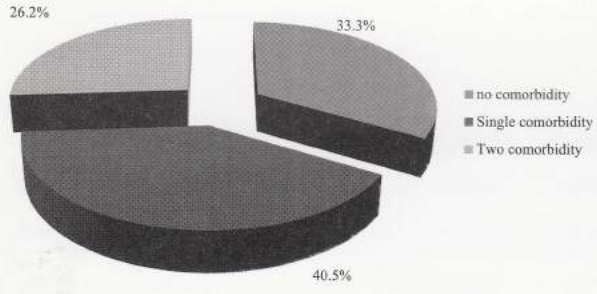

Fig 1 : *Frequency of co-morbid illness*

Comorbid illness was found among 28(66.7%). Type and frequency of comorbidity is shown in Table-II. Among comorbid illness hyperkinetic disorder was most frequent (54.8%). More than two co morbid illness present in 26.2% of cases. Electroencephalographic (EEG) findings are presented in Table-III. EEG report revealed normal activity, epilepogenic discharge and, non-epileptogenic discharge in 57.1%, 28.6%, 14.3% cases respectively. Table-IV shows the findings of MRI of brain of the cases. Abnormality in MRI findings was found in 35.7% cases. Table-V shows the relation between co morbid illness with EEG and MRI of the brain findings.EEG abnormality with co morbidity and MRI abnormality with co morbidity found in 66.7% and 73.3% cases respectively. There is an increase number of co morbidity related with EEG abnormality (Table-VI).

Table-I

Characteristics of Subjects

Variables		Frequency	Percent
Age in Category	2 -5 year	20	47.6
	6-9 year	17	40.5
	10-13 year	5	11.9
Sex	Male	33	78.6
	female	9	21.4
Habitat	rural	8	19
	urban	34	81
	Variables	Frequency	Percent
Socio-economic status	High	16	38.1
	Middle	25	59.5
	Low	1	2.4
Education	No education	37	88.1
	Main stream education	3	7.1
	Special education	2	4.8

Table-II

Types and frequency of co-morbid illness

	Mental retardation		Hyperkinetic disorder		Seizure	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Present	14	33.3	23	54.8	2	4.8
Absent	28	66.7	19	45.2	40	95.2
Total	42	100.0	42	100.0	42	100.0

Table-III

Electro encephalogram (EEG) findings

	Frequency	Percent
Normal	24	57.1
Epileptiform discharge	12	28.6
Generalized Absence	1	2.4
Localized epileptiform discharge	3	7.1
GTCS	8	19.0
Non Epileptiform discharge	6	14.3
Nonspecific changes	3	7.1
Generalized slow activities	3	7.1

Table-IV

Findings of MRI of brain

		Frequency	Percent
Normal			
Abnormal		15	35.7
	ganglia	2	4.8
	Enlarged ventricle	8	19.0
	cortical atrophy	3	7.1
	others	2	4.8
Total		42	100.0

Table-V

Relation between co-morbid illnesses with EEG & MRI finding

			Co morbid illness					
			Present			Absent		
	Frequency of MRI & EEG Changes		Frequency	% within EEG/MRI abnormality	% within illness	Frequency	% within EEG/MRI abnormality	% within illness
EEG. Abnormality	present	18	12	66.7%	42.9%	6	33.3%	42.9%
	absent	24	16	66.7%	57.1%	8	33.3%	57.1%
MRI Abnormality	present	15	11	73.3%	39.3%	4	26.7%	28.6%
	Absent	27	17	63.0%	60.7%	10	37.0%	71.4%

Table-VI

Relationship between number of co-morbid illness and EEG abnormality

Number of Comorbid illness	EEG.Abnormality		
	present	absent	Total
0	6	8	14
1	4	13	17
2	8	3	11
Total	18	24	42

Discussion :

This study explored the possible association of neuroimaging in autism. Though seizure disorder was present only among 4.8% (n=2) of patients, EEG changes were detected among 42.9% that was considerably significant. Of the two abnormalities, one had EEG changes suggestive of GTCS while another one had nonspecific EEG changes. Among non epileptic patients, 27.5% had epileptiform discharge and 12.5% had Nonspecific abnormalities .This result differs from a study which showed 18.2% of autistic patients with co-morbid epilepsy had non – epileptiform abnormality and 37.5% had epileptiform discharge; while among the patients not having epilepsy, 81.8% had non epileptiform abnormality and 62.5% had epileptiform discharge.[30] However a clear inference cannot be drown as number of patients having seizure in this study was only two. EEG changes were found in 33.3% of patients without presence of any co morbidity. Above findings suggest an association between ASD and EEG changes. As this study was not a case control study, it was not possible to find out any significant change in EEG pattern from normal individual. Duffy and Als (2012)[31] found that these two groups differed significantly on the basis of variables generated from EEG-based coherence data. Classification success suggests a stable coherence loading pattern that differentiates ASD-from Control group subjects. This might constitute an EEG coherence-based phenotype of childhood autism . Therefore; broad based case control study can reproduce the data. In another study, Kim et al.[32] found majority (69%) of patients had EEG abnormality comprising of Non Epileptogenic abnormality, Epileptogenic abnormality and combination. No patients with autism had recorded epileptic seizures, despite the high prevalence of Interictal EEG abnormalities. In this study more than one third of the patients had abnormal structural MRI findings. Changes in basal ganglia were found among 4.8% such as multiple hypodense area seen in both lentiform nuclei and head of left caudate nuclei that is dystrophic calcification and enlarged basal ganglia. Though many articles for decades showed increased brain volume.[33,34.21] This study failed to replicate this findings; rather we found generalized mild cortical atrophy, focal area- right high anterior frontal cortex, bilateral temporal cortical atrophy. More extensive neuroimaging study on large sample comparing with control group could help in drawing conclusion. Other changes included prominent cistern magna with smaller posterior vermis of the cerebellum (lobule VI – VII) which is consistent with a study done by Kaufmann et al.[35] There is a similarity between this study and study done by Courehence where the author found enlargement of central nervous system fluid space i.e. enlarged lateral ventricle, enlarged fronto-temparo- parietal cistern, prominent cistern magna etc.[36]

Present study revealed that co morbidity with autism is high (67%). Of the psychiatric co-morbidities hyperkinetic disorder and mental retardation were found 55% and 33% respectively. This finding simulates with the report of the first clinical study of Autism in a tertiary hospital in Dhaka. This study found 64% and 48% co-morbidity of hyperactivity and mental retardation respectively.37 Of the co-occurring medical condition, seizure disorder was found 5% in our study. Co occurring seizure disorder was found 20% in report of the clinical study of Autism in a tertiary hospital in Dhaka. [37] Possible explanation of lower proportion of seizure disorder in our study might be due to the difference in pattern of attendance of the two study centres. In private consultation centre, the autistic patents with seizure disorders usually go for pediatric or neurologic consultation. In tertiary hospital setup, these patient populations attend more in psychiatry outpatient department. Further exploration is required to confirm these findings. Though neuroimaging abnormalities with or without co-morbidities are not significant, overall these abnormalities are higher in autistic patients with co-morbidities. The co-morbidities might be associated with increased structural and/or/functional brain abnormalities either as the manifestation of multiple or common etiological pathways. In-depth and extensive studies are required in this area that will certainly contribute in exploring aetiology of autism.

Conclusion :

The present study indicates that structural and physiological dysfunctions are related to childhood autism. Further explorations are needed to understand the aetiological aspects of Autism and its clinical implications. High number of co-morbidities that found in this study

number of co-morbidities that found in this study indicates biological or genetic aetiology of childhood autism. Targeting the evaluation of comorbid mental illness and intention for early intervention will improve the quality of life of children with autism.

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