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Neurodevelopmental Comorbidities in Children with Epilepsy in a Tertiary Care Hospital

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Abstract **Original Research Article**

***Background*:** Epilepsy is chronic neurological disorder characterized by recurrent unprovked seizure of cerebral origin with motor, sensory or autonomic disturbance with or without loss of consciousness. A wide spectrum of comorbid conditions either coexist at the time of presentation in a child with epilepsy or develop subsequently. These are often concern to the parents-at times even more than the seizures themselves as the seizures may be under controlled with AEDs. In children it is occassionaly associated with variable comorbidites although the frequency of such comorbidity is often difficult to determine. Many comorbidites associated with epilepsy are age dependent, earliar the insult of seizure, more damage to the growing brain. So, very early onset (<6months) seizure group showed more impairments that early onset group(>6months of age). ***Objectives*:** To identify neurodevelopmental comorbidites of children with epilepsy attending in child development center of ICMH. ***Methods*:** This cross sectional study was done from 8th March 2016 to 8th September 2016 at SCDDMC of ICMH. Detailed information were obtained in each cases according to protocol. Complete history was taken either from patient or accompying attendants. All epilepsy (15months to 15years) patient attending in Saleh child development & disability management center, had been follow-up there for at least 1year. ***Result*:** In this study, among the 175 children with epilepsy, Mean age of the studied children was 4.7(±2.8):age range 1- 2years.Male were 129(73.7%) and female were 46(26.3%),male female ratio was M:F-2.8:1.Demographic characteristics of epilepsy among studied cases showed that 27(15.4%) children came from low income group,129(73.7%) children came from middle income group,19(10.9%) came from high income group. In this study, 102(58.3%) patients had onset of seizure before 1months of age. Mean age of onset of seizure was found 9.9±21.4months. Majority 102(58.3%) patients had generalized clonic, 92(52.6%) had generalized tonic, 38(21.7%) had generalized myoclonic seizure. Symptoms associated with seizure were sensory symptom found in 56(32.0%) & sudden fall from standing / sitting position was in 54(30.9%). In this study, it was observed that, majority 128(73.1%) patient had speech delay,110(62.9%) had gross motor impairment, 110(62.9%) had cognitive delay, 92(52.6%) had fine motor impairment, 81(46.3%) had school dropout/ absence. ***Conclusion*:** This study found the co-morbidities associated with epilepsy in children. Out of 175 children with epilepsy 128 (73%) had speech delay. 110 (62.9%) had gross motor, 92 (52.6%) had fine motor impairment, cognitive delay found in 110 (62.9%), 31.4% had behavioral problem, 20.6% had conduct problems, 46.3% children were dropped out from school. Gross motor, fine motor, speech, hearing, conduct problems and school dropout was significantly associated with age of onset of seizure. Associated impairments/disabilities in different domains were significantly associated with clinical type and severity of seizure.

Keywords: Epilepsy, comorbidities, seizure, autism spectrum.

INTRODUCTION

Epilepsy defined as two or more unprovokated epileptic seizures occurring more than 24 hours apart in a child more than one month old. Bangladesh is one of the densely populated countries in the world where infectious diseases, malnutrition & many chronic neurological diseases are quite common [1]. Epilepsy is one of the most common diseases of central nervous system in children. Roughly 50% of the epilepsies

begin during childhood [2]. Studies in developed countries prevalence rate of epilepsy is about 5 per 1000 population whereas in developing countries it is higher [2]. Based on the prevalence rate of 10 per 1000 populations, the number of epilepsy patient in Bangladesh is about 1.3million [1]. There is considerable overlap between epilepsy & neurodevelopmental disorder. Behavioral disturbances and cognitive impairments are reported in nearly 20-30% of children [3]. Studies showed that 70-76% of children with epilepsy have some types of disability or handicap affecting their daily life [4, 5].

Neurodevelopmental disorders are a group of conditions with onset in the developmental period of brain [6]. These disorders typically manifest early in development, often before the child enters grade school, and are characterized by developmental deficits that produce impairments of personal, social, academic or occupational functioning [6]. These comorbidities are often associated with epilepsy. One study showed that, epileptic children are upto 4.7 times more likely to have behavioral problems than children with other chronic non-neurological condition [7].

Epilepsy is a heterogenous condition of recurrent seizure with varied etiologies & consisting of different seizure types. The unpredictability and distressing nature of the seizure and social stigma associated with epilepsy are assumed to influence psychological development & often impact on quality of life, causing neurobehavioral disorders [8, 9]. A spectrum of neurodevelopmental disorders are found to occur at a high rate in children and adolescents with epilepsy. These include intellectual disabilities, motor disabilities, autism, attention deficits /hyperactivity disorder, anxiety and psychotic disorder [10].

Most of the evidence of neurobehavioral disorders in children with epilepsy comes from studies done in developed countries and there is limited data of epilepsy and its comorbidities from developing countries. The present study's primary objective was to determine the prevalence and type of neurobehavioral disorders in children with active epilepsy using a standardised questionnaire [11].

Individuals with autism and epilepsy have poorer cognitive (lower IQ), adaptive, behavioral, and social outcomes than those with autism without epilepsy, and epilepsy accounts for increased morbidity and mortality in individuals with autism (Gillberg *et al.*, 2010) [12].

Autism is a neurodevelopmental disorder affecting primarily social cognition but associated with language impairments, restricted interests, and repetitive behaviors. The term autism spectrum disorders (ASDs) is used interchangeably with autism and includes a broader group of children including those with autistic disorder, pervasive developmental disorders not otherwise specified, and Asperger syndrome.

OBJECTIVE

General Objective

To identify neurodevelopmental comorbidities of children with epilepsy attending in child development center of ICMH.

Specific Objective

1. To find out socio-demographic characteristic of children with epilepsy.
2. To determine the age of onset of seizure, clinical type & severity of seizure.
3. To identify neurodevelopmental comorbidities among children with epilepsy.
4. To find out association between onset of seizure, type of seizure, severity of seizure with comorbidities.

METHOD

Study Design: Cross sectional study.

Place of Study

Saleh Child Development and Disability Management Center, Institute of Child and Mother Health (ICMH) Matuail, Dhaka.

Study Period: 8th March 2016 to 8th September 2016.

Study Population

Children (age range 15 months to 15 years) attending in child development and disability management center, had two or more unprovoked seizure & had been followed up for at least 1 year in epilepsy clinic.

Sample Size: Minimum sample size is 319
Sampling Method: Purposive sampling.

Selection Criteria
Inclusion Criteria:

1. Children in the age group of 15 months to 15 years having two or more afebrile, unprovoked seizure.
2. They had been followed-up for at least 1 year in the epilepsy clinic & had a routine EEG done during their follow-up period.

Exclusion Criteria:

1. Febrile seizure, seizure due to ongoing CNS infections, head injury that causing acute seizure was excluded.
2. Seizure associated with any syndromic child.

Procedures of Collecting Data

Face to face interview. Previous data (EEG reports, result of IQ test).

Procedure of Data Analysis

Statistical analyse was carried out by using the Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated by frequencies and percentages Chi-Square test was used to analyze the categorical variables, shown with cross tabulation. P values <0.05 was considered as statistically significant.

RESULTS

Table I: Age group distribution of studed patients (n=175)

Age (years)	Number of frequency	Percentage
1-2 yrs	55	31.4
>2-4 yrs	36	20.6
>4-6 yrs	37	21.1
>6-8 yrs	20	11.4
>8-10 yrs	27	15.4
Mean±SD (yrs)	4.7±2.8	

Table I shows age group distribution of the patients. It was observed that majority 55 (31.4%) patients belonged to age 1-2 years and mean age was found 4.7±2.8 years.

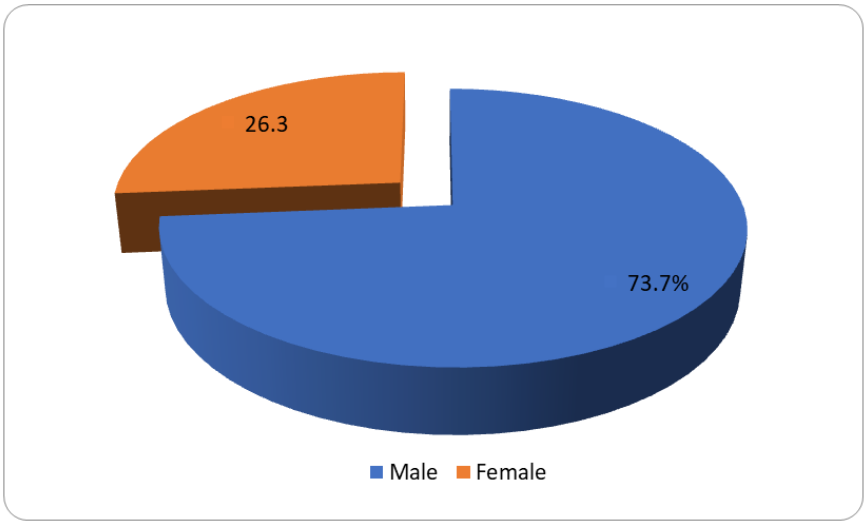

Figure I: Sex distribution of the study patients

Figure I show sex distribution of the patients. Male was found 129(73.7%) and female was 46(26.3%). Male female ratio was 2.8:1.

Table II: Socio-economic status of the study patients (n=175)

Socio-economic status	Number of frequency	Percentage
<5000 Tk/Low income group	27	15.4
5000-10000 Tk/middle income group	129	73.7
>10000 Tk/High income group	19	10.9

Table II shows socio-economic status of the patients. It was observed that majority 129(73.7%) patients came from middle (5000-10000 Tk) socio-economic income group family.

Table III: Socio demographic characteristics of the parents (n=175)

Mother occupational status	Number of frequency	Percentage
Housewife	129	73.7
Service holder	46	26.3
Mother educational status		
Illiterate	19	10.9
Primary	137	78.3
Secondary	9	5.1
Graduate	10	5.7

Father occupational status		
Service holder	56	32.0
Businessman	73	41.7
Farmers	18	10.3
Day labor	28	16.0
Father educational status		
Primary	73	41.7
Secondary	83	47.4
Higher secondary	9	5.1
Graduate	10	5.7
Residence area		
Rural	147	84.0
Urban	28	16.0

Table III shows mother occupational status, it was observed that majority 129(73.7%) mother were housewives and 46(26.3%) were service holder. Majority 137(78.3%) mother were primary education level followed by 19(10.9%) were illiterate, 10(5.7%) were graduate, 9(5.1%) were secondary. Regarding father occupational status, majority 73(41.7%) father were businessman, 56(32.0%) were service holder, 28(16.0%) were day labor, 18(10.3%) were farmers. Majority 83(47.4%) father were secondary education level, 73(41.7%) were primary level, 10(5.7%) were graduate and 9(5.1%) were higher secondary level. Majority 147(84.0%) patients were came from rural area and 28(16.0%) came from urban area.

Table IV: Age of onset of seizure (n=175)

Age of onset (months)	Number of frequency	Percentage
<1	102	58.3
1-6	37	21.1
7-12	9	5.1
>12	27	15.4
Mean±SD	9.9±21.4	

Table IV shows age of onset of seizure, it was observed that majority 102(58.3%) patients had onset of seizure in duration of <1 months. Mean age of onset of seizure was found 9.9±21.4 months.

Table V: Distribution of the study patients by symptoms associated with seizure (n=175)

Symptoms associated with seizure	Number of frequency	Percentage
Sensory symptom	56	32.0
Sudden fall from standing/ sitting position	54	30.9
None	65	37.1

Table V shows symptoms associated with seizure sensory symptom was found 56(32.0%) and sudden fall from standing/sitting position was 54(30.9%).

Table VI: Distribution of the study patients by frequency of seizure (n=175)

Frequency of seizure	Number of frequency	Percentage
Less then 1/week (Mild)	37	21.1
One or more /week (Moderate)	99	56.6
Daily (Severe)	29	16.6

Table VI shows rate of seizure of the patients. It was observed that majority 99(56.6%) patients had one or more seizure per week.

Table VII: Distribution of the study patients by seizure frequency beginning to present state (n=175)

Seizure frequency from beginning to present state	Frequency	Percentage
Decreasing	146	83.4
No change	29	16.6

Table VII shows seizure frequency from beginning to present state, it was observed that 146(83.4%) patients had decreasing and no change was found 29 (16.6%).

DISCUSSION

Epilepsy is a chronic neurological disorder characterized by unprovoked recurrent seizures. In this study it was observed that more than half that is 55(31.4%) patients belonged to age group 1-2 years and mean age of studied children was found 4.7±2.8 years. Moinuddin *et al.,* stud found mean age of the controlled group and poorly controlled group of children were 79 months and 40.3 months respectively [12]. The study done by Akhter and Mannan showed that mean age was 3.2 ± 2.6 years (median age 2 years) were studied [2]. Banu *et al.,* found that age range between 2 months to 15 years, median age was 3 years) [11]. In the study of Liptak *et al.,* mean age of CP was 9.6 years SD ±4.6 that is dissimilar in this study [13]. All these study findings of mean age of epilepsy in children is consistent with this study.

In this study it was observed that male was found 129(73.7%) and female was 46(26.3%). Male female ratio was 2.8:1. In Moinuddin *et al.,* study 76 (63.3%) children were male and 44 (36.7%) children were female [12]. This finding was consistent to another study [14], which was1.85: 1. Berg *et al.,* found equal ratio of both male and female [15]. Most studies reported a slightly higher incidence in boys than girls [16]. The high ratio of male might be due to the fact that boys get preference in the family in seeking healthcare.

In this current study it was observed that majority 102(58.3%) patients had onset of seizure in duration of <1 months. Mean age of onset of seizure was found 9.9±21.4 months. Moinuddin *et al.,* onset of epilepsy was before 1 year of age among 78% cases in poorly controlled group, compared to 25.3% cases in controlled group [12]. Banu *et al.,* before and at 12 months of seizure was found 56.3% and after 12 months of age was 43.7% [11].

In this series it was observed that majority 102(58.3%) patients had general clonic, 92(52.6%) had general tonic, 38(21.7%) had generalized myoclonic. Moinuddin *et al.,* study showed focal epilepsy was found in 30 (68%) cases in controlled and 14 (31.8%) cases in poorly controlled group; generalized epilepsy was found in 49 (72%) cases in controlled and in 19 (28.8%) cases in poorly controlled group [12]. Banu *et al.,* Generalized, partial, and unclassifiable epilepsy were found in 63.6%, 25.2%, and 11.2% respectively [11].

In this study it was observed that majority 99(56.6%) patients had one or more seizure per week. Moinuddin *et al.,* Frequency of seizure before treatment (1 or more per week) 43.0% in controlled group and 92.7% in poorly controlled group [12].

In this study it was observed that majority 128(73.1%) patients had speech, 110(62.9%) had gross motor, 110(62.9%) had cognition, 92(52.6%) had fine motor impairment & 81(46.3%) had school dropout/absence. In this study, it is showed there is association of impairments in different domains with age of onset of epilepsy. In very early onset(<6months) & early onset epilepsy group, gross motor impairment found in 90% Vs 10% in both group(P vaiue=0.001), fine motor impairment 9.6.7% Vs 3.3% among both groups. This study found out the association of the impairments or disabilities with age of onset of seizure, type of seizure & severity of seizure & also found that earlier the insult of seizure, more damage to the growing brain, so very early onset seizure group showed more impairments than that of early onset (>6months age).

In study of Mezaal *et al.,* showed that 48 motor disabilities was 60%, followed by epilepsy 42%, hearing loss 63%, cognitive delay 40%, speech delay 30% that studies nearly similar to in this study [17]. In Mezaal *et al.,* study visual impairment 2% that is distinct in this study [17].

CONCLUSION

This study found the co-morbidities associated with epilepsy in children. Out of 175 children with epilepsy 128 (73%) had speech delay. 110 (62.9%) had gross motor, 92 (52.6%) had fine motor impairment, cognitive delay found in 110 (62.9%), 31.4% had behavioral problem, 20.6% had conduct problems, 46.3% children were dropped out from school. Gross motor, fine motor, speech, hearing, conduct problems and school dropout was significantly associated with age of onset of seizure. Associated impairments/disabilities in different domains were significantly associated with clinical type and severity of seizure.

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