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Risk Factors for the Development of Epilepsy Among Children with Cerebral Palsy

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Abstract: *Background:* Cerebral palsy is the most common physical disability in children. Epilepsy is one of the most common and important co-morbidity among patients with cerebral palsy. Epilepsy is said to occur in 15–90% of children with CP. There is a paucity of studies among these individuals to determine the risk factors predicting the development of epilepsy. The aim of this study was to determine the risk factors predicting the development of epilepsy considering antenatal, natal, and postnatal characteristics associated impairments and cranial imaging findings in a patient with cerebral palsy. *Methods:* This case-control study was conducted in the Department of Pediatric Neurology at the National Institute of Neurosciences and Hospital, Dhaka, Bangladesh during the period from January 2020 to December 2020. In total 150 children with cerebral palsy were enrolled in this study who were divided into two groups. In CP with epilepsy, there were 50 patients were taken as the case group, and in CP without epilepsy, there was 100 age- sex-matched patients were taken as a control group. Informed consent was taken from all the parents. Demographic features, clinical findings, functional disability, psychological assessment, computerized tomography (CT) scan, and EEG findings in epilepsy cases were collected in a predesigned questionnaire and analyzed. *Results:* In this study, 56.0% had age at onset of epileptic seizure less than 12 months. The total mean age at the onset of epilepsy was 13.58 ± 14.47 months. Epilepsy was most common in spastic quadriplegic CP (54%). 38.0% had focal epileptiform activity on EEG. Clinically focal epilepsy was found in 36.0%, generalized epilepsy in 32.0%, syndromic epilepsy in 28.0%, and unknown epilepsy in 4.0%. Focal epilepsy is more common in spastic hemiplegia CP. Generalized and syndromic epilepsy is a more common spastic quadriplegic CP. After logistic regression analysis, a significant positive correlation was found between the history of neonatal seizure (OR, 6.769), 1st Seizure during the 1st year of life (OR, 3.660), family history of epilepsy (OR, 16.453), CT scan abnormalities (OR, 4.045), severe intellectual disability (OR, 6.042) and spastic quadriplegic CP (OR, 6.163) with the occurrence of epilepsy in cerebral palsy cases. A statistically significant positive correlation was not found between functional severities of CP by GMFCS, MACS and moderate intellectual disability as a risk factor to develop epilepsy in CP patients. *Conclusion:* Cerebral palsy is associated with higher incidence of epilepsy. This study determined the presence of history of neonatal seizure, 1st Seizure during the 1st year of life, family history of epilepsy, CT scan abnormalities, severe intellectual disability and spastic quadriplegic CP were the risk factors for the development of epilepsy in children with cerebral palsy.

Keywords: Cerebral Palsy, Epilepsy, Children, Risk Factors

1. Introduction

Cerebral palsy is a common physical disability in childhood [1]. Cerebral palsy describes a group of permanent disorders of development of movement and posture, causing activity limitations that are attributed to non-progressive disturbances that occur in developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication and behavior, by epilepsy and by secondary Musculo skeletal problems [2]. It can result in spasticity, dystonia, muscle contractures, weakness and difficulty in co-ordination that ultimately affects the ability to control movements [3]. The occurrence of cerebral palsy is approximately 2 per 1000 live births. Globally, there are an estimated 17 million people living with CP [4]. A community-based study conducted by Tabib SMSB et al. [5] during the period from July 2006 to June 2007 mentioned that the prevalence of CP was 6.1/1000 children. There are an estimated 2, 33, 514 children with CP in Bangladesh [6, 7]. Most of the CP patients also have some associated problems like epilepsy, mental retardation and problem related to speech, hearing, vision or behavior. Among them epilepsy is one of the commonest associated problems in patients of CP [8]. The incidence of epilepsy among CP patients varies with a wide range of 15–90% [9]. The most commonly reported risk factor for later epilepsy was found to be history of neonatal seizures [8, 10]. But additional data regarding birth history parameters that could increase the risk for the development of epilepsy in these children were less consistent [11, 12]. It has been observed that seizures in the CP children tend to have an earlier onset, necessitating the use of more than one antiepileptic drugs [13, 14]. The present study aims are to determine the risk factors predicting the development of epilepsy considering antenatal, natal and postnatal characteristics, CP subtype, severity of CP, the nature of epilepsy, intellectual disabilities as well as cranial imaging findings at a referral neurology hospital in Bangladesh. Knowing the risk factors could provide close follow-up of these patients like evaluating these patients more frequently in an outpatient clinic, informing the families about the seizures, advising to video recording of the events in case of suspicion of seizure and if necessary, requesting early EEG [15]. So, that rapid identification in patient with highest risk would allow physicians to consider them earlier for treatment with recently approved medications and other surgical and nonsurgical treatments [16, 17].

2. Methods

This prospective observational case-control study was conducted in the outpatient and inpatient Department of Pediatric Neurology at National Institute of Neurosciences and Hospital, Dhaka, Bangladesh (January 2020 to December 2020). A total of 150 children with cerebral palsy were enrolled in this study who were divided into two groups. In CP with epilepsy there were 50 patients were taken as the case group and in CP without epilepsy, there were 100 age-sex-matched patients were taken as a control group. The study was approved by the ethical committee of the mentioned hospital. Informed written consent (both Bengali and English) was obtained from parents or caregivers who were enrolled in this study after a full explanation of the details of the research process before data collection. Obeying proper inclusion as well as exclusion criteria we selected the total respondents.

Inclusion criteria:

1. Patient of cerebral palsy with epilepsy (case) and without epilepsy (control).
2. Age between 18 month to 12 years.

Exclusion criteria:

1. Nonspecific motor delay.
2. Suspected cases of neurometabolic disease.
3. Suspected case of neurodegenerative disorder.
4. Provoked seizure (eg. febrile seizure).

Every morning first case of CP with epilepsy was enrolled as a case group. Age (±2 months) and sex-matched the next two cases of CP without epilepsy were enrolled as the control group sequentially. Diagnosis of cerebral palsy was clinical, based on the disorder of posture and movement of cerebral origin with improving developmental trends and findings related to centers controlling such posture and movement as documented by findings related to pyramidal, extra pyramidal and cerebellar systems. Clinically types of CP were divided into four variants spastic, dyskinetic (dystonic or choreoathetotic), ataxic, and mixed. Spastic, dyskinetic, and ataxic clinical types of CP were classified according to the classification of SCPE (European Cooperation on Surveillance of Cerebral Palsies in Europe) [18]. It was named a mixed type of CP when there was more than one type of CP in the same patient. Spastic CP was re-divided into three types according to topographical involvement of extremities as quadriplegia, hemiplegia, and diplegia.

Epilepsy was considered to be present when two or more unprovoked seizures occurred in a time frame of longer than 24 hours. Diagnosis of epilepsy was based on history from a reliable eyewitness or video documentation if available and EEG. All the diagnoses were made by the pediatric neurologist(s) based on the study definition.

The motor disorders were evaluated and classified according to the Gross Motor Function Classification System (GMFCS) into five levels [19]. Levels I, II, and III were named as mild- moderate GMCFS level and levels IV and IV were named as severe GMCFS level. Fine motor disorders were classified according to Manual Ability Classification System (MACS) [20, 21]. It was developed to evaluate each hand function separately and it has five levels. Levels I, II, and III were named as mild-moderate MACS level and levels IV and IV were named as severe MACS level.

The children's intelligence was evaluated based on age-appropriate psychometric tests by psychologist. The standardized, Reynell-Zinkin developmental scale (RZS) was applied to evaluate cognitive development in non-verbal with

visually impaired children aged 5 years and below [22]. Wechsler Preschool and Primary Scale of Intelligence III (WPPSI-III) junior intelligence was designed for children ages 2 years 6 months to 2 years 11 months and senior for children ages 4 years to 7 years 7 months [23]. Wechsler Intelligence Scale for Children-IV (WISC-IV) was used to assess the intelligence quotient (IQ) for children above 6 years of age [24]. Children with a total intelligence score (IQ) level < 70 were diagnosed as intellectual disability. Children with an intelligence score of < 35 were diagnosed as having a severe intellectual disability, 49–35 were diagnosed as moderate intellectual disability, and 69–50 were diagnosed as mild intellectual disability [25].

CT scan of the head was done at the Neuroradiology Department of the National Institute of Neurosciences and Hospital (NINS&H) by HitachiEclos (Japan) with 16-mm axial slices, skilled professionals and expert opinions were taken from neuroradiologists and carefully reviewed by the pediatric neurologist.

A written structured questionnaire was used for the collection of data regarding demographic characteristics, maternal antenatal problems, natal events, post-natal complications, 1st seizure during the 1st year of life, family history of epilepsy, occipitofrontal circumference, functional disabilities, CT scan findings of the head, intellectual disabilities, type of CP and type of epilepsy, were compared statistically between the groups of CP patients with epilepsy and CP patients without epilepsy.

The main analyses were performed with the use of SPSS software, version 22.0 (IBM). Besides standard descriptive statistical methods (mean ± standard deviation), an unpaired t-test was used in the comparison of groups, the chi-square test was performed during the evaluation of qualitative data. Binary logistic regression was used for determining the risk factors for the development of epilepsy by using independent variables that were calculated as $p < 0.05$. The odds ratio and 95% confidence interval were calculated. Statistical significance was defined as $p < 0.05$.

3. Results

In this case control study, all diagnosed cases of cerebral palsy were selected as per inclusion criteria. CP with epilepsy were enrolled as case group (n=50) and age (18 months -12 years ± 2 months) -sex matched CP without epilepsy were enrolled as control group (n=100) sequentially. The commonest age in both group 48 months to 72 months, in case of CP with epilepsy 18 (36%) and CP without epilepsy 42 (42%) respectively. Male sexes were more, 31 (62.0%) in case of CP with epilepsy 59 (59.0%) in case of CP without epilepsy. Socio economic status is represented on the basis of parent's monthly income, mother's and father's level of education. We found 82% patients belonged to lower and middle socioeconomic background (Table 1). Hypertension was found in the most of the patients in both CP with epilepsy 11 (22.0%) and CP without epilepsy 15 (15.0%). Term delivery (Gestational age 38 to 41 weeks), normal vaginal delivery (NVD), Normal birth weight (2500 to 4000 g) were more in both in group, in case of CP with epilepsy 36 (72.0%), 29 (58%), and 36 (72%), in case of CP without epilepsy 56 (56%), 53 (53%) and 54 (54%) respectively. In CP with epilepsy home delivery 26 (52%) and obstructed labour 17 (34%) were more. On the other hand, hospital delivery 60 (60%) and prolong lobour 27 (27%) were more in CP without epilepsy. Comparison Regarding postnatal complication neonatal seizure was significantly higher in CP with epilepsy 24 (48.0%) than CP without epilepsy 12 (12.0%) ($p=<0.001$) when compared between two groups (Table 2). First seizure during 1st year of life was observed significantly higher in CP with epilepsy 35 (70%) than CP without epilepsy 23 (23%) ($P= < 0.001$). Family history of epilepsy in CP with epilepsy 10 (20.0%) and CP without epilepsy 2 (2.0%), their differences were statistically significant ($P= < 0.001$). Microcephaly was found in CP with epilepsy 44 (88.0%) and CP without epilepsy 81 (81.0%) but no significant difference was observed in between groups ($P= 0.278$). Distribution of severity of functional dysfunction of CP patient by GMFCS was significantly different when compared between groups ($p<0.001$). Severe disability was higher in CP with epilepsy 32 (64.0%) and mild to moderate disability was higher in CP without epilepsy 69 (69.0%). Significant difference was also observed when CP functional level by MACS was compared between groups ($p<0.001$). Severe disability was higher in CP with epilepsy 26 (52.0%) and mild to moderate disability was higher in CP without epilepsy 78 (78.0%). Significant difference was observed when distribution of severity of intellectual disability of CP patient was compared between groups ($p<0.001$). Severe disability was higher in CP with epilepsy 30 (60.0%) and moderate disability was higher in CP without epilepsy 51 (51.0%). Distribution of types of CP patient was significantly different when compared between groups ($p=<0.001$). Spastic quadriplegia was higher in CP with epilepsy 27 (54.0%) and Spastic diplegia was higher in CP without epilepsy 36 (36.0%) (Table 3). Abnormal CT scan findings of head were significantly higher in CP with epilepsy 42 (84.0%) than CP without epilepsy 46 (46.0%) ($p=<0.001$) (Table 4). In this study distribution of CP patients with epilepsy by EEG findings, it was found that 28 patients (56.0%) had focal origin (focal epileptiform activity 38.0%, multifocal epileptiform activity 14.0%, focal epileptiform activity with 2nd generalization 4.0%), 9 patients (18.0%) had epileptic encephalopathy and 2 patients (4.0%) had generalized epileptiform activity (Table 5). In this study 28 patients (56.0%) had age at onset of epileptic seizure less than 12 months (Figure 1). Clinically Focal epilepsy was found in 18 patients (36.0%), generalized epilepsy in 16 patients (32.0%), unknown epilepsy in 2 patients (4.0%) and syndromic epilepsy in 14 patients (28.0%) (Figure 2). Focal epilepsy is more common in spastic hemiplegia CP. Generalized and syndromic epilepsy is more common spastic quadriplegic CP (Table 6). The mean age at onset of epilepsy was 8.30 ± 3.34 months. The onset of epileptic seizure was earlier in spastic quadriplegic patient and later in spastic

hemiplegic patients (Figure 3). By calculating the Odds ratio by logistic regression analysis significant positive correlation was found between history of neonatal seizure (OR, 6.769), 1st Seizure during the 1st year of life (OR, 3.660), family history of epilepsy (OR, 16.453), CT scan abnormalities (OR, 4.045), severe intellectual disability (OR, 6.042) and spastic quadriplegic CP (OR, 6.163) with occurrence of epilepsy in cerebral palsy cases. Statistically significant positive correlation was not found between functional severities of CP by GMFCS, MACS and moderate intellectual disability as a risk factor to develop epilepsy in CP patients (Table 7).

Table 1. *Distribution of the CP patients according to basic demographic characteristics (n=150).*

Characteristics	CP with epilepsy (n=50)	CP without epilepsy (n=100)	p-value
Age (months)			0.802
<24	8 (16.0)	12 (12.0)	
24 – 48	18 (36.0)	42 (42.0)	
48 – 72	9 (18.0)	18 (18.0)	
72 – 144	15 (30.0)	28 (28.0)	
Mean ± SD	48.7 ± 30.3	49.0 ± 30.5	0.958
Sex			0.724
Male	31 (62.0)	59 (59.0)	
Female	19 (38.0)	41 (41.0)	
Monthly family income (Taka)			0.323
<10,000	13 (26.0)	12 (12.0)	
10,000 - 30,000	31 (62.0)	67 (67.0)	
>30,000	6 (12.0)	21 (21.0)	
Mean ± SD	15860 ± 8896	23445 ± 21794	0.02
Fathers' education			0.461
Illiterate	5 (10.0)	11 (11.0)	
Below SSC	24 (48.0)	36 (36.0)	
SSC	6 (12.0)	16 (16.0)	
HSC	8 (16.0)	12 (12.0)	
Graduate	7 (14.0)	25 (25.0)	
Mathers' education			0.895
Illiterate	6 (12.0)	7 (7.0)	
Below SSC	23 (46.0)	46 (46.0)	
SSC	9 (18.0)	16 (16.0)	
HSC	6 (12.0)	15 (15.0)	
Graduate	4 (8.0)	10 (10.0)	

Table 2. *Distribution of the CP patients according to maternal antenatal problem, natal events and postnatal complication (n=150).*

Parameters	CP with epilepsy (n=50)	CP without epilepsy (n=100)	p-value
Type of maternal antenatal problem			0.857
DM	2 (4.0%)	4 (4.0%)	
HTN	11 (22.0%)	15 (15.0%)	
PET	2 (4.0%)	10 (10.0%)	
Fever with rash	2 (4.0%)	4 (4.0%)	
UTI	4 (8.0%)	8 (8.0%)	
Others	8 (16.0%)	14 (14.0%)	
Type of natal events			
Gestational age (weeks)			0.088
<37 wk (Preterm)	11 (22.0%)	40 (40.0%)	
38-41 wk (Term)	36 (72.0%)	56 (56.0%)	
>42 wk (Post term)	3 (6.0%)	4 (4.0%)	
Mode of delivery			0.204
NVD	29 (58.0%)	53 (53.0%)	
LUCS	21 (42.0%)	47 (47.0%)	
Place of delivery			0.064
Home	26 (52.0%)	40 (40.0%)	
Hospital	24 (48.0%)	60 (60.0%)	
Birth weight (g)			0.17
VLBW (<1500 g)	2 (4.0%)	6 (6.0%)	
LBW (1500-2499g)	9 (18.0%)	34 (34.0%)	
NBW (2500-4000 g)	36 (72.0%)	54 (54.0%)	
Macrosomia (>4000 g)	3 (6.0%)	6 (6.0%)	
Complication during labour			0.216
Prolonged labour	15 (30.0%)	27 (27.0%)	

Parameters	CP with epilepsy (n=50)	CP without epilepsy (n=100)	p-value
Obstructed labour	17 (34.0%)	23 (23.0%)	
History of Postnatal complication			
Perinatal asphyxia	44 (88.0%)	86 (86.0%)	0.734
Neonatal seizure	24 (48.0%)	12 (12.0%)	<0.001
Neonatal jaundice	12 (24.0%)	32 (32.0%)	0.31

Table 3. *Clinical feature of CP patients with epilepsy and CP patients without epilepsy (n=150).*

Clinical features	CP with epilepsy (n=50)	CP without epilepsy (n=100)	p-value
1st Seizure during 1st year of life			<0.001
Yes	35 (70.0%)	23 (23.0%)	
No	15 (30.0%)	77 (77.0%)	
Family history of epilepsy			<0.001
Yes	10 (20.0%)	2 (2.0%)	
No	40 (80.0%)	98 (98.0%)	
OFC			0.278
Normal	6 (12.0%)	19 (19.0%)	
Microcephaly	44 (88.0%)	81 (81.0%)	
GMFCS			<0.001
Mild to moderate	18 (36.0%)	69 (69.0%)	
Severe	32 (64.0%)	31 (31.0%)	
MACS			<0.001
Mild to moderate	24 (48.0%)	78 (78.0%)	
Severe	26 (52.0%)	22 (22.0%)	
Intelligence			<0.001
Normal	1 (2.0%)	3 (3.0%)	
Mild disability	7 (14.0%)	29 (29.0%)	
Moderate disability	12 (24.0%)	51 (51.0%)	
Severe disability	30 (60.0%)	17 (17.0%)	
Type of CP			<0.001
Spastic hemiplegia	8 (16.0%)	21 (21.0%)	
Spastic diplegia	6 (12.0%)	36 (36.0%)	
Spastic quadriplegia	27 (54.0%)	15 (15.0%)	
Dyskinetic	3 (6.0%)	11 (11.0%)	
Mixed	6 (12.0%)	17 (17.0%)	

Table 4. *Distribution of the CP patients according to CT scan findings of head (n=150).*

CT scan of head	CP with epilepsy (n=50)	CP without epilepsy (n=100)	p-value
Abnormal findings	42 (84.0%)	46 (46.0%)	<0.001
Non-specific cerebral atrophy	14 (28.0%)	13 (13.0%)	
Encephalomalacia	10 (20.0%)	09 (9.0%)	
Hydrocephalus	4 (8.0%)	7 (7.0%)	
Calcification	0 (0.0%)	1 (1.0%)	
Infarction	5 (10.0%)	8 (8.0%)	
Cystic lesion	3 (6.0%)	4 (4.0%)	
Cerebral malformation	2 (4.0%)	2 (2.0%)	
Periventricular Hypodensity	4 (8.0%)	2 (2.0%)	

Table 5. *EEG findings of CP patients with epilepsy (n=50).*

EEG findings	Frequency (n)	Percentage (%)
Normal findings	4	8
Generalized epileptiform activity	2	4
Focal origin		
Focal epileptiform activity	19	38
Multifocal epileptiform activity	7	14
Focal epileptiform activity with secondary generation	2	4
Epileptic encephalopathy	9	18
Hypoarrythmia	4	8
Burst suppression	2	4
Electrical status epilepticus	1	2

Table 6. *Epilepsy type (clinical) in different type of cerebral palsy (n=50).*

Clinical Epilepsy type	Spastic Hemiplegia	Spastic Diplegia	Spastic Quadriplegia	Dyskinetic	Mixed
Focal	7 (87.5%)	1 (16.7%)	6 (22.2%)	2 (66.7%)	2 (33.3%)
Generalized	0 (0.0%)	5 (83.3%)	7 (25.9%)	1 (33.3%)	3 (50.0%)
Unknown	0 (0.0%)	0 (0.0%)	2 (7.4%)	0 (0.0%)	0 (0.0%)
Combined generalized and focal	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
West syndrome	0 (0.0%)	0 (0.0%)	8 (29.6%)	0 (0.0%)	1 (6.7%)
Lennox Gastaut syndrome	1 (12.5%)	0 (0.0%)	4 (14.8%)	0 (0.0%)	1 (16.7%)

Table 7. *Logistic regression of risk factors of epilepsy in CP patients (n=150).*

	p-value	OR	95%CI	
			Lower	Upper
H/O neonatal seizure	0	6.769	2.983	15.362
1st Seizure during the 1st year of life	0.049	3.66	1.003	13.352
Family H/O epilepsy	0.004	16.453	2.487	108.84
GMFCS	0.147	2.301	0.746	7.091
MACS	0.578	1.379	0.444	4.282
CT scan (abnormal)	0.014	4.045	1.325	12.343
IQ				
Moderate disability	0.699	0.821	0.301	2.237
Severe disability	0	6.042	2.275	16.046
Spastic quadriplegia	0	6.163	2.849	13.33

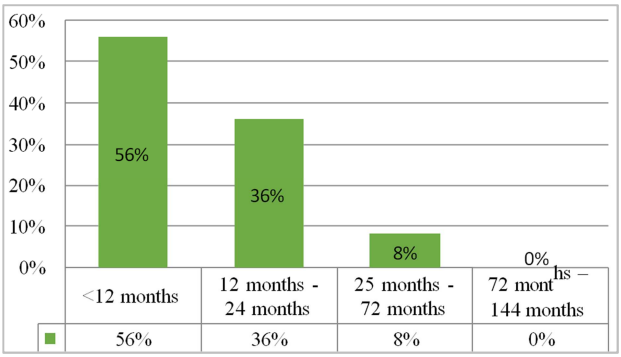

Figure 1. *Distribution of patients according to age at onset of epileptic seizure (n=50).*

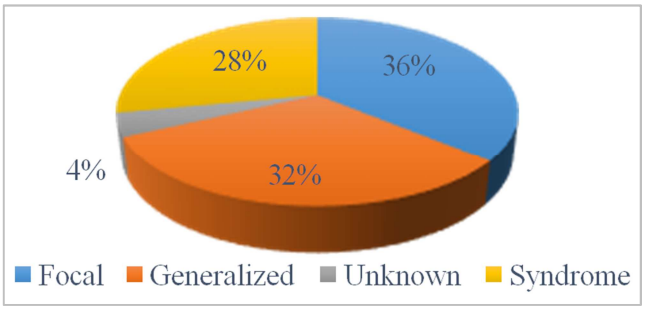

Figure 2. *Clinical epilepsy type of CP patients (n=50).*

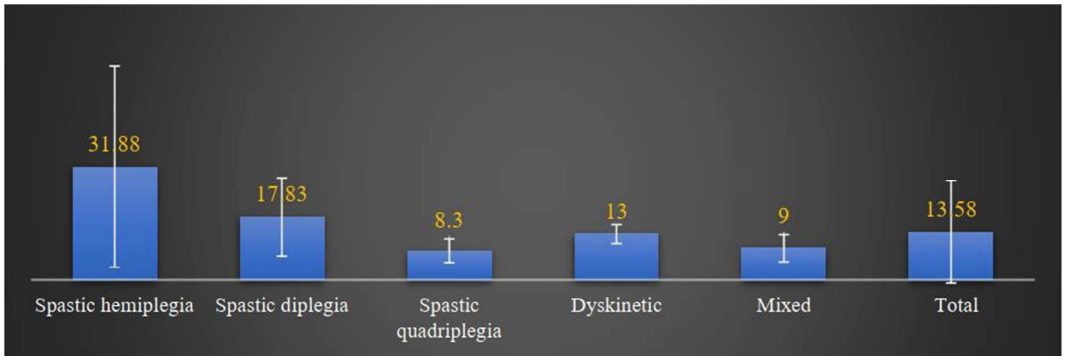

Figure 3. *Mean age (in month) at onset of epileptic seizure in children with different type of cerebral palsy (n=50).*

4. Discussion

This study was conducted on 150 children with CP (age-sex matched 50 patients CP with epilepsy and 100 patients CP without epilepsy) in National Institute of Neurosciences and Hospital Dhaka, Bangladesh. The aim of this study was to determine the risk factors for the development of epilepsy among children with cerebral palsy. There are several studies to find out the risk factors for epilepsy in children with Cerebral Palsy. In this Case-control study, epileptic and non-epileptic patients with CP were compared according to demographic, clinical, neuroimaging features, and etiological aspects to find out the risk factors predicting the development

of epilepsy. Positive seizure history in neonatal period, 1st seizure during the 1st year of life, Positive family history of epilepsy, quadriplegic type of CP, severe degree of gross and fine motor disorders, neuroimaging abnormalities and severe intellectual disability were determined as risk factors for the development of epilepsy in CP patients. Children age range between 18 months to 12 years were included in our study and found the age range between two to less than four years were commonest in both CP with epilepsy group 18 (36.0%) and CP without epilepsy group 42 (42.0%). In this study 90 patients (60%) were male. A similar observation was found by Pratibha Singhi et al. [26]. In their study they found 65 patient (62%) out of 105 Cerebral Palsy cases were male. Male cases were more, 31 (62.0%) in CP with epilepsy and 59 (59.0%) in CP without epilepsy. There was no significant difference in terms of age and sex between CP patients with epilepsy and CP patients without epilepsy. Karatoprak E et al. [15] also did not found any relation between age-sex and risk for epilepsy development. In this study socio economic status is represented on the basis of parent's monthly income, mother's and father's level of education. We found 82% patients belonged to lower and middle socioeconomic background. A study done by Israt Jahan et al. [27] found that 73.9% were from low-income families. Our study found that, parent's educational level was below SSC more. In case of father 24 (48.0%) in CP with epilepsy and 36 (36.0%) CP without epilepsy. In case of mother 22 (44.0%) in CP with epilepsy and 45 (45.0%) CP without epilepsy. Around 42.33% of parents of CP children were below SSC level; out of this 9.7% were illiterate. This finding is consistent with that of Israt Jahan et al. [27]. It is known that antenatal, natal and postnatal problems are the major cause of CP but there is little known about the effect of these factors on the development of epilepsy. So, we determined the detailed history of antenatal, natal and postnatal problems. In our study as per analysis of antenatal events, we did not find any significant difference between CP with epilepsy and CP without epilepsy (P = 0.857). Karatoprak et al. [15] also did not find any relation between these antenatal problems and risk for epilepsy development. The results from various studies determining the relation between gestational age, mode of delivery, place of delivery, birth weight, complication during labour, and epilepsy development in CP patients were conflicting. Mert et al. [28] found that both prematurity and low birth weight were not related to Epilepsy development. Kulak et al. [10] did not find any relation between gestational age and the risk of epilepsy development. But they determined an increased risk of epilepsy in patients with low birth weight. On the other hand, Zelnik et al. [29] demonstrated that epilepsy was more frequent in term infants than in premature infants whereas they found no relation between birth weight, mode of delivery and risk of epilepsy development. Gruraj et al. [8] also reported that term delivery had an increased association with epilepsy development. Sellie ret al. [9] determined association between epilepsy development and term and ≥ 2500 g infants in 17 European registers. Karatoprak E et al. [15] did not find any relation between these labour problems and the risk for epilepsy development. In our study regarding the gestational age, mode of delivery, place of delivery, birth weight and complication during labour, when compared we also did not find any significant difference between groups (P= 0.088, 0.204 0.064, 0.170, 0.216). As per analysis of postnatal events previous studies reported that history of neonatal seizure in patients with cerebral palsy is a risk factor for epilepsy development [8, 9, 10, 28, 29]. Bruck I et al. [30] reported that 30 out of 62 (48.4%) children with a history of neonatal seizure subsequently developed epilepsy. Similar to the literature, in our study during the analysis of postnatal events neonatal seizure was significantly higher in CP with epilepsy 24 out of 50 (48.0%) than in CP without epilepsy (12.0%) (p=<0.001). In contrast to our finding Kulak et al., [10] and Kwong et al. [31] noted neonatal seizure in 17% and 19% of children with CP and epilepsy respectively. In our study 1st seizure during 1st year of life was significantly higher in CP with epilepsy 35 (70%) than in CP without epilepsy 23 (23%) (P= < 0.001) which is in accordance with Zafeiriou et al. [32] they found that first seizures occurred during the first year of life in 69.7%. In our study, a family history of epilepsy was significantly higher in CP with epilepsy 10 (20.0%) than CP without epilepsy 2 (2.0%) (P= < 0.001). Kulak et al. [10] and Bruck I et al. [30] found 10.9%, and 29% epileptic children with cerebral palsy had a family history of epilepsy. In the current study, we did not found association between microcephaly and risk for epilepsy development between groups (P= 0.278). Zelnik et al. [29] also found that the ratio of microcephaly did not differ among the CP with epilepsy and CP without epilepsy patients. In this study distribution of severity of functional dysfunction of CP patients by GMFCS severe disability was significantly higher in CP with epilepsy 32 patients (64.0%) than in CP without epilepsy 31 patients (31.0%) (p=<0.001) and by MACS severe disability was also significantly higher in CP with epilepsy 26 patients (52.0%) than CP without epilepsy 22 patients (22.0%) (p=<0.001).

Karatoprak et al. [15] also found severe functional disability in CP with epilepsy by GMFCS was 57.1% and by MACS was 46.8% respectively. Bruck et al. [30] also found the degree of CP severity was associated with a higher incidence of epilepsy. We demonstrated a higher proportion of CT abnormalities in children with CP with epilepsy 42 patients (84.0%) compared with the CP without epilepsy in 49 patients (49.0%) and their differences were statistically significant (p=<0.001). Kulak et al. [10] also found CT abnormalities in CP with epilepsy was 68 patients (82.9%) compared with the CP without epilepsy 56 patients (48.2%). Regarding the abnormal findings cerebral atrophy was most often associated with epileptics, a finding consistent with data found in the literature [8, 10, 29]. In the present study, we found that severe intellectual disability was significantly higher in CP with epilepsy 30 patients (60.0%) than CP without epilepsy 17 patients (17.0%) (p=<0.001). Karatoprak et al. [15] also found severe intellectual disability in CP with epilepsy (46%) and CP without epilepsy (12.0%)

respectively. In contrast to our study El- Tallawy et al. [33] observed no relationship between total IQ and epilepsy development in children with epilepsy than in those without epilepsy (84.6% versus 66.7%). In this current study, distribution of types of CP patient was significantly different when compared between groups (p=<0.001). Spastic quadriplegia was higher in CP with epilepsy 27 (54.0%) and Spastic diplegia was higher in CP without epilepsy 36 (36.0%). Karatoprak et al. [15] also found in CP with epilepsy spastic quadriplegia was 66.1% and in CP without epilepsy spastic diplegia was 40.6%. In contrast Singhi et al. [34] reported that the rate of epilepsy was the highest in spastic hemiplegic patients (65.9%). In our study it was found that 28 patients (56.0%) had age at onset of epileptic seizure less than 12 months. Zaferiou et al. [32] also found that 69% of patients with CP had their first epileptic attack before they were a year old. This indicates the severity of underlying brain injury. In our study we found the mean age of onset of epilepsy was 31.88 ± 28.27 months in spastic hemiplegia patients, 17.83 ± 11.03 months in spastic diplegia patients and 8.30 ± 3.34 months in spastic quadriplegia patients respectively. Smililar to our study Carlsson et al. [35] reported that the mean age of epilepsy onset 2.5 years in hemiparetic cerebral palsy, 12 months in diparetic cerebral palsy and 6 months in quadriparetic cerebral palsy. In this current study we found that the total mean age at onset of epilepsy was 13.58 ± 14.47 months. These findings were consistent with the previous study by Bruck I et al. [30] they found the average age at onset of epilepsy was 12.59 months. In contrast to our study Delgado et al. [14] found mean age at onset of epilepsy 2.5 years (range, 1 month to 11 years). EEG is essential in the work-up of children with CP and suspected seizures. It can lend support to the diagnosis of epilepsy and assist in seizure/epilepsy classification to better guide the choice of antiseizure drugs. In our study regarding EEG findings, we found epilepsy of focal origin was more common 28 patients (54.0%) in CP patients with epilepsy. Similar to our study focal epileptiform activity was the common EEG findings observed by Şenbil et al. [36] (48.39%). In contrast to our study generalized epileptiform abnormality was detected in a large proportion of patients with cerebral palsy and epilepsy 50 patients (41.4%) by Hanci et al. [37]. In our study clinical focal epilepsy (18 patients 36.0%) were more common in CP. Similarly focal epilepsy was more commonly observed by Gururaj et al. [8] (39.3%), Kwong et al. [31] (37.5%), Aksu et al. [13] (93.1%), Delgado et al. [14] (71%), in CP with epilepsy. In contrast to our study Hadjipanayis et al. [38] reported generalized epilepsy (36.8%) followed by focal epilepsy (33%) in cerebral palsy with epilepsy. Classification of the type of epilepsy is difficult in children with CP for the following reasons. First, partial seizure onset that rapidly becomes generalized may not be witnessed or reported reliably. Second, impairment of consciousness during an episode may be impossible to clarify in patients with multiple handicaps. Third, the differentiation between myoclonic, tonic, and atonic seizures occasionally could be extremely difficult without ictal EEG or video EEG. In this current study we found focal epilepsy was more common in the hemiplegic variety of CP and epilepsy was less common in dyskinetic CP. Other studies have found a similar high incidence of focal epilepsy in this variety of CP ranging from 69 to 73% [39]. In the dyskinetic type of CP, epilepsy is believed to be uncommon [40].

Limitations of the Study

This was a single centered study with small sized samples. Moreover, the study was conducted in a tertiary care hospital or referral center. Although they came from different tier of the society and district of Bangladesh, they were not the representative of all children with CP in this country.

5. Recommendation

For getting more specific results we would like to recommend for conducting similar more large-scale multicenter studies with big sample size. Further studies looking in to possible genetic and early prenatal factors may lead to better understanding of the risk factor of epilepsy in CP.

6. Conclusion

This study determined the presence of history of neonatal seizure, 1st Seizure during the 1st year of life, family history of epilepsy, CT scan abnormalities, severe intellectual disability and spastic quadriplegic CP were the risk factors for the development of epilepsy in children with cerebral palsy. Preconception on the risk factors for the development of epilepsy in children with cerebral palsy may be helpful for physician to consider for early diagnosis and proper management to prevent undesirable morbidity.

Approval

Got from the respective department.

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