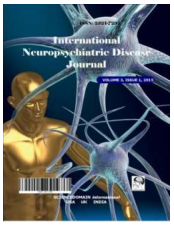

International Neuropsychiatric Disease Journal
6(2): 1-8, 2016; Article no.INDJ.22785
ISSN: 2321-7235, NLM ID: 101632319

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Epilepsy among Cerebral Palsy Children: Clinical Predictors and Frequency

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Authors' contributions

This work was carried out in collaboration between all authors. Author OAS designed the study and wrote the protocol. Author AE preformed the statistical analysis. Author MES managed the literature search and wrote the first draft of the manuscript with assistance from author OAS. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/INDJ/2016/22785
Editor(s):
(1) Zhefeng Guo, Department of Neurology, University of California, Los Angeles, USA.
Reviewers:
(1) Jera Kruja, University of Medicine, Tirana, Albania.
(2) Antonio Diaz Negrillo, Infanta Elena Hospital, Madrid, Spain.
(3) Debopam Samanta, University of Arkansas for Medical Sciences, USA.
Complete Peer review History: http://sciencedomain.org/review-history/12694

Original Research Article

Received 26th October 2015
Accepted 1st December 2015
Published 16th December 2015

ABSTRACT

Introduction: Epilepsy is one of the most common neurological disorder in childhood. The risk of epilepsy is highest in children with brain abnormalities, such as cerebral palsy. There are a lot of studies showing that epilepsy varies from 12-19 percent in children with CP.
Objective: The objective of this study is to determine the relationship between cerebral palsy (CP) and epilepsy and how to predict development of seizures among cerebral palsy children.
Subject and Methods: A prospective study included 82 patients with cerebral palsy and history of seizure. Seizure were classified according to ILAE classification, an EEG and neuro-imaging were obtained in all cases. We analyzed the incidence of different types of epilepsy in relation to different subtypes of cerebral palsy. Other factors associated with epilepsy such as age of starting first attack, neonatal seizures and familial factors were also analyzed.
Results: In our study the most common risk factors were perinatal factors 40 patients (48.8%): 16 of them had epilepsy. While the less common risk factors were postnatal factors 10 patients (12.2%): 6 of them had epilepsy. The incidence of epilepsy in our sample was significantly higher

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with very sever types of CP affecting 58.8% of very sever CP (P = 0.007). In contrary the mild type of CP was significantly associated with 3% only of the prevalence of epilepsy (P = 0.05). Abnormal CT brain findings were found in only 19 (39.6%) patients and there was no abnormality in CT brain in 29(60.4%) patients. High prevalence of epilepsy was associated with neonatal seizures and positive family history of epilepsy (p<0.005).

Conclusions: Epilepsy among children with CP is common and the most common risk factors were perinatal factors. The predominant form of epilepsy was generalized. Brain CT imaging allowed definition of extent of associated brain damage and mostly significant frequency of abnormal findings were detected in epileptic CP children.

Keywords: Epilepsy; cerebral palsy; EEG.

1. INTRODUCTION

Cerebral palsy (CP) was first described in 1862 by an orthopedic surgeon named William James Little [1], a motor disorder resulting from non-progressive (static) hurt of the immature nervous system caused by several factors that have occurred in prenatal, perinatal or postnatal periods [2-5]. It is one of the three most common lifelong developmental disabilities, the other two being autism and mental retardation causing severe disabilities affecting children and their families [6]. It can manifest itself in different pictures, mainly as spastic, athetoid and ataxic palsies; moreover, it is one of the most common causes of motor disability in children and frequently is associated with other problems, such as mental retardation, speech disorder and other disabilities such as epilepsy [7].

The prevalence of epilepsy in general childhood population, is between 3 and 6 per 1000 [8]. Overall, this prevalence raising between 15 and 55% of children and adults with CP [9,10]. Also, if learning disability associated, the risk to children with CP to develop epilepsy is much higher, rising to 71% [11].

Some authors contend that in certain types of CP occur higher rate of epilepsy [12] and has been seen that about one third of the patients with CP exhibit seizures and this is proportional to the degree of motor and cognitive disabilities [13,14].

Neurophysiology and neuro-imaging are inclined to be supportive in the identification of the underlying pathology, and in diagnosis and management [15]. EEG is extremely critical assistant of the analysis for epilepsy. EEG could be precise useful, both in adding support to a probable diagnosis of epilepsy, further more for serving to categorize the vicinity or absence of a certain epilepsy syndrome [16].

Imaging might both identify underlying reason for neurological deficits and provide information about the feasibility and practicalities of surgical treatment. A wide range of developmental and acquired lesions might be recognized [15,17]. Specially to genetic and prognostic factors, it will be essential that the underlying lesion is defined as completely as possible [15].

2. OBJECTIVE

The objective of this study is to determine the relationship between cerebral palsy (CP) and epilepsy and to determine the risk factors and to classify seizure incidence and type in relation to the CP subtypes and how to predict development of seizures among cerebral palsy children.

3. SUBJECT AND METHODS

82 patients with cerebral palsy were included in this prospective study and conducted at outpatient clinic of both Neurology and Pediatrics Departments, at Saudi German Hospital, KSA since Jan 2014 till Oct 2015, in corporation with Neurology Department Mansoura University, Egypt. Thorough history taking was done for all children with CP including age at time of gestation, occurrence of pregnancy-related complications, mode of delivery and prenatal, perinatal and postnatal complications, maturity (pre-term, full term, or post-term). Age and gender of patients were defined. The etiology might have been recognized perinatal if there was history of pregnancy prompted hypertension, hypoxic ischemic encephalopathy, neonatal sepsis, alternately historical backdrop of punctual hospitalization after conception. Though the history proposed manifestation after 7 days, the cause was considered to be postnatal. CP might have been ordered as stated by tone and motor deficit into atonic and spastic (diplegia, hemiplegia, and tetraplegia including dyskinetic type).

The severity of CP was classified into:

1. Very severe: child cannot move with assistance and require wheelchair.
2. Severe: can walk with maximum support with significant limitations of daily activities.
3. Moderate: can walk with some assistance.
4. Mild mean child can move without assistance and without limitation of daily activities [18] the patient was studied in detail for clinical type of epileptic seizure, its frequency, and its response to anti-epileptic drugs, and seizures were classified according to ILAE classification [19], EEG and CT brain were done for all cases.

4. RESULTS

In our study epileptic patients (34 patients) were classified into four main categories: generalized, partial, infantile spasms and undeterminate (ILAE - 1989) [19]. Active epilepsy was considered when two or more unprovoked seizures occurred during the previous year [20,21].

The study included 82 children (mean age, 7.56±4.89 years; range, 2-17 years), of whom 47(57.3%) were males and 35 (42.7%) were females, with a male to female ratio was 1.3:1. Also, the incidence of epilepsy in CP patients. While, 48 children with cerebral palsy (58, 5%), weren't epileptic. 52.1% of the non-epileptic cases are males (n=25 patients), and (47,9%) are females (n=23 patients).

Spastic type was the most common type (85.4%), including spastic quadriplegia in 40.2% of patients, spastic hemiplegia in 29.3% of patients, and spastic diplegia in 15.9% of patients. While, patients presented by dyskinesia in 2.4% of cases, ataxia in 3.7% of cases, hypotonia in 2.4% of cases and mixed type in 6.1% of patients (Table 2).

In our study the most common risk factors were perinatal factors 40 patients (48.8%): 16 of them had epilepsy. The second most common risk factors were prenatal factors in 29 patients (35.4%): 11 of them had epilepsy. While the less common risk factors were postnatal factors 10 patients (12.2%): 6 of them had epilepsy, and with unknown etiological factors 3 patients (3,7%): 1 of them had epilepsy.

Frequency of epilepsy in CP patients was significantly higher with very sever types of CP affecting 58.8% of very sever CP (P = 0.007). while, less sever and moderate types of CP were associated with less prevalence of epilepsy (20.6% and 17.6 respectively). In contrary the mild type of CP was significantly associated with 3% only of the prevalence of epilepsy (P = 0.05).

The recurrence of epilepsy was highest in patients with spastic quadriplegic type disease (50%) but not statistically significant (P=0.1294), followed by hemiplegic type in 13 patients (38.2%), then diplegic type affecting 3 patients only (8.8%), and lastly the mixed type in one patient (3%) only. While there were no epileptic cases among dyskinetic, ataxic, and hypotonic types.

A total of 41% of the CP patients had epilepsy, 24% had mental retardation, 23% of patients had speech impairments, and 22% of CP patients had visual disorders. While, growth retardation, behavioral disorders, teeth problems, and dysphagia were less common manifestations of CP patients (Fig. 1).

Total number of epileptic patients was 34 (41.5%). 19 patients (55.9%) of the epileptic CP patients had generalized epilepsy, 10 patients (29.4%) had partial, two patients (5.9%) had infantile spasms and three patients (8.8%) had undeterminate epilepsy (Fig. 2).

Thirty-four CP patients were epileptics and abnormal CT brain findings were found in 28(82.4%) patients (ventriculomegaly,focal infarctions, periventricular leukomalacia, cortical and subcortical atrophy, basal ganglionic lesions), and there was no abnormality in CT brain in 6(17.6%) patients.

Table 1. Age and sex distribution in CP patients

Variable		Epileptic	Non-epileptic	Total	Test of significance
Age mean (range) Y		8.1±5.22 (2-17)	7.9±4.53(3-15)	7.56±4.89 (2-17)	P value 0.895
Sex	Male	22(64,7%)	25(52.1%)	47(57.3%)	Chi-square= 1.2962
	Female	12(35,3%)	23(47,9%)	35(42.7%)	P value =0.2549
Total		34(41, 5%)	48(58, 5%)	82(100%)	

Table 2. CP subtypes

CP Subtype	Number (n=82)	Ratio (%)
Spastic	70	85.4%
Quadriplegic	33	40.2%
Hemiplegic	24	29.3%
Diplegic	13	15.9%
Dyskinetic	2	2.4%
Choreathetoic	1	1.2%
Dystonic	1	1.2%
Ataxic	3	3.7%
Hypotonic	2	2.4%
Mixed	5	6.1%
Total	82	100

Forty-eight CP patients were non-epileptics and abnormal CT brain findings were found in only 19(39.6%) patients and there was no abnormality in CT brain in 29(60.4%) patients. High prevalence of epilepsy was associated with neonatal seizures and positive family history of epilepsy (p<0.005).

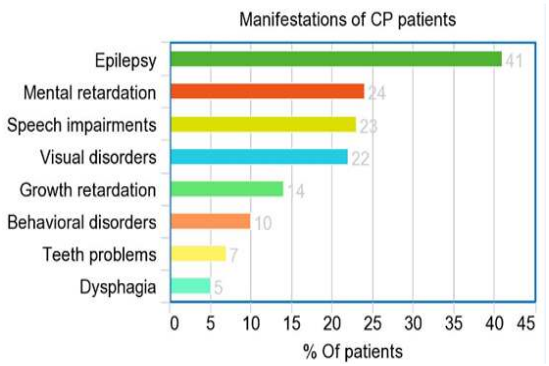

Fig. 1. Manifestations of CP patients

Table 3. Risk factors for cerebral palsy

Risk factor	With epilepsy	Without epilepsy	Ratio (%)	Test of significance
Prenatal	11	18	35.4%	chi-square = 1.6818
(Peri)natal	16	24	48.8%	P-Value = 0.640995
Postnatal	6	4	12.2%	
Unknown	1	2	3,7%	
Total	34 (41,25%)	44 (58,75%)	82 (100%)	

Table 4. Prevalence of epilepsy in relation to severity of different types of cerebral palsy (CP)

CP type	Very sever		sever		Moderate		Mild		Total
	ve+	-ve	+ve	-ve	+ve	-ve	+ve	-ve	
Quadriplegic	13	11	3	2	1	3	0	0	33
Diplegia	2	1	1	5	0	2	0	2	13
Hemiplegic	4	1	3	2	5	6	1	2	24
Dyskinetic	0	0	0	0	0	1	0	1	2
Ataxic	0	0	0	0	0	2	0	1	3
Hypotonic	0	0	0	0	0	1	0	1	2
Mixed	1	1	0	1	0	1	0	1	5
Total	20	14	7	10	6	16	1	8	82(100%)
N (%) of epileptic cases	20 (58. 8%)		7 (20.6%)		6(17. 6%)		1(3%)		
Test of significance	Chisquare= 7.2121 P = 0.007*		P = 0.978		P = 0.1142		Chisquare= 3.837 P = 0.05*		

Table 5. Frequency of epilepsy in relation to types of CP

CP type	With epileptic	Non without epileptic	Total	Test of significance
Quadriplegic	17(50%)	16(33.3%)	33	P =0.1294
Diplegia	3(8.8%)	10(20.8%)	13	P =0.1423
Hemiplegic	13(38.2%)	11(22.9%)	24	P =0.1331
Dyskinetic	0	2(4.2%)	2	P =0.228
Ataxic	0	3(6.3)	3	P =0.1375
Hypotonic	0	2(4.2%)	2	P =0.228
Mixed	1(3%)	4(8.3%)	5	P =0.314
Total	34 (41, 5%)	48 (58, 5%)	82(100%)	

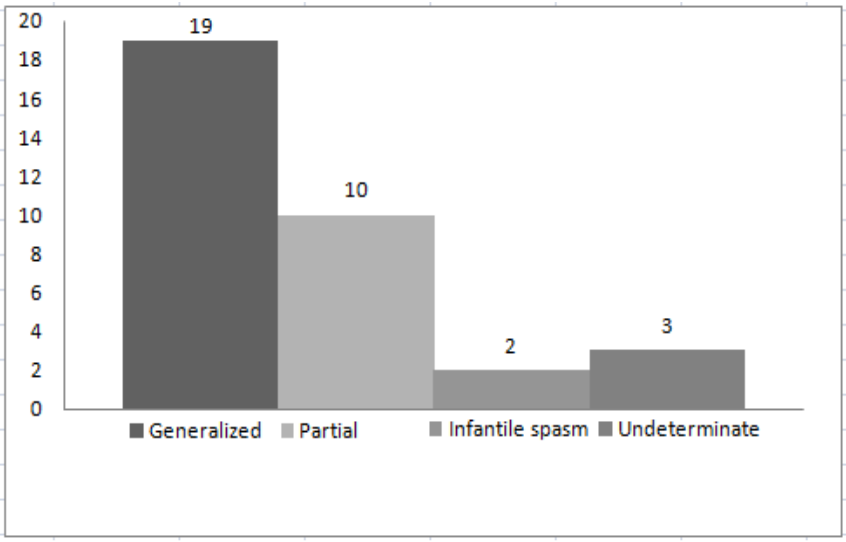

Fig. 2. Number of epileptic CP patients according to type of epilepsy

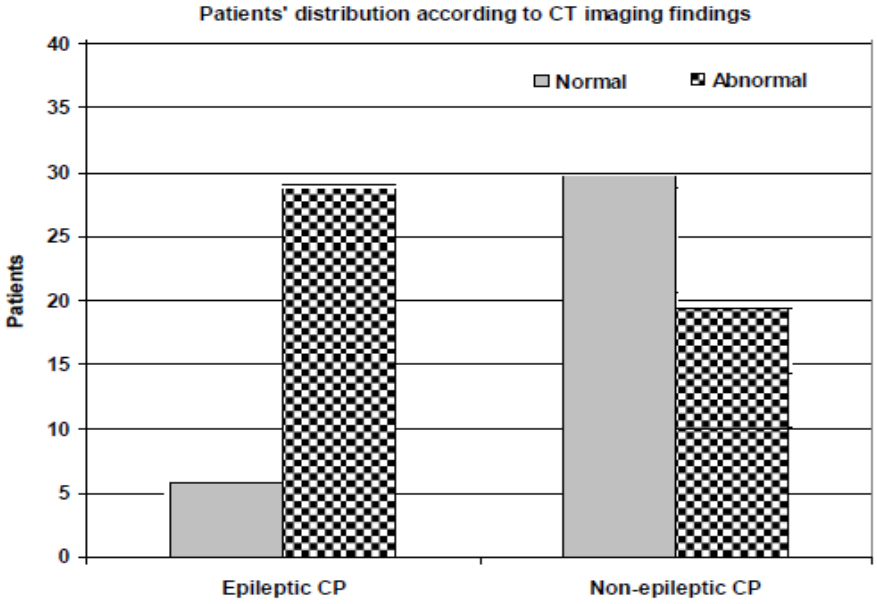

Fig. 3. Showing significant higher frequency of abnormal CT brain in epileptics CP patients in comparison to non-epileptic CP patients (p<0.001)

Table 6. CT imaging and associated factors with incidence of epilepsy in CP

Associated factors		Epileptics	Non-epileptics	Total	Test of significance
Neonatal seizures		20	2	22	Chi-square =30.286 p<0.005*
Positive family history		9	0	9	Chi-square =14.27 p<0.005*
CT imaging	Abnormal	28 (82.4%)	19 (39.6%)	47 (57.3%)	Chi-square = 14.8812.
	Normal	6 (17.6%)	29(60.4%)	35 (42.7%)	p<0.005*
		34 (41, 5%)	48(58.5%)	82(100%)	

** This result is significant at p < 0.05*

5. DISCUSSION

Epilepsy is a standout amongst the vast majority pervasive neuro-impairment in childhood and is appeared in 4.0 to 8.8 per 1000 in population-based studies [22].

In our study the most common risk factors were perinatal factors 40 patients (48.8%): 16 of them had epilepsy. The second most common risk factors were prenatal factors in 29 patients (35.4%): 11 of them had epilepsy. While the less common risk factors were postnatal factors 10 patients (12.2%): 6 of them had epilepsy, and with unknown etiological factors 3 patients (3,7%): 1 of them had epilepsy.

The incidence of epilepsy in our sample was significantly higher with very sever types of CP affecting 58.8% of very sever CP (P = 0.007). While, less sever and moderate types of CP were associated with less prevalence of epilepsy (20.6% and 17.6 respectively). In contrary the mild type of CP was significantly associated with 3% only of the prevalence of epilepsy (P = 0.05). May be identified with those of higher degree of motor and mental disorder of the patients concerned in these population, this is in accordance with several studies found that the incidence of epilepsy in cerebral palsy children is related to severe form of motor and mental abnormalities in the patients included in their group [23-26].

The predominant type of seizure in our study was generalized, which is in accordance with other studies concerned with children with or without CP [25,27,28]. Niedemayer [29] advocated this findings stating that the generalized epileptiform activity can be attributed whichever with a genetic predisposition, or to a quick secondary bilateral synchronization, for example the one induced sometimes by a frontal focus. On extraordinary occasions, deep subcortical cerebral lesion could also produce this type of epileptiform activity.

Also we found that The frequency of epilepsy was highest in patients with spastic quadriplegic type disease (50%) but not statistically significant (P=0.1294), followed by hemiplegic type in 13 patients (38.2%), then diplegic type affecting 3 patients only (8.8%), and lastly the mixed type in one patient (3%) only. While there were no epileptic cases among dyskinetic, ataxic, and hypotonic types. That is go in hand with Bruck et al. [30] who specified that there may be straight association between epilepsy and degree of motor dysfunction, furthermore their association with mental retardation. Also in their study they found that the majority of tetraplegic patients presented epilepsy and intellectual impairment.

Thirty-four CP patients were epileptics and abnormal CT brain findings were found in the majority (82.4%) of them, while normal CT findings were concluded in only 6 of 34 patients with CP and epilepsy and there is a significant higher frequency of abnormal CT brain in epileptics CP patients in comparison to non-epileptic CP patients ($p<0.001$). These findings indicated the applicability of neuroimaging for evaluation of both CP and epileptic patients. However, still CT imaging is not conclusive in patients with cerebral palsy as it is restricted in diagnosis of many cases with congenital abnormalities and cortical dysplasia, and so, in farther studies we recommend to do MRI imaging rather than CT studies. In line with this finding, Banerjee et al. [31] found that out of the epileptics who had brain CT scans 23.4% demonstrated single or multiple lesions suggestive of neurocysticercosis. Grigore & Diaconu reported that in 85.28% of CP patient's MR/CT imaging showed different types of abnormalities, CT/MR abnormalities might have been cohorted on 65.45% of cases with mental retardation, furthermore 44.54% exhibited epileptic seizures, also closed that in CP neuroimaging findings are common, but variable and MRI/CT change correlates with neurological appraisal [32]. Tripathi et al. [33] reported that radiological findings of structural cerebral abnormality is significant predictor of response, delayed milestones, high initial seizure frequency of more than you quit offering on that one for every month.

6. CONCLUSION

The obtained results concluded that epilepsy among children with CP is common and the most common risk factors were perinatal factors. with predominant of generalized form. Also; abnormal neuro-radiological findings associated with brain damage and EEG are mostly significant and we recommend to do them for all cerebral palsy children specially moderate or severe form and spastic quadriplegic type, for early detection of epilepsy in CP children and so the best line of management could be carried out.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
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