

Maternal Risk Factors for Epilepsy in Children with Cerebral Palsy Attending in Chittagong Medical College Hospital, Chattogram

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Abstract

Background: Cerebral palsy is a group of disorders that results from nonprogressive interference of the developing brain. It is a major cause of childhood disability in various parts of the world and is often associated with epilepsy and epileptic seizure. Epilepsy has been observed to be more common among children with cerebral palsy which causes additional challenge during their management. Definite risk factors for epilepsy in cerebral palsy have been less highlighted though it is associated with one-third of such patients. The aim of the study was to identify the maternal risk factors of epilepsy in children with cerebral palsy.

Materials and methods: This retrospective nested case-control study was conducted both in the Outpatient and Inpatient wards of Department of Pediatrics, Chattogram Medical College Hospital, Bangladesh. The study duration was six months from 01.05.2021 to 31.10.2021. Fifty children of cerebral palsy with epilepsy were selected for the case group, and another age matched 50 children of cerebral palsy having no epilepsy were selected for the control group. Data were collected from the hospital records and available family history of both the groups.

Results: Majority of the children of both groups belonged to 1-5 years old age group. Spastic quadriplegia in case group and hypotonic in control group were the predominant types of Cerebral Palsy (CP). Generalized tonic and clonic types of seizure were found in majority of the CP patients who had epilepsy. Single associated impairment had a higher prevalence in the control group, but multiple associated impairments were higher in the case group, and the difference was statistically significant. Risk factors that showed significant positive correlation to develop epilepsy in CP were positive family history of epilepsy, history of prolonged rupture of membrane, delivery by untrained birth attendant and LSCS as mode of delivery. No statistically significant positive correlation

was found between maternal age at delivery, pre and post conceptional maternal diseases and preterm labour as risk factors to develop epilepsy in CP.

Conclusion: The study found that apart from family history, history of prolonged rupture of membrane, maternal pregnancy related issues including mode of delivery may cause significant impact on children of CP having epilepsy.

Key words: Cerebral palsy; Children; Epilepsy; Neonatal; Seizure.

Introduction

Cerebral Palsy (CP) is a combination of persistent, although not always stable, movement and/or postural and motor function problems caused by a nonprogressive interference, lesion, or anomaly of the developing/immature brain.¹ Epilepsy is a distinct and significant clinical concern in children with CP. It is well acknowledged that the general incidence of epilepsy in children and people with CP ranges from 15% to 55%. Cerebral Palsy (CP) is characterized by abnormalities in muscle tone, mobility, and motor abilities as a result of harm to the developing brain. Clinically, the condition develops over time and however, suggestive signs and symptoms may be present at a younger age. Epilepsy is frequent in CP, affecting around 30% of individuals. In most cases, the beginning occurs within the first two years of life. Children with spastic hemiplegia are most likely to develop epilepsy, followed by quadriplegia and diplegia.² In high-income nations, the epidemiology of CP has been widely researched. However, there is a scarcity of evidence-based on large, general population-representative samples that can give accurate, impartial data in Low- and Middle-Income Countries (LMICs). A meta-analysis and systematic review of the prevalence of CP was comprised of 49 investigations, 46 of which were done in high-income countries.³ The etiology of CP may predict the onset of epilepsy. Certain risk factors increase the likelihood that a newborn may have CP. Epilepsy is strongly linked to CP. Family history, anatomical abnormalities (Most notably

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brain atrophy and gray matter involvement) newborn seizure, poor Apgar scores, and mental retardation are all important risk factors for the development of epilepsy in CP patients. Seizures are more prevalent in CP patients with spastic quadriplegia or acquired hemiplegia, but are less common in moderate symmetric spastic diplegia and CP that is mostly athetoid. Risk factors for the development of epilepsy are mainly positive family history and history of neonatal seizures. According to recent research by Sadowska, the risk variables related to the occurrence of epilepsy in the investigated group of children were arterial hypertension during pregnancy, cesarean birth, and newborn convulsions.⁴ Knowledge of epileptic risk factors in children at risk of CP necessitates extra care and behavioral monitoring, as well as recurring EEG screening. All children with CP, but notably those at higher risk, should be extensively examined for probable epilepsy incidence to commence early treatment, which may be critical to enabling these kids' improved development. Epilepsy is the leading cause of morbidity in children globally, with 80 percent of those affected living in underdeveloped nations. Epidemiological surveys in Bangladesh support the prevalence of seizure disorders. In one research, children aged 2 to 9 years had a prevalence rate of 68 out of 1000 for any seizure history and 9 out of 1000 for any unprovoked seizure.⁵ Epilepsy is frequent in CP patients, affecting around 30% of them. Bangladesh has an estimated frequency of CP of 3.4/1000, which is 1.5 times higher than in Europe.⁶ If modifiable risk factors for CP and related seizures can be identified early, and the effective preventative program can be developed by prioritizing them. So, the present study was conducted to find out the maternal risk factors of epilepsy among children presenting with cerebral palsy.

Materials and methods

This retrospective nested case-control study was conducted at both the outpatient and inpatient wards of Department of Pediatrics, Chittagong Medical College Hospital (CMCH) Bangladesh. The study duration was six months, from 01.05.2021 to 31.10.21. A total of 320 CP patients were enrolled and epilepsy was found in 104 patients. Among them 50 patients were selected for the case group and another age matched 50

children of CP having no epilepsy were selected for the control group. Diagnosis of Cerebral palsy and Epilepsy were established either by Child Developmental Centre of CMCH or by Pediatricians after thorough clinical & laboratory evaluation. Inclusion criteria for the selected patients were: CP patients with epilepsy attending in pediatric wards and OPD (For cases), age - matched children of CP patients without epilepsy (For control) and patients whose parents had given consent to participate in the study (For both groups). On the other hand, patients having Autism Spectrum and other developmental disorders, Down's syndrome, patients with known neurometabolic, neurodegenerative and neurogenetic conditions (e.g. Tuberous sclerosis, neurofibromatosis etc.) and patients whose parents refused to participate were excluded from the study. Convenient sampling method was used for the selection of the participants. A mixed type of questionnaire-based case record form was used to collect data. After obtaining informed consent from the respective parents' information regarding demographic profile, family history, type of CP, type and age of onset of seizure, pre and post-conceptual maternal diseases, antenatal care etc. were carefully documented from individual interviews and also from present and previous hospital records. Ethical approval was obtained from the ethical review committee of the study hospital. Data were tabulated according to key variables. Analysis of different variables were done using SPSS (Statistical Package for Social Science) for Windows version 25. Continuous data were expressed as mean (\pm Standard deviation). They were compared by independent sample t-test. Categorical data were expressed as frequency (Percentage) and compared between groups by Chi-square test. Independent predictive factors for epilepsy were determined by logistic regression analysis. p-value when less than 0.05 was considered as statistically significant and confidence interval was set at 95% level.

Results

Majority of the children of both groups were between 1-5 years old. Male patients were more in case group (60% vs 48%). Predominant type of CP in case group was spastic quadriplegia whereas hypotonic type of CP was found more in control group (Table I). Though most of the patients in

both the group had developmental delay, multiple associated impairments were higher in the case group. About 64% of the patients with epilepsy had generalized tonic & clonic types of seizure and half of the patients having epilepsy reported of not having well-controlled seizure. Among the total 100 participants from both groups, 24 patients had singular impairment and 76 patients had multiple associated impairments. Sixteen patients from the control group had singular associated impairments compared to the 8 patients from the case group. On the other hand, multiple associated impairments were more prevalent in the case group (84% vs 64%) (Table II). Statistically significant difference was found in case of family history of epilepsy between the groups, where 8% of patients from the case group had a family history of epilepsy. The most prevalent perinatal risk factor was consanguinity, prevalent in 12% of the case group participants and 16% of control group participants. Maternal hypertension also had a high prevalence among the case group participants, at 10%. Preeclampsia and antepartum hemorrhage were only present in 1 parent each from the case group, while all of these factors were statistically non-significant between case and control groups (Table III). About 52% of the case group and 36% of the control group participants had prolonged labor, while 14% of the case group and 8% of the control group had prolonged membrane rupture. Labor induction was necessary for 44% of the case group and 10% of the control group participants. Delivery by untrained birth attendant (UTBA) was done in 24% of the case group and 4% of the control group participants, while history of LSCS was among 28% of the case group and 8% of the control group. The pregnancy-related risk factors as prolong membrane rupture, delivery by UTBA and history of LSCS were constantly higher among the case group participants, and the difference between case and control groups was statistically significant, but induction of labour shows statistically highly significant difference (Table IV). Regarding risk factors, positive family history of epilepsy, prolong membrane rupture, history of induction of labour, delivery by UTBA and history of LSCS were independently associated with epilepsy (Table V).

Table I Demographic profile and predominant CP motor type of the patients

	Case		Control		p-value
	Number	Percentage	Number	Percentage	
Age of Patient					
<1 year	13	26%	12	24%	0.973
1-5 year	34	68%	35	70%	
>5 years	3	6%	3	6%	
Gender					
Male	30	60%	24	48%	0.229
Female	20	40%	26	52%	
Predominant CP motor type					
Spastic	25	50%	15	30%	
Hypotonic	19	38%	20	40%	0.079
Dyskinetic	1	2%	1	2%	
Ataxic	5	10%	14	28%	

Table II Associated impairments present in the children with cerebral palsy

Associated Impairments	Case		Control		p-Value	
	Number	Percentage	Number	Percentage		
Singular Impairments (n=22)	Speech	2	4%	7	14%	0.01
	Intellectual	4	8%	4	8%	
	Strabismus	2	4%	2	4%	
	Hearing	0	0%	3	6%	
Multiple Impairments (n=76)	Speech+ Intellectual + Strabismus	6	12%	10	20%	
	Speech+ Intellectual + Hearing	4	8%	1	2%	
	Speech+ Intellectual + Visual	12	24%	0	0%	
	Speech+ Intellectual	12	24%	13	26%	
	Intellectual+ Visual	1	2%	0	0%	
	Speech+ Hearing + Visual	1	2%	1	2%	
	Speech+ Intellectual + Strabismus + Visual	1	2%	2	4%	
	Hearing + Visual	1	2%	3	6%	
	Speech + Intellectual + Hearing + Visual	1	2%	2	4%	
	Intellectual + Hearing + Visual	1	2%	0	0%	
Intellectual + Strabismus	2	4%	1	2%		
Speech + Strabismus	0	0%	1	2%		

Table III Maternal risk factors

Maternal Risk Factors	Case		Control		p value
	Number	Percentage	Number	Percentage	
Family History of epilepsy	4	8%	0	0%	0.041
Family history of disability	3	6%	3	6%	1.00
Consanguinity	6	12%	8	16%	0.564
Maternal Hypertension	5	10%	1	2%	0.295
Maternal Epilepsy	1	2%	2	4%	0.134
Polyhydramnios	1	2%	1	2%	1.00
Maternal Fever	2	4%	1	2%	0.558
Urinary Tract Infection	0	0%	1	2%	0.315
Preeclampsia	1	2%	0	0%	0.315
Antepartum Hemorrhage	1	2%	0	0%	0.315
Pre-term Birth	1	2%	1	2%	1.00

Table IV Distribution of delivery-related factors

Variables	Case		Control		p-Value
	Number	Percentage	Number	Percentage	
Prolonged Labor	28	56%	19	38%	0.071 (ns)
Prolonged Membrane Rupture	15	30%	5	10%	0.012 (s)
Labor Induction	22	44%	5	10%	<0.001 (hs)
Delivery by UTBA	12	24%	2	4%	0.004 (s)
Delivery by LSCS	14	28%	4	8%	0.009 (s)

Table V Adjusted Odds Ratio for risk of epilepsy among children presenting cerebral palsy

Variables	Adjusted OR	95% CI		p value
		Lower	Upper	
Positive family history	2.087	1.694	2.571	0.041 ^s
Prolonged membrane rupture	2.250	1.028	4.925	0.012 ^s
Induction of labour	3.329	1.478	7.495	<0.001 ^{hs}
Delivery by UTBA	3.907	1.068	14.290	0.004 ^s
LSCS	2.524	1.042	6.118	0.009 ^s

CI = Confidence Interval, OR = Odds Ratio, s = significant, hs = highly significant.

Discussion

Cerebral palsy can manifest as worldwide mental and physical dysfunction or as discrete problems in locomotion, cognition, development, or sensory. It is the most prevalent physical handicap in childhood, affecting 2 to 2.5 children out of every 1,000 born in the United States.⁷ Cerebral palsy is caused by brain damage or issues during pregnancy, birth, or within the first 2 to 3 years of a child's life. It can be caused by premature delivery, brain trauma, a lack of oxygen, and a variety of other circumstances. Cerebral Palsy (CP) can often lead to epilepsy, a neurological condition marked by a lasting proclivity to induce epileptic seizures as well as its psychological repercussions.⁸ Epilepsy affects 15-60% of children with cerebral palsy, however, the clinical course is unknown.^{9,10} Freud noticed the increased risk of seizures in people with Cerebral Palsy (CP) more than a century ago. His descriptions of the convulsions' features show that he recognizes their symptomatic nature. Much more recently, the significance of epilepsy as a negative factor for cognitive performance in children with hemiplegic CP has been emphasized.¹¹ The present study was conducted to observe the possible risk factors of epilepsy among children with cerebral palsy. The study was conducted with

the case group, containing 50 children with CP who also had epilepsy, and the control group of another 50 children who only had CP and no epilepsy. To better observe and analyze the risk factors of epilepsy, both maternal and family risk factors were also documented. The majority of both case and control groups participants were from the age group of 1-5 years. The difference of prevalence between case and control group participants was not significant. Among the case group participants, the majority were male, but among the control group participants, the female prevalence was observed. But this difference was not statistically significant. In the present study, the spastic type of predominant CP had the highest prevalence in the case group at 50%, but in the control group, 40% had a hypotonic type and 30% had a spastic type of CP. Spastic type of cerebral palsy is more common compared to other types of cerebral palsy, having as high as 80% incidence rate worldwide, as observed in various other studies.^{12,13} Hypotonic CP had the second-highest prevalence among the case group participants. Cerebral palsy is almost always associated with impairments, from motor disability to cognitive impairments.^{14,15} In the present study, the majority of the participants had multiple impairments, and only 22 had singular impairments, 6 from the case group and 16 from the control group. On the other hand, 84% of the case group and 64% of the control had multiple associated impairments present. The combination of speech and intellectual impairment had the highest prevalence in both the case group and control group. The difference of associated impairments between the case group and control group had high significance. Antiepileptic medicine was used for 98% of the case group children and for only 4% of control group participants, which was statistically significant. Among the perinatal risk factors found in this study, the most prevalent was consanguinity or marrying into the family. Consanguinity was observed to have a high association with cerebral palsy and epilepsy in various global studies.¹⁶⁻¹⁹ In a study from Jordan, it was observed that first cousin marriages had higher incidence rates of cerebral palsy and epilepsy.²⁰ Maternal hypertension had a higher incidence among the case group participants compared to the control

group. 8% of the case group participants had a family history of epilepsy, while none from the control group had such a family history. Pregnancy-related complications also play a role in both epilepsy and cerebral palsy, and the difference between these two had high significance. In the case group, 52% had prolonged labor, while only 36% from the control group had prolonged labor. Labor induction was necessary for 44% of the case group participants, while it was only necessary for 10% of the control group participants. Pregnancy-related risk factors had been constantly high in the case group, suggesting a high correlation between such factors and epilepsy among children, supported by multiple studies.²¹⁻²³ Present study shows, history of LSCS was among 28% of the case group and 8% of the control group patients ($p=0.009$). Delivery by cesarean section increased the risk of epilepsy in the CP patients over two-fold ($OR = 2.17$, $p = 0.012$).⁴

Limitation

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

Conclusion

The study found that lack of proper and adequate care during pregnancy, various antenatal complications can have a significant impact on children having epilepsy like preterm membrane rupture, induction of labor, mode of delivery etc. Family history of epilepsy, hypertension, and consanguinity also had a role in epilepsy.

Recommendation

Similar study can be done for long duration with large sample size in multiple centre for actual results.

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Contribution of authors

ZC- Conception, design, acquisition of data, data analysis, manuscript writing & final approval.

KN-Data analysis, interpretation of data, manuscript writing & final approval.

AF- Acquisition of data, critical revision & final approval.

DB- Data analysis, manuscript writing & final approval.

AB-Acquisition of data, manuscript writing & final approval.

MD- Interpretation of data, critical revision & final approval.

Disclosure

The authors declared no conflicts of interest.

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