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Original Research Article

# A Cross-Sectional Study Done to Determine the Prevalence, Describe the Clinical Profile and Identify the Risk Factors of Epilepsy in Children with Cerebral Palsy

**Murugan T.P.[1], Koshy Alan Valiaveetil[2], Amanda Grace Sajem[3], Samuel Philip Oommen[4]**

[1]Associate Professor, Department of Paediatrics, Christian Medical College Hospital, Vellore, India
[2]Associate Professor, Department of Paediatrics, Christian Medical College, Vellore, India
[3]Senior Resident, Department of Anaesthesia, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India
[4]Professor, Department of Paediatrics, Christian Medical College, Vellore, India

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**Corresponding Author: Dr. Samuel Philip Oommen**
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**Abstract:**

**Background:** The non-progressive motor impairment condition known as cerebral palsy (CP) is brought on by brain lesions during early development, making it a major cause of childhood disability. CP is commonly associated with comorbidities like epilepsy, learning disabilities, and behavioral disorders. The incidence of epilepsy in CP kids ranges from 20-45%, with an increased incidence in those with spastic quadriplegia. Epilepsy in CP is often drug-resistant and can significantly affect the quality of life, requiring polytherapy for control.

**Aim:** This study aimed to determine the prevalence of epilepsy in children with CP and to identify the correlated risk aspects, including demographic, clinical, and aetiological factors.

**Methodology:** A cross-sectional study was conducted at the Christian Medical College, India, with a sample size of 100 kids diagnosed with CP. The children were categorized based on the category of CP, severity of movement disorders, and brain imaging results. Psychological assessments were used to evaluate intellectual development. Epilepsy was diagnosed following the International League Against Epilepsy (ILAE) criteria. The study utilized statistical analyses to determine significant associations between selected parameters and epilepsy.

**Results:** Children with epilepsy showed a higher prevalence of microcephaly, lower social quotient, neonatal seizures, and a family history of seizures. Perinatal and neonatal disorders were the most common aetiologies, with perinatal asphyxia and intrauterine growth restriction being prevalent. The majority of CP children with epilepsy had generalized seizures, and a significant portion exhibited drug-resistant epilepsy.

**Conclusion:** Epilepsy is highly frequent in kids with CP, particularly those with microcephaly, developmental delays, and perinatal risk factors. The study highlights the need for early diagnosis and intervention to manage epilepsy and improve outcomes in this vulnerable population.

**Keywords:** Cerebral Palsy, Drug-Resistant Epilepsy, Epilepsy, Perinatal Asphyxia.



## Introduction

A collection of non-progressive yet frequently variable motor dysfunction symptoms arising from brain abnormalities or lesions that manifest early in development is usually referred to as cerebral palsy (CP) [1]. It is recognised as one of the three most prevalent lifelong developmental impairments, alongside autism and intellectual disability, and is a primary contributor to childhood disability [2]. The incidence of cerebral palsy in developed nations is approximately 2 to 2.5 per 1,000 live births. Notwithstanding advancements in obstetric care, this aspect generally remained static, partially due to the enhanced survival rates of premature infants [3]. The Gross Motor Function Classification System (GMFCS), first introduced in 1997 and subsequently refined by Palisano et al. in 2007 (GMFCS-E&R), is the most widely utilised clinical functional classification for cerebral palsy, despite numerous classifications based on topography, neuropathology, aetiology, and physiology. [4] The five tiers of the GMFCS ordinal scale are predicated on the mobility and ambulation of children with cerebral palsy. Cerebral palsy (CP) is frequently associated with comorbidities including seizures, particularly drug-resistant epilepsy, learning disabilities, feeding challenges, behavioural issues, visual impairment, auditory impairment, and malnutrition [5].

Seizure burden occurs frequently in children with cerebral palsy, affecting approximately 20-45% of this population. The estimated prevalence of cerebral palsy in Indian children ranges from 35 to 50 percent [6]. Children with cerebral palsy (CP) exhibit a markedly elevated risk of epilepsy development associated with low birth weight, neonatal seizures, seizures during the first year of life, a familial history of epilepsy, or severe CP [7]. Children with cerebral palsy and concurrent epilepsy exhibit a poor prognosis. Early warning signs may include prolonged fisting, early-handedness, mental slowness, and toe walking.

Early onset epilepsy in children with cerebral palsy is characterised by a high initial frequency and the presence of multiple seizure subtypes. This condition is primarily drug-resistant and necessitates polytherapy with anti-seizure medications (ASMs). Status epilepticus occurs nine times more frequently in these children [8]. Generalised seizures represent the most prevalent category of seizures. These occurrences are observed with greater frequency in children diagnosed with diplegia (20–27%), spastic hemiplegia (27–45%), and spastic quadriplegia (65–72%) [9]. Seizures occur in approximately 50.1% to 60.01% of children with cerebral palsy before reaching one year of age. Increased seizure risk is observed in cerebral palsy patients with more extensive cortical grey matter involvement. The 2017 classification by the International League Against Epilepsy (ILAE) is the currently recommended framework for epilepsy [10]. The ILAE 2017 classification system highlights the significance of determining aetiology because of its therapeutic implications and is designed for classification in diverse clinical contexts. This study presents a cross-sectional analysis aimed at determining the prevalence and risk factors associated with childhood cerebral palsy and epilepsy.

## Methodology

**Study Design:** The research was carried out in the Outpatient Department of Paediatrics at Christian Medical College Hospital, Vellore, India for one year.

**Sample Size:** The sample size for this study was 100 children with CP, selected based on the inclusion and exclusion criteria outlined below.

### Inclusion and Exclusion Criteria

**Inclusion Criteria:**

- Children between the ages of four and seventeen at the time of hospitalisation or enrolment.
- A cerebral palsy diagnosis that has been confirmed by a seasoned paediatric neurologist.
- Neuroimaging data are available by Computed Tomography (CT) or Magnetic Resonance Imaging (MRI).

**Exclusion Criteria:**

- Children under the age of four or older than seventeen at the time of admission or hospitalisation.
- No neuroimaging results were found.
- Symptoms that point to progressive encephalopathies.
- The existence of inborn metabolic errors.

**Procedure:** The analysis of the selected sample involved classifying the types of cerebral palsy (CP), assessing the severity of movement disorders, and evaluating brain imaging results. The CP types were categorized using Ingram's classification, which includes diplegia, hemiplegia, tetraplegia, extrapyramidal form, ataxic form, and mixed form. The severity of movement disorders was assessed using the Gross Motor Function Classification Scale (GMFCS). For MRI brain imaging, the results were classified according to the Magnetic Resonance Imaging Classification System (MRICS) recommended by the Surveillance of Cerebral Palsy in Europe (SCPE). The classification categories included maldevelopments (such as disorders of cortical formation and other maldevelopments), predominant white matter injury (including periventricular leukomalacia (PVL), sequelae of intraventricular haemorrhage (IVH), and combinations of PVL and IVH sequelae), predominant grey matter injury (such as basal ganglia/thalamus lesions, cortico-subcortical lesions, and arterial infarctions), miscellaneous findings, and normal results.

Intellectual developmental levels were assessed by psychologists using various psychological tests for the 100 children in the study. These tests included the Wechsler Intelligence Scale for Children—Revised (WISC-R), Wechsler Adult Intelligence Scale-Revised (WAIS-R), Psyche Cattell Infant Intelligence Scale, Columbia Mental Maturity Scale (CMMS), Leiter International Performance Scale, Intelligence and Development Scales—Preschool (IDS-P), and the H.C. Gunzburg Scale of Measurement of Social Development in children with mental disabilities. Based on the results of these assessments, the children were classified into five groups: those with standard or below-standard psychological assessment, mild impairment, moderate impairment, significant impairment, and deep impairment.

Epilepsy was diagnosed following the criteria established by the International League Against Epilepsy (ILAE). A separate group was identified for drug-resistant epilepsy, defined as the failure of adequate trials of two tolerated, appropriately chosen, and used antiepileptic drug schedules (either

as monotherapy or in combination) to achieve sustained seizure freedom. Seizure freedom was defined as the absence of seizures for more than one year or seizures that occurred at a frequency separated by a period three times longer than the longest interval between seizures before treatment.

**Statistical Analysis:** Statistical analysis was performed using STATISTICA 13.0 software. Continuous variables were summarized as mean values (M) and standard deviations (SD), while categorical variables were presented as absolute (n) and relative frequencies (%). The Mann-Whitney U test compared continuous variables, and the $\chi^2$ test with Yates's correction assessed categorical variables. Univariate and multivariate logistic regression models were used to calculate the odds ratio (OR) with 95% confidence intervals (CI) for the relationship between selected parameters and epilepsy or drug-resistant epilepsy. A p-value of $\leq 0.05$ was considered statistically significant.

## Result

Table 1 presents the demographic and clinical characteristics of children with and without epilepsy. The groups are similar in gender distribution, with slightly more girls in both groups, and the median age is comparable (46 months for non-epileptic children vs. 44 months for epileptic children; $p$=0.78). Parental consanguinity and socio-economic status do not differ significantly between the groups. However, microcephaly is significantly more prevalent among children with epilepsy (79.5% vs. 63.9%; $p$<0.001), as is a social quotient below 80 (92.3% vs. 67.2%; $p$<0.001). History of neonatal seizures (35.9% vs. 13.1%; $p$<0.001) and family history of seizures (30.8% vs. 1.6%; $p$<0.001) are also significantly associated with epilepsy. No significant differences were found in rates of malnutrition or stunting between the two groups.

**Table 1: Clinical features and cohort demographic information**

| Clinical and Demographic Characteristics | **Children with Epilepsy (%)** | **Children without Epilepsy (%)** | **P-Value** |
|---|---|---|---|
| Total number of kids | 39 (39.0) | 61 (61.0) | - |
| Girls | 25 (64.1) | 41 (67.2) | - |
| Boys | 14 (35.9) | 20 (32.8) | - |
| Median age of children | 44 months | 46 months | 0.78 |
| Range (in months) | 12 to 177 | 12 to 195 | - |
| IQR | 26 to 75 | 27 to 68 | - |
| Parental consanguinity | 6 (15.4) | 8 (13.1) | 0.65 |
| Socio-economic status | | | |
| Upper class | 15 (38.5) | 24 (39.3) | |
| Middle class | 10 (25.6) | 21 (34.4) | 0.18 |
| Lower class | 14 (35.9) | 16 (26.2) | |
| Microcephaly | 31 (79.5) | 39 (63.9) | <0.001 |
| Malnutrition | 25 (64.1) | 37 (60.7) | 0.79 |
| Stunting | 29 (74.4) | 40 (65.6) | 0.52 |
| Social quotient (<80) | 36 (92.3) | 41 (67.2) | <0.001 |
| History of Neonatal seizures | 14 (35.9) | 8 (13.1) | <0.001 |
| Family History of seizures | 12 (30.8) | 1 (1.6) | <0.001 |

Table 2 shows the causes of conditions in the children, comparing those with epilepsy to those without epilepsy. Syndromes of prenatal onset accounted for a total of 13 cases (13%), with slightly more children without epilepsy (6%) than with epilepsy (2%) associated with brain malformation conditions. Disorders of neonatal and perinatal onset were the most prevalent, comprising 92 cases (92%), with prematurity, intrauterine growth restriction (IUGR), and perinatal asphyxia being the leading causes, affecting both groups but more frequently those without epilepsy. For instance, IUGR alone contributed to 34% of the total cases, with 15% having epilepsy. Disorders of postnatal onset after the neonatal period were less common, representing 16% of the cases, with unclassifiable or unknown causes being the most frequent within this category (11%). Overall, children without epilepsy made up 78% of the cohort, while 43% had epilepsy, highlighting distinct distributions across aetiological categories.

| Table 2: Etiology of children in the cohort: a comparison between those with epilepsy and those without. | | | |
|---|---|---|---|
| Etiology | **No Epilepsy** | **Epilepsy** | **Total** |
| Disorders of Prenatal Onset | | | |
| Migration Disorders | 6 (6%) | 2 (2%) | 8 (8%) |
| Disorders of Organization | 1 (1%) | 1 (1%) | 2 (2%) |
| Other Disorders of Brain Malformation | 2 (2%) | 0 (0%) | 2 (2%) |
| | 1 (1%) | 0 (0%) | 1 (1%) |
| **Neonatal and Perinatal Onset Disorders** | | | |
| Prematurity | 22 (22%) | 8 (8%) | 30 (30%) |
| IUGR | 4 (4%) | 2 (2%) | 6 (6%) |
| Perinatal Asphyxia | 19 (19%) | 15 (15%) | 34 (34%) |
| TORCH Infection Sequelae | 1 (1%) | 1 (1%) | 2 (2%) |
| Perinatal Sepsis or Meningitis | 2 (2%) | 3 (3%) | 5 (5%) |
| Multiple Maternal Risk Factors | 3 (3%) | 1 (1%) | 4 (4%) |
| Perinatal Arterial Stroke | 1 (1%) | 0 (0%) | 1 (1%) |
| Neonatal Hyperbilirubinemia Sequelae | 8 (8%) | 2 (2%) | 10 (10%) |
| **Postnatal Onset Disorders (after Neonatal Period)** | | | |
| Unclassifiable or Unknown Etiology | 6 (6%) | 5 (5%) | 11 (11%) |
| Postnatal Non-Infectious Cause | 0 (0%) | 1 (1%) | 1 (1%) |
| Postnatal Infection - Meningitis, Encephalitis | 2 (2%) | 2 (2%) | 4 (4%) |
| Total | **78 (78%)** | **43 (43%)** | **100 (100%)** |

## Discussion

The analysis of demographic and clinical characteristics (Table 1) reveals significant differences between children with and without epilepsy in specific parameters, despite comparable gender distribution, median age, parental consanguinity, and socio-economic status. Microcephaly is markedly more prevalent among children with epilepsy, with 79.5% affected compared to 63.9% in the non-epileptic group ($p<0.001$). Similarly, a low social quotient (<80) is significantly more common in the epileptic group (92.3% vs. 67.2%; $p<0.001$). A notable association is seen between neonatal seizures and family history of seizures, where the prevalence in children with epilepsy (35.9% and 30.8%, respectively) is significantly higher than in those without epilepsy (13.1% and 1.6%, respectively, $p<0.001$). No significant differences were found in malnutrition or stunting rates. The ILAE 2017 categorization also included epilepsy types: 37% of children had focal seizures, 58% had generalized seizures, and 5% had both focal and generalized seizures. When included under epilepsy syndrome, they were categorized as developmental and epileptic encephalopathy. According to Zafeiriou et al., the distribution of children with cerebral palsy was comparable. Nonetheless, both focal and generalized seizures were taken into account in their investigation, along with seizures with secondary generalization [11]. Partial seizures were the most common (48.2%) in research by Mert et al., most likely because they included 42.9% of spastic hemiplegics in their analysis [12]. Just 39.3% of participants in another research by Gururaj et al. experienced partial seizures, while the remaining participants experienced different kinds of generalized seizures. The kind of CP was more important than the variable distribution [13].

According to population-based research done in Australia on 3466 CP infants born between 1996 and 2005, the frequency of epilepsy rose as the degree of motor impairment grew; it was lowest in diplegic patients (14%) and greatest in tetraplegic kids (53%) [14]. The Turkish study examined how coexisting morbidities affected the intellectual development of kids with cerebral palsy. The scientists verified that there is a statistically significant correlation between intellectual developmental level and epilepsy. Severe intellectual developmental impairment was present in 68% of epileptic individuals [15].

The aetiological comparison of the cohort (Table 2) indicates that perinatal and neonatal disorders constitute the most significant category, affecting 92% of cases. These conditions, including prematurity, intrauterine growth restriction (IUGR), and perinatal asphyxia, are more frequent in children without epilepsy, though IUGR also contributes substantially to the epileptic group. Prenatal onset disorders, such as brain malformations, are relatively rare, accounting for only 13% of cases, with slightly higher prevalence in the non-epileptic group. Postnatal onset disorders after the neonatal period, including infections and non-infectious causes, contribute to 16% of cases, with unclassifiable or unknown causes being most common within this category. The overall distribution highlights distinct aetiological patterns, with 78% of the total cohort comprising children without epilepsy, while 43% of the cohort has epilepsy. These findings underline the multifactorial

nature of epilepsy and the potential influence of perinatal and neonatal events. The primary cause of both epilepsy and cerebral palsy in our research was perinatal asphyxia (There were 99 kids with CP and 107 kids with CP without epilepsy). Neonatal hyperbilirubinemia (32 infants) and preterm (80 children) were the other significant causes. There were fewer prenatal reasons, such as TORCH sequelae, intrauterine growth restriction, perinatal arterial stroke, postnatal meningitis/sepsis, neonatal hypoglycemia, migrational and organizational problems, and others. Prematurity and prenatal asphyxia were the most prevalent aetiologies, according to other research conducted in underdeveloped nations [16]. However, according to Carlsson et al., The prevalence of epilepsy was higher in children with cerebral palsy, meningitis, and neurodevelopmental migrational and organisational disorders [17].

## Concussion

This study reveals a significant incidence of epilepsy in kids with CP (cerebral palsy), with neonatal seizures, low social quotient, microcephaly, and a family history of seizures being strong indicators. Perinatal asphyxia and intrauterine growth restriction (IUGR) were identified as the leading causes of both CP and epilepsy. Epilepsy in these children is primarily characterized by generalized seizures and a high incidence of drug-resistant epilepsy. The study also highlights the association between intellectual developmental delays and epilepsy in CP. Early diagnosis and intervention are crucial for improving outcomes, and further research is needed to optimize treatment strategies for this population.

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