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# Prevalence and risk factors for epilepsy in children with spastic cerebral palsy

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## Abstract

***Background*** Epilepsy in cerebral palsy (CP) is usually difficult to treat and can lead to poor prognosis due to increased risk for motor and cognitive disorders. The prevalence and risk factors of epilepsy in children with CP vary among studies.

***Objective*** To determine the prevalence and risk factors for epilepsy in spastic CP.

***Methods*** We performed a retrospective study using medical records of patients with spastic CP at the Departement of Child Health, Cipto Mangunkusumo Hospital from January 2003 until December 2008. Prevalence ratio was calculated by comparing the prevalence of epilepsy in subjects with and without risk factors. We excluded patients with metabolic disorder, genetic syndrome, and onset of CP after 3 years of age.

***Results*** Two hundred thirty six out of 238 spastic CP patients were analyzed. The mean age at diagnosis of spastic CP was 28.8 months. Male to female ratio was 1.4:1. The prevalence of epilepsy in spastic CP was 39%. The risk factors for epilepsy in spastic CP were central nervous system infection, the ocurrence of seizure in the first year of life, and abnormality of EEG.

***Conclusions*** The prevalence of epilepsy in spastic CP is 39%. The risk factors for epilepsy in spastic CP are post central nervous system infection, and ocurrence of seizure in the first year of life. **[Paediatr Indones. 2010;50:11-7]**.

***Keywords:*** *spastic cerebral palsy, epilepsy, risk factor*

Cerebral palsy (CP) is a permanent non-progressive brain damage occurring in early age which results in the disorders of brain development, position, muscle tone, motoric coordination, and other neurological manifestations.[1-2] The prevalence of CP in various countries is estimated around 2-2.5 for every live birth.[3] Generally, CP is classified into spastic, athetoid, ataxic, and mixed type,[4] among which the most common is the spastic type.[5-6]

Epilepsy is known to have a higher association with CP. It is usually difficult to control and increases the severity of motor and cognitive disorders making the prognosis worse.[7-8] Some risk factors are believed to be associated with CP such as low birth weight, neonatal seizures, seizure onset before 1 year old, family history of epilepsy, mental retardation, and abnormality on brain magnetic resonance imaging (MRI) or computed tomography scan (CT scan).[7]

The prevalence of epilepsy in children with CP ranged from 15 to 90%.[7] The studies of Ashwal et al[9] dan Sianturi et al[10] reported the prevalence of epilepsy

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of 36-62% and 37.3%. Epilepsy is more commonly found in the hemiplegia and quadriplegia spastic type.[11-12] This study aimed to find the prevalence and risk factors of epilepsy in children with CP in Cipto Mangunkusumo Hospital, Jakarta.

## Methods

This cross-sectional retrospective study was carried out at the Neurologic outpatient clinic of the Department of Child Health Cipto Mangunkusumo, Jakarta in February 2009. Subjects were all spastic CP patients registered at the hospital in 2003 to 2008. Children with inborn errors of metabolism, genetic syndrome, or onset of motor, posture, and tonus disorders after 3 years of age were excluded.

We obtain data from medical records which included the following variables: asphyxia, preterm gestational age, birth process, low birth weight, central nervous system (CNS) infection, neonatal seizure, onset of seizure before 1 year old, family history of epilepsy, head circumference, types of spastic CP, and abnormality of brain CT or MRI, and EEG abnormality.

Statistical analyses were done using the SPSS 15.0 for Windows. The prevalence ratio (PR) was calculated to compare the prevalence of epilepsy between subjects with and without a particular risk factor and was considered to have significant value if it was >1.5. This study was approved by the Ethics Committee of Medical School, University of Indonesia.

## Results

There were 238 spastic CP patients during the period of 2003-2008 in the Department of Child Health, Cipto Mangunkusumo Hospital Jakarta, but only 236 of them fullfilled the eligibility criteria. The mean age of the establishment of CP diagnosis was 28.8 months with a range of 7-60 months (**Table 1**).

Epilepsy was most frequently found in spastic hemiplegia CP (50%), followed by the spastic quadriplegia type (38%) and diplegia type (35.4%). General tonic clonic epilepsy was the most common type of epilepsy found in the subjects (68.5%), followed by myoclonic type (15.2%), partial complex (12%), and focal epilepsy (4.3%). The distribution of epilepsy types is shown in **Table 2.** Several risk factors were found to have significant association with the ocurrence of epilepsy in the subjects of this study (**Table 3**). They were CNS infection (PR 1.76; 95% CI 1.07 to 2.90), first onset of seizure before 1 year old (PR 3.43; 95% CI 2.04 to 5.75), and EEG abnormality (PR2.56; 95%CI 1.33 to4.96). Other risk factors could

**Table 1.** Subjects' characteristics

| Characteristics | Total (n=236) | % |
|---|---|---|
| Sex | | |
| Boy | 137 | 58.1 |
| Girl | 99 | 41.9 |
| Delivery process | | |
| Non-spontaneous | 40 | 16.9 |
| Spontaneous | 196 | 83.1 |
| Prematurity | | |
| Yes | 43 | 18.2 |
| No | 193 | 81.8 |
| Low birth weight | | |
| Yes | 50 | 21.2 |
| No | 186 | 78.8 |
| Head circumference abnormality | | |
| Yes | 197 | 83.5 |
| No | 39 | 16.5 |
| Types of spastic CP | | |
| Hemiplegia | 30 | 12.7 |
| Quadriplegia | 158 | 66.9 |
| Diplegia | 48 | 20.3 |
| Epilepsy | | |
| Yes | 92 | 39 |
| No | 144 | 61 |

**Table2.** The distribution of epilepsy in different types of CP

| Types of epilepsy | Types of spastic CP | | | Total (%) |
|---|---|---|---|---|
| | Hemiplegia | Quadriplegia | Diplegia | |
| Epilepsy | 15 (50%) | 60 (38%) | 17 (35.4%) | 92 (39%) |
| Focal (tonic/clonic) | 0 | 2 | 2 | 4 (4.3%) |
| Partial complex | 7 | 3 | 1 | 11 (12%) |
| Tonic Clonic | 7 | 46 | 10 | 63 (68.5%) |
| Myoclonic | 1 | 9 | 4 | 14 (15.2%) |
| No epilepsy | 15 (50%) | 98 (62%) | 31 (64,6%) | 144 (61%) |
| Total | 30 (100%) | 158 (100%) | 48 (100%) | 236 (100%) |

Table 3. Risk factors of epilepsy in children with spastic CP

| Risk factors | Spastic CP with epilepsy | Spastic CP without epilepsy | PR* | 95%CI** |
|---|---|---|---|---|
| Asphyxia (n=236) | | | | |
| Yes | 34 | 56 | 0.95 | 0.68-1.32 |
| No | 58 | 88 | | |
| Prematurity (n=236) | | | | |
| Yes | 12 | 31 | 0.67 | 0.40-1.12 |
| No | 80 | 113 | | |
| Delivery process (n=236) | | | | |
| Non-spontaneous | 16 | 24 | 1.03 | 0.67-1.56 |
| Spontaneous | 76 | 120 | | |
| Low birth weight (n=236) | | | | |
| Yes | 14 | 36 | 0.66 | 0.41-1.07 |
| No | 78 | 108 | | |
| CNS infection (n=196) | | | | |
| Yes | 67 | 79 | 1.76 | 1.07-2.90 |
| No | 13 | 37 | | |
| Neonatal seizure (n=219) | | | | |
| Yes | 15 | 13 | 1.33 | 0.90-1.95 |
| No | 77 | 114 | | |
| Onset of seizure ≤1 years old(n=219) | | | | |
| Yes | 79 | 61 | 3.43 | 2.04-5.75 |
| No | 13 | 66 | | |
| Family history of epilepsy (n=231) | | | | |
| Yes | 3 | 2 | 1.56 | 0.74-3.25 |
| No | 87 | 139 | | |
| Head circumference abnormality (n=236) | | | | |
| Yes | 73 | 124 | 0.76 | 0.52-1.10 |
| No | 19 | 20 | | |
| Type of spastic CP (n=236) | | | | |
| Hemiplegia | 15 | 15 | 1.41 | 0.84-2.38 |
| Quadriplegia | 60 | 98 | 1.07 | 0.69-1.65 |
| Diplegia | 17 | 31 | 1 | Reference |
| Brain CT scan/MRI (n=108) | | | | |
| Yes | 42 | 52 | 0.89 | 0.50-1.58 |
| No | 7 | 7 | | |
| EEG abnormality (n=108) | | | | |
| Yes | 77 | 13 | 2.56 | 1.33-4.96 |
| No | 6 | 12 | | |

*PR = prevalence ratio **95% CI = 95% confidence interval

not be proven to play a role in epilepsy occurring in our subjects, which were asphyxia, gestational age, operative delivery, low birth weight, neonatal seizures, head circumference abnormality, type of CP, family history of epilepsy, and abnormal brain CT or MRI (**Table 3**).

## Discussion

This was a retrospective study using data from medical records which unfortunately were not well-documented and became the main limitation of this study. Not all records contained data regarding a particular risk factor. Besides, the brain CT or MRI data were mostly without complete description of the results pointing to a specific lesion for epilepsy, only stated as normal or abnormal. Similar problems were also found with EEG results.

Preterm births, low birth weight, or non-spontaneous delivery process were not frequently found in this study (18.2%, 21.2%, and 16.9% of all subjects, respectively). This suggested that the predominant etiology of spastic CP found in this study was probably due to postnatal events.

The most common manifestation of spastic CP

found was head circumference abnormality (197 subjects or 83.5%). It suggested that the abnormality possibly happened after birth due to deleterious events before 3 years old when the brain development has not been completed. The most probable cause was CNS infection which was found in 74.5% of the subjects. The infection of CNS could cause either damage of brain mass resulting in microcephaly or obstruction of cerebrospinal fluid flow resulting in hydrocephalus.[13]

The most common type of CP found was the quadriplegia type, which caused the most severe motor disorders compared to other types. It involves all extremities and is associated with mental retardation as well as seizures due to relatively more massive brain damage compared to that of other types of CP.[2] In this study, the high prevalence of the quadriplegia type was in parallel with the high occurrence of CNS infection, which usually results in massive brain damage. Previous studies also found the spastic quadriplegia as the most common type of CP found.[7,10,14]

There were 92 of 236 (39%) spastic CP subjects who had epilepsy. This result was similar to the result found by Kulak et al who found 76 of 172 (44.2%) spastic CP children in their study suffered from epilepsy. Sianturi et al found a smaller frequency (30.2%) of epilepsy in the spastic CP children. This difference was maybe due to the smaller number of epilepsy found either in the spastic hemiplegia (20%) or the spastic quadriplegia (37.1%) CP subjects. In this study, epilepsy was found in 50% and 38% subjects with spastic hemiplegia and spastic quadriplegia CP, respectively.

Bruck et al[15] found a higher prevalence of epilepsy in spastic CP children (62%). This might be due to the higher number of epilepsy found in the spastic hemiplegia (70.6%) and spastic quadriplegia (66.1%) patients compared to this study. Other studies reported that spastic hemiplegia and spastic quadriplegia CP had the severest brain destruction resulting in a bigger possibility of developing epilepsy.[16,17] Another possible cause of the difference in prevalence was that almost 30% of subjects had not routinely visit the neurology clinic and they were lost to follow up before the clinical manifestation of epilepsy appeared.

Our series indicated that the most common type of epilepsy found was generalized tonic clonic epilepsy, i. e., 68.5% cases. This result may be associated with the high number of spastic quadriplegia found in this study that showed the most severe brain destruction. Previous studies also found 38-61% CP patients had generalized tonic clonic epilepsy.[2-3,5-6]

Every change occurring in the brain can be a risk factor to the development of epilepsy. Several risk factors that might be an etiology of epilepsy are central nervous system malformation, central nervous system infection, neurological impairment, neonatal seizure, seizure in the first year of life, history of epilepsy in the family, abnormal neuroimaging and EEG.[18]

Central nervous system infection is commonly found in developing countries and 30-50% cases will develop sequele. Several literatures stated that CP as a complication of central nervous system infection will significantly increase the risk of developing epilepsy.[19] Central nervous system infection was considered as a risk factor of epilepsy in CP children (PR 1.76; 95% CI 1.07 to 2.90). This result may be associated with the high incidence of central nervous system infection in Indonesia and the high proportion of subjects with central nervous system infection in the spastic CP with epilepsy (84%) in this study. Lagunju et al[19] also reported that central nervous system infection had a role in the development of epilepsy in CP.

Previous studies reported that seizure in the first year of life was a risk factor in the development of epilepsy. This was due to the vulnerability of the brain in this age group because it's still in a developing phase. Any insult to the brain in this phase will cause brain destruction. The risk of brain destruction increases if the seizure occured in a long period of time. In this study, seizure in the first year of life was considered a risk factor for epilepsy in spastic CP children (PR 3,43; 95% CI 2,04 to 5,75). Seizure in the first year of life was found in 86% spastic CP subjects with epilepsy. Kulak et al and Lagunju et al[19] also reported that seizure in the first year of life was a risk factor of epilepsy in CP children.

Epilepsy is a clinical disorder and diagnosis does not depend on EEG examination. Brain dysfunction does not always appear in EEG recording.[19-20] Kulak et al reported that abnormal EEG was not a risk factor in the development of epilepsy in children with CP. EEG examination in that study was performed in all subjects and 76 of 82 (92.7%) subjects in the CP group with epilepsy showed abnormal EEG. In this study, EEG examination was performed in 108 of 236 (44.8%)

spastic CP subjects and 77 of 83 (92.8%) subjects in the epilepsy group showed abnormal EEG. Although EEG data was not available in more than 20% subjects in this study, statistical analysis for this risk factor was still performed and showed that abnormal EEG was considered a risk factor for the development of epilepsy. Approximately 92.8% spastic CP subjects with epilepsy in this study had abnormal EEG but the abnormality found might not be specific for epilepsy. This could happened due to limited time spent in performing EEG examination so the specific feature for epilepsy might not appear.

We also found other risk factors such as asphyxia, prematurity, delivery process, low birth weight, neonatal seizure, abnormal head circumference, history of epilepsy in the family, subtype of spastic CP, and abnormal neuroimaging. However we could not proved these factors had a role in the development of epilepsy in spastic CP paients.

Asphyxia is a condition that could cause hypoxia, ischemia, and hypercapnia of the brain leading to brain destruction and will result in CP in the future, and if it involves certain area such as the cerebral cortex and temporal lobe, it will cause epilepsy.[21] We noted that there were 34 of 92 (37%) subjects with spastic CP and epilepsy had a history of asphyxia. This study could not prove the association of asphyxia and epilepsy in spastic CP children (PR 0.95; 95%CI 0.68 to 1.32). This may be due to the small number of asphyxia found in spastic CP with epilepsy group thus implicating that asphyxia tend to cause CP but not epilepsy. Kulak et al also found that asphyxia was not a risk factor for epilepsy in CP children.

Babies with intrauterine growth retardation have a higher risk of neurological problems and other morbidities compared to babies without intrauterine growth retardation.[22] In this study, prematurity and low birth weight was not proven to be associated with epilepsy in spastic CP children. This may be due to unclear information about history of intrauterine growth retardation in subjects with low birth weight and history of preterm delivery. This information was important because children with a history of intrauterine growth retardation had higher risk of neurological problem and other morbidities. Birth process in this study was also not proven to be a risk factor of epilepsy in spastic CP children. This result showed that prematurity, low birth weight, and non spontaneous birth process could not be a risk factor of epilepsy in spastic CP if it was presented alone.

Neonatal seizure increases risk of mortality and neurological sequele in neonates such as epilepsy. Studies reported that neonatal seizure was a risk factor of epilepsy in CP patients.[8,12] Study by Widiastuti et al[23] in 3 teaching hospitals in Jakarta found neonatal seizure mortality rate was 47.4%. The high mortality rate of neonatal seizure was associated with the severe neonatal clinical condition after birth. In this study, history of neonatal seizure was found in 15 out of 92 (16.3%) spastic CP subjects with epilepsy. This could not proven neonatal seizure as a risk factor for epilepsy in spastic CP children. This result may be associated with the high mortality rate of neonatal seizure in Indonesia.

History of epilepsy in the family increases individual risk of developing epilepsy. In countries where consanguinity is high, such as in Jordan, Turkey, and Pakistan, epilepsy genetic transmission is also high. History of epilepsy in the family in patients with CP will increase the risk of developing epilepsy.[24] In this study, history of epilepsy in the family was not proven to be a risk factor for epilepsy in spastic CP children. Kulak et al and Bruck et al[15] showed different result that may due to information bias about the history of epilepsy in the family in this study. This could happen because of the low education level of parents which causes limited knowledge of epilepsy.

Abnormal head circumference is caused by central nervous system malformation that could be detected from neuroimaging studies (CT scan or MRI).[14] Abnormal head circumference in this study was not proven as a risk factor for epilepsy in spastic CP children. In with subjects CP and epilepsy, 79.3% subjects had abnormal head circumference, but this could not be considered as a risk factor for epilepsy. Neuroimaging confirmation was still needed to confirm specific brain abnormality that caused epilepsy.

Epilepsy is mostly found in hemiplegia and quadriplegia spastic CP patients due to the cerebral cortex involvement and the more severe brain destruction. This study could not prove spastic hemiplegia and spastic quadriplegia CP subtype as a risk factor for epilepsy. This may be due to approximately 30% spastic CP patients in this study did not performed regular visits, especially the quadriplegia subtype, resulting in many lost to follow

up patients before epilepsy occured. Other possible causes for this result may be due to the different classification used for CP, not based on the degree of motoric dysfunction. Literatures stated that severe motoric dysfunction in a CP patients would increase the risk of developing epilepsy. Kulak et al[7] and Bruck et al[15] reported that severity of CP played a significant role in the development of epilepsy.

Neuroimaging studies in this study was performed in 108 of 236 (45.8%) subjects and 87% of them showed abnormality. In this study, abnormal neuroimaging was not proven to be a risk factor for epilepsy in spastic CP children which may be due to more than 20% subjects had no report of the neuroimaging result. However, it could be clinically important since 42 of 49 (85.7%) subjects with epilepsy had abnormality in brain imaging although detail descriptions of the abnormality were lacking.

In conclusion, the prevalence of epilepsy in children with spastic CP is 39%. Statistically significant risk factors of epilepsy in children with spastic CP are central nervous system infection, seizure in the first year of life and abnormality of EEG. Further study with cohort methods and multicenter study with more subjects is suggested to evaluate risk factors of epilepsy in spastic CP children.

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