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Risk factors of cerebral palsy in the perinatal period

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Abstract

Background Cerebral palsy is an irreversible yet preventable condition, thus it is necessary to know the risk factors of the disease. The potential risk factors that are found in the perinatal and neonatal period i.e. asphyxia, sepsis, very low birth weight, premature birth, and neonatal seizure. No available data for the risk factors of cerebral palsy in Indonesia.

Objective To identify the perinatal risk factors in cerebral palsy.

Methods We performed an age and sex-matched nested case-control study. The case group was children with cerebral palsy who were born at Sardjito Hospital during 1997-2005. The control group was selected from the same population as the case group. Risk factors during the perinatal period consisted of asphyxia, sepsis, very low birth weight, premature birth and neonatal seizure. Logistic regression was used to determine the association between risk factors and cerebral palsy.

Results Univariate analysis showed that the following factors were risk factors for cerebral palsy, i. e., asphyxia (OR 5.6, 95%CI 2.48; 12.53); premature birth (OR 4.5; 95%CI 1.55; 13.13); and neonatal seizure (OR 7.5, 95%CI 3.13; 18.03). On multivariate analysis risk factors associated with cerebral palsy were asphyxia (*a*OR 6.3, 95%CI 2.42; 16.66) and neonatal seizure (*a*OR 10.9,95%CI 4.03; 29.97).

Conclusion Asphyxia and neonatal seizure are significant risk factors of cerebral palsy in perinatal period **[Paediatr Indones 2008;48:175-9]**.

Keywords**:** *cerebral palsy, asphyxia, sepsis, very low birth weight, premature birth, neonatal seizure, perinatal risk factor.*

Cerebral palsy is a disorder characterized by abnormal motoric movement or body posture control, irreversible and non progressive brain damage. Such motoric disorders includes muscle tone alteration i.e. spasticity in most cases, uncontrolled movement, ataxia, and/or combination of those disorders.[1] Up until now, cerebral palsy is still the major cause of abnormality in children. The occurrence cerebral palsy varies about 2-3 per 1 000 live births. The incidence is higher in newborn with very low birth weight. The prevalence of cerebral palsy in developed countries, such as the United States is two per 1 000 live births, while in developing countries, such as Bangladesh, is as high as 70 per 1 000 live birth.[2]

In general, risk factors of cerebral palsy are divided into antenatal factors, perinatal/neonatal factors, and factors in the infancy. Meberg and Broch[3] reported that among 166 cases found in Norway during the 30-year period of 1970-99, the originetiology of cerebral palsy could be was classified as prenatal in 37 (22%), perinatal/neonatal in 78 (47%) and unclassified able in 51 (31 %) cases. Furthermore, Costello *et al.*[4] reported

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that 36% of term babies and 61% of preterm babies with cerebral palsy had perinatal risk factors.

Since perinatal risk factors accounted for significant proportion of cerebral palsy, assessment of the possible perinatal risk factors associated with cerebral palsy is important for planning further measures of prevention. Therefore, the aim of this study is to identify perinatal risk factors associated with cerebral palsy.

Methods

We conducted a sex and age-matched case-control study. The case group was children with cerebral palsy who were born at Sardjito Hospital within 1997-2005, who fulfilled the inclusion criteria. The control group was selected from the same population as the case group. Risk factor was defined as the factor that was capable to increase the risk of cerebral palsy during the perinatal period, i. e., asphyxia, sepsis, very low birth weight, premature birth, and neonatal seizure.

All children with the diagnosis of cerebral palsy who were born in Dr. Sardjito Hospital during 1997-2005 were selected as cases; they should have complete birth medical record, and without congenital abnormality. Sex and age-matched normal children who were born in Sardjito Hospital were recruited as controls. Logistic regression analysis was performed to determine the association between the five potential risk factors and the development of cerebral palsy.

Results

The total subjects of study was 138, consisting of 55% males and 44% females. The mean age of subjects was 6.1±1.7 years with the range of 2 to 8 8 years at the time of the recritment. **Table 1** showed characteristics of subjects; it shows that males significantly outnumbered females.

Univariate analysis showed that asphyxia (OR 5.6, 95%CI 2.48; 12.53), premature birth (OR 4.5, 95%CI 1.55; 13.13), and seizure in neonates (OR 7.5, 95%CI 3.13; 18.03) were associated with cerebral palsy. On the other hand very low birth weight was not significantly associated with cerebral palsy (OR 4.1, 95%CI 0.44; 2.64) . See **Table 2**.

Univariate analysis on risk factors of cerebral palsy in the perinatal period resulted that variables which had significance were asphyxia, premature birth, seizure in neonates and very low birth weight. The last variable, i.e. very low birth weight, was taken as one factor to be analyzed in the multivariate analysis because it had P<0.3. Furthermore, the four variables were included in the logistic regression of multivariate analysis. The results of logistic regression of multivariate analysis showed that seizure in neonates was the strongest risk factor to increase cerebral palsy in perinatal period in study population with aOR (adjusted Odds Ratio) 10.9

Table 1. Characteristic of the study subjects

Sex	Cases n = 46	Controls n = 92	Odds ratio (RO)	95%CI	P
Boys n (%)	34 (74)	43 (47)	1.6	1.19; 2.08	0.003
Girls n (%)	12 (26)	49 (53)			

Table 2. Risk factors associated with cerebral palsy

Variable	Case n = 46	Control n = 92	Odds Ratio (OR)	95%CI	P
Asphyxia, n (%)	23 (50)	14 (15)	5.6	2.48; 12.53	<0.001
Premature, n (%)	11 (24)	6 (7)	4.5	1.55; 13.13	0.04
Neonatal seizure n(%)	22 (48)	10 (11)	7.5	3.13; 18.03	0.001
Low Birth Weight n(%)	2 (4)	1 (1)	4.1	0.36; 46.86	0.26
Sepsis n (%)	9 (20)	17 (18)	1.0	0.44; 2.64	1.0

(95%CI 4.0; 29.9). Subsequently, asphyxia with aOR 6.3 (95% CI 2.4; 16.6). Premature birth and very low birth weight were not risk factors that increased cerebral palsy because P>0,05 (**Table 3**).

Cerebral palsy were potential to lead cerebral disorder as complication, the cerebral palsy complications found in this study were presented in **Table 4**.

The mental retardation data (n=13) in this study were obtained from the child's development record, the data were from children studying in special school other patients were not checked for the data. Diagnosis of strabismus was established through physical examination on child's eyes during home visit.

As additional results, the most frequent cause of seizure in neonates was hypoxia-ischemia encephalopathy (n=9; 41%) followed by hypoglycemia (n=5; 23%), hypocalcaemia (n=5; 23%), intracranial infection (n=2; 9%) and subdural bleeding (n=1; 4%). The delivery methods of the case group were caesarian section (n=2; 4%), vacuum extraction (n=12; 26%), buttocks extraction with Brach method (n=2; 4%), and normal delivery (n=30; 66%). There were 22 (48%) children with APGAR's score at the second five minutes less than seven. All children with caesarian section, vacuum extraction, and buttocks extraction with Brach method suffered from asphyxia with Apgar's score less than seven.

Discussion

In this study, asphyxia shows significant association and increases the risk of cerebral palsy (OR 5.6; 95%CI: 2.48;12.53; P<0,001). Probably, it is caused by the high prevalence of asphyxia in this study population. Dewi5 with the same population, i.e. children in Dr.Sardjito Hospital, reported the prevalence of neonatal asphyxia was 22.51%. It is higher than that estimated by International Guidelines for Neonatal Resuscitation 2000, which estimated that 5% to 10% of newborn in population need active resuscitation at the time of birth.[5] One possible explanation is the majority of asphyxia babies in Dr. Sardjito Hospital are referral cases (58.5%).[5]

Table 3. Risk factors of cerebral palsy

Variable	aOR	95%CI	P
Asphyxia	6.3	2.42; 16.66	<0.001
Neonatal seizure	10.9	4.03; 29.97	<0.001
Premature	3.0	0.75; 12.40	0.12
Low birth weight	3.3	0.18; 60.25	0.41

Table 4. Complications of cerebral palsy

Variable	n (%)
Impaired language and communication	24/46 (52)
Epilepsy	23/46 (50)
Mental retardation	13/46 (28)
Strabismus	3/46 (7)

The study of Murphy *et al*[7] reported that seizure in neonatal increased cerebral palsy occurrence (OR 10.0, 95%CI 4.1; 24.7). In this study, seizure in neonatal period was associated with less less occurrence of cerebral palsy compared with that observed e done by Murphy *et al*[7] (OR 7.5, 95%CI 3.1; 18.0; P<0,001).[6] The high odds ratio of seizure in neonatal in this study might be due to very high prevalence of asphyxia in this study and the most common etiology was hypoxia-ischemia encephalopathy, i.e. 41%. It was almost the same as that studied by Hill[8] that reported a significant association between occurrence of cerebral palsy and seizure in neonates with the etiology of hypoxia-ischemia encephalopathy (P<0,001).

Premature birth increases the risk of cerebral palsy occurrence.[7] Costello *et al*[4] reported that 36% of cerebral palsy in term babies and 61% in preterm babies was associated with perinatal risk of cerebral palsy.[4] Univariate analysis in this study shows that premature birth increases the risk of cerebral palsy as much as four times (OR 4.5, 95%CI 1.5; 13.1; P=0,5).

Sepsis and very low birth weight are not associated with cerebral palsy occurrence in this study population. Very low birth weight does not increase the risk of cerebral palsy in univariate analysis, it may be due to the sample size of very low birth weight in this study (n=2; 4%). Therefore, it is not eligible to be included in multivariate analysis (P<0.3 and OR>1).

Multivariate analysis was done on the four variables that significantly influenced cerebral palsy occurrence in this study. It was done to know the role of the four variables, asphyxia, premature birth, very low birth weight and seizure in neonates together on cerebral palsy occurrence. In multivariate analysis, the odds ratio of neonatal seizure is higher, i.e. 10.9 with 95%CI 4.03;29.97; and P value of <0,001. Logistic regression shows that asphyxia also increases the risk

of cerebral palsy as much as six times (OR 6.3, 95%CI 2.42; 16.66; P<0,001). Premature birth and very low birth weight are not the risk factors increasing cerebral palsy because the value of P>0,05. The ORs are as follow: premature birth OR 3.0 (95%CI 0.75; 12.40; P=0,12) and very low birth weight OR 3.3 (95%CI 0.18; 60.25; P=0.41).

Epilepsy is one of cerebral palsy complications. According to the previous studies, epilepsy occurs 12-90% in cerebral palsy occurrence.[1] Cerebral palsy and mental retardation in combination have association with the developing risk to become epilepsy.[9] The study of Bruck *et al*[10] reported a significant association between epilepsy and cerebral palsy (P<0.001; OR 13.00, 95%CI 2.35; 4.57). The etiology of cerebral palsy and epilepsy in the perinatal period were central nervous system infection (5%) and substantia alba damage (42%).[10] The epilepsy occurrence in this study is 50% (n=23).

The other cerebral complications are speaking and language disorders. Oral speaking is an oral communication mechanism, while language involves understand, processing, and production.[11] Various central nervous system and peripheral organ disorders can result in language and speaking perception, processing and production disorders. Speaking and language disorders can results from hearing disorder, mental retardation, autism, cerebral palsy and behavior and psychosocial deprivation disorders.[4] Speaking and language disorders in this study, in association with cerebral palsy, account for 52%.

The cause of mental retardation in cerebral palsy patients is a primarily cause by brain damage.[3] The highest rate is in slight and intermediate mental retardation patients.[3] As reported by Malin *et al*,[12] mental retardation occurrence in cerebral palsy patients accounted for 50-70%. Mental retardation with epilepsy in cerebral palsy children was differentiated into normal intelligence (27%, OR 1; P=0), slight mental retardation (24%, OR 3.31; P=0.01) and severe mental retardation (49%, OR 13; P<0.0001). Meanwhile, 30% of cerebral palsy patients have normal intelligence.[13] In this study, mental retardation in cerebral palsy patients accounts for 28% (n=13); P<0.001. The data was obtained from patients studying at a special school (Sekolah Luar Biasa). Because of the limitation of this study, intelligence assessment on the other cerebral palsy patients was not done.

Conclusion

Based on the hypothesis in this study, we conclude asphyxia and seizure in neonate are one of the risk factors of cerebral palsy, and seizure in neonates independent risk factors of cerebral palsy. We suggest to conduct further studies with sufficient samples (calculating the minimum sample size is 74), so that samples recruited are more representative.

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Conclusion

Based on the hypothesis in this study, we conclude that asphyxia and seizure in neonate are independent risk factors of cerebral palsy. We suggest to conduct further studies with sufficient samples (calculating the minimum sample size is 74), so that samples recruited are more representative.

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