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Original Article

Prenatal, Perinatal and Postnatal Risk Factors from Mother and Child to The Incidence of Epilepsy

Susan Megawati Sibuea, Endang Kustiowati, Maria Immaculata Widiastuti Samekto, Dodik Tugasworo, Aris Catur Bintoro, Elta Diah Pasmanasari

Department of Neurology, Medical Faculty of Diponegoro University / Central General Hospital of Kariadi Semarang, Indonesia

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Author Affiliation:
Department of Neurology,
Medical Faculty of Diponegoro University/
Central General Hospital of Kariadi Semarang,
Indonesia

Author Correspondence:
Susan Megawati Sibuea
Dr. Sutomo 16 street, Semarang,
Central Java 50244, Indonesia

E-mail:
susanmega2@gmail.com

Abstract

Background : Epilepsy is a health problem that affects sufferers and their families, characterized by at least two seizures without provocation with an interval of more than 24 hours between seizures, one seizure without provocation with the possibility of recurring within 10 years, a diagnosis of epilepsy syndrome has been established. The risk of epilepsy can be influenced by the condition of the mother and child in the prenatal, perinatal and postnatal periods. This study analyzed the risks of several prenatal, perinatal, and postnatal factors of mother and child as risk factors for epilepsy incidence.
Methods : A case control study was conducted at RSUP Dr. Kariadi Semarang from July 2022 to March 2023. A total of 90 eligible subjects were divided into 45 case with epilepsy and 45 control with a non-epileptic diagnosis. Inclusion criteria were aged over 17 years to 40 years and exclusion criteria were subjects with mothers who had died or could not be interviewed, data were incomplete and had structural brain disorders or other diseases with clinical symptoms of seizures for the control group. The data obtained were analyzed using chi squares test for bivariate association, followed by multivariate analysis with multiple logistic regression.
Results : Maternal age during pregnancy (p=0.016), low birth weight (p=0.007), surgical birth (p=0.004), head trauma at the age of less than 6 years (p=0.008) have been shown to influence the occurrence of epilepsy with significance respectively.
Conclusion : Prenatal factors of the mother which is maternal age during pregnancy, perinatal and postnatal factors of the child which are low birth weight, surgical birth, and head trauma at the age of less than 6 years are risk factors that influence the occurrence of adulthood epilepsy.

Keywords : Adulthood epilepsy, prenatal, perinatal, postnatal, risk factors.

INTRODUCTION

Epilepsy is one of the prominent health problems in society, because the problem is not only from a medical perspective but also from a social and economic perspective that affects subjects and their families. Epilepsy does not occur due to a single cause. There are several factors that can damage brain cells or interactions between brain cells.[1] The factors that have been widely studied are the perinatal conditions of individuals with epilepsy. However, another thing that needs to be investigated is the mother's factor during prenatal conditions. The medical condition of the mother influences the nature of the condition in utero (environment) which regulates brain development in the offspring that are born. When information about environmental is examined, it can provide important clues about how the mother's medical complications affect the developmental trajectory of the child's brain.[2]

METHODS

The research conducted was an analytic observational study using a case control design at RSUP Dr. Kariadi Semarang in the period July 2022 to March 2023. Research subjects were selected based on epilepsy (ICD-10 G40) and non-epilepsy diagnoses (ICD-10) obtained from medical records, then tracing was carried out on the patient's mother whether she had the risk factors being studied or not by telephone or home visit. This study involved 90 subjects, with 45 cases and 45 controls. The inclusion criteria for both groups were subjects with age 17–40 years old. Exclusion criteria for both groups were subjects whose mothers had died or could not be interviewed and data were incomplete, with additional criteria for control group of had structural brain disorders or other diseases with clinical symptoms of seizures (acute symptomatic seizure). Furthermore, interviews were conducted using a questionnaire with the subject's mother directly, by telephone or home visit to obtain research variable data. The data obtained were analyzed using univariate analysis for subjects characteristics, Chi-Square and Odd Ratio as bivariate analysis, and multiple logistic regression analysis as multivariate analysis.

RESULTS

This study involved 90 subjects who met the inclusion criteria, with 45 in case group and 45 control group. The characteristics of the research subjects were presented in Table 1.

In this study, the mean age in control group was older than the mean age of case group. There were more males than females in both case and control groups. The educational level of both groups were mostly senior high school. There was 1 case subject who was born to a grand multipara mother (number of parities > 4). There was no difference between the case and control groups, so it can be assumed that demographic characteristics were similar between two groups.

Table 2 showed that there was no difference in the mean age of the mother and the parity status of the mother between the case and control groups. Based on the age category of the mother during pregnancy, it was found that mothers with vulnerable age for pregnancy was more likely found in the case group. Based on statistical analysis, subjects born to mothers at a vulnerable age to get pregnant have 8.734 times higher risk of experiencing epilepsy.

A history of preeclampsia during pregnancy was only found in the case group. Mother was asked whether

TABLE 1
Demographic Characteristics of the subjects

		Epilepsy	Non epilepsy	*p*
Mean age (in years)		25.71 (6.43)	31.38 (5.682)	0.152
Gender; n (%)	Male	24 (53.3%)	24 (53.3%)	1.0
	Female	21 (46.7%)	21 (46.7%)	
Education level	Special school	3 (6.7%)	0 (0%)	0.13
	Elementary school	3 (6.7%)	1 (2.2%)	
	Junior high school	6 (13.3%)	4 (8.9%)	
	Senior high school	22 (48.9%)	20 (44.4%)	
	Diploma/bachelor	11 (24.4%)	20 (44.4%)	
Parity of subject's mother	≤ 4	44 (97.8%)	45 (100%)	1.0
	> 4	1 (2.2%)	0 (0%)	

TABLE 2
Characteristics of mother during pregnancy

Characteristics of mother		Group		*p*	OR
		Epilepsy	Non epilepsy		
Parity status	Parity 1–4	44 (97.8%)	45 (100%)	1.0	
	Parity ≥ 5	1 (2.2%)	0 (0%)		
Mean maternal age during pregnancy (in years)		27.8 (7.42)	28.89 (3.588)	0.87	
Categories of maternal age during pregnancy	20–35 years old	32 (71.1%)	43 (95.6%)	0.005	8.734
	<20, >35 years old	13 (28.9%)	2 (4.4%)		
Preeclampsia	No	33 (73.3%)	45 (100%)	0.01	2.364
	Yes	12 (26.7%)	0 (0%)		
History of systemic infection during pregnancy	No	38 (84.4%)	43 (95.6%)	0.160	
	Yes	7 (15.6)	2 (4.4%)		

TABLE 3
Characteristics of subjects at birth

Characteristics of subjects at birth		Epilepsy	Non epilepsy	*p*	OR
Gestational age at birth	Full term	40 (88.9%)	43 (95.6%)	0.431	
	Premature	5 (11.1%)	2 (4.4%)		
The process of birth	Normal	35 (77.8%)	43 (95.6%)	0.03	6.143
	With procedure	10 (22.2%)	2 (4.4%)		
Birth weight	Normal	33 (73.3%)	44 (97.8%)	0.03	16
	Low birth weight	12 (26.7%)	1 (6.5%)		
Asphyxia	No	37 (82.2%)	45 (100%)	0.01	2.216
	Yes	8 (17.8%)	0 (0%)		

there was high blood pressure started on second trimester accompanied by abnormal blood and urine examination which caused mother was hospitalized, or whether mother had been diagnosed with preeclampsia. There was no history of preeclampsia in the control group. Based on statistical analysis, subjects born to mothers with preeclampsia during pregnancy had a 2.364 times higher risk for experiencing epilepsy.

A history of maternal systemic infection during pregnancy was more common in the case group. Mother was asked whether mother had fever during pregnancy which led to inpatient with abnormal blood examination or whether mother had been diagnosed with infection during pregnancy. Based on statistical analysis, there was no difference between the case and control groups.

Table 3 showed that based on the category of maternal gestational age when the subjects were born, most of the subjects were born at term, and based on statistical analysis, there was no significant difference between the two groups.

Based on the category of birth process, most of subjects were born with normal delivery. Labor with procedure such as caesarean section (SC) and vacuum extraction were more common in the case group. There were no subjects with a history of birth with forceps extraction in both groups. Based on statistical analysis, subjects who were born with surgical or assisted deliveries had a 6.143 times higher risk of experiencing epilepsy.

Based on the category of birth weight, more subjects were born with low birth weight in the case group. Based on statistical analysis, subjects born with low birth weight have a 16 times higher risk for developing epilepsy.

Subjects who were born with asphyxia were only found in the case group. Mother was asked whether the

TABLE 4
Characteristics of patient at postnatal

Characteristics of patient at postnatal		Epilepsy	Non epilepsy	*p*	OR
History of head trauma (before seizure onset)	No	37 (82.2%)	44 (97.8%)	0.035	9.514
	Yes	8 (17.8%)	1 (2.2%)		
Neonatal infection	No	39 (86.7%)	45 (100%)	0,035	2.429
	Yes	6 (13.3%)	0 (0%)		

TABLE 5
Multiple logistic regression analysis on risk factors for epilepsy

Variable	*p*	Adjusted OR
Maternal age during pregnancy	0.016	1.149
Birth with procedure	0.007	15.854
Low birth weight	0.004	36.774
History of head trauma	0.008	36.656

patient did not cry immediately when he/she was born, had a slow breathing rate, pale or blue skin, or a history of intensive care immediately after birth. If the patient was born at home or midwife, there was a history of being referred to hospital for intensive care. There was no history of asphyxia in the control group. Based on statistical analysis, subjects born with asphyxia have a 2.216 times higher risk of experiencing epilepsy.

Table 4 showed that a history of head trauma which is a hard impact to the head or from a height of ± 1 meter which cause the patient to be hospitalized with or without impaired consciousness was more common in the case group. Based on statistical analysis, subjects who had a history of head trauma with a height of ± 1 meter have a 9.514 times higher risk of experiencing epilepsy.

A history of infection as a neonate obtained from mother which was characterized by fever that caused hospitalization or diagnosed with infection within the first four weeks of life was only found in the case group. There was no history of neonatal infection in the control group. Based on statistical analysis, subjects who had a history of neonatal infection were 2.429 times more likely experiencing epilepsy.

Table 5 showed that variables of maternal age during pregnancy, birth procedure, low birth weight, and history of head trauma partially (separately) influence the incidence of epilepsy. The most influence variable in this study was low birth weight, where subjects born with low birth weight had a 36.774 times greater risk for experiencing epilepsy later in life.

DISCUSSION

In this study, maternal parity status which was divided into non-grand multipara (parity 1–4) and grand multipara (parity ≥ 5) did not prove to be significant as a risk factor for epilepsy. This could be because of the total case and control subjects, there was only 1 subject who came from a mother with a parity of ≥ 5. This can be influenced by increased family awareness regarding family planning programs and the introduction of contraception. So now it is rare to find mothers with children ≥5.

Based on the age category of the mother, most of them are the age group of 20–35 years which is a safe age for pregnancy. In this study, subjects born to mothers at a vulnerable age for pregnancy, namely < 20 years and > 35 years, had an 8.734 times greater risk of experiencing epilepsy. Mothers who get pregnant at an older age often suffer from diseases such as hypertension, eclampsia, cervical cancer, diabetes and heart disease.[3] Hypertension, eclampsia, and diabetes may lead to various structural and functional changes of placenta and impaired vascularization during pregnancy, even leading to preterm birth and abortion. Heart disease affects the mother's strength to push during labor, which can lead to hypoxia or asphyxia to the baby. Cervical cancer can cause birth canal disturbances that cause prolonged labor and hypoxia to the baby. These conditions can lead to epileptogenesis.[3] At older age, the birth canal is less elastic than before, resulting in difficult and long labor. This is coupled with decreased strength of

mother to expel the baby due to age and concurrent comorbidities. This condition may cause asphyxia and/or experience birth trauma in the form of intracranial bleeding which can progress to epilepsy in the future.[4]

Based on bivariate analysis, pregnancy with preeclampsia is a risk factor for epilepsy. Bivariate analysis found that subjects born from mothers with preeclampsia have a tendency to experience epilepsy. However, after multivariate analysis, preeclampsia was not statistically significant as a risk factor for epilepsy. This could be due to several risk factors influencing one another in their contribution to the incidence of epilepsy. This effect is further reduced in multivariate analysis.

In this study a history of systemic infection in the mother during pregnancy was not proven to be statistically significant, either simultaneously or partially as a risk factor for epilepsy. This is not in accordance with cohort research previously by Whitehead E who followed the progress of the patient from 1986 to 2001, it was found that infection during pregnancy in the mother is a factor that increases the risk of developing epilepsy.

Bivariate analysis found that subjects born prematurely had a tendency to experience epilepsy. However, after multivariate analysis, premature birth was not statistically significant as a risk factor for epilepsy. This could be due to several risk factors influencing one another in their contribution to the incidence of epilepsy. This effect is further reduced in multivariate analysis. In this study, only 7 subjects were born prematurely. This is in accordance with research by Tri Budi Raharjo in 2007. Different with previous research by Wanling Li et al in 2019 which showed premature birth as a significant risk factor for epilepsy.[5] This result may be due to the fact that children born prematurely may still experience optimal brain development according to their age and have sufficient birth weight, thus indicating that organ development is viable enough, including the brain. Based on research by Yuelian Sun in 2007 it was found that among children who were born prematurely, only children who had lower birth weight below the 5th percentile Z score had higher incidence rate ratio of epilepsy than children with birth weight above the 15th percentile Z score.[6] In addition, this can also be influenced by the nutritional conditions given to subjects who were born prematurely, to catch up on brain development so that it can be optimal.[7]

Based on multivariate analysis, subjects who were born with a history of labor with action, either cesarean section or vacuum extraction have a 15.854 times higher risk of having epilepsy. These factors are related to prolonged labor and labor with action, and are thought to be related to cephalopelvic disproportion.[8] The incidence of seizures and encephalopathy is nearly double in infants born by vacuum extraction after >41 weeks gestation, compared with 39–41 weeks gestation. Mothers with dystocia can be assisted in delivery procedures, both vacuum extraction and SC, but babies born from vacuum extraction are exposed to higher risks, both in terms of duration and pressure (from the vacuum device) during the delivery process itself.[9]

Based on the multivariate analysis test, subjects who were born with low birth weight had a 36.774 times higher risk of experiencing epilepsy. Infants born with low birth weight may soon experience hypoxic ischemia and/or intraventricular haemorrhage, with clinical manifestations in the form of seizures. This situation, can develop into epilepsy later in life.[3]

The perinatal risk factor that was also studied was asphyxia. From the bivariate analysis it was found that subjects born with asphyxia have a tendency to experience epilepsy. However, after multivariate analysis, perinatal asphyxia was not statistically significant as a risk factor for epilepsy. This may be due to several risk factors influencing one another in their contribution to the incidence of epilepsy. This effect is further reduced in multivariate analysis. In this study, only 8 subjects were born prematurely. This is in accordance with research conducted by Supriadi, perinatal asphyxia is not significant as a risk factor for epilepsy.[10] This could be due to the bivariate analysis of several risk factors influencing each other in their contribution to the incidence of epilepsy.

Based on statistical analysis, a history of head trauma was a risk factor that can increase the risk of up to 10.884 times the incidence of epilepsy. The impact that is not significant gives sequelae in the form of scar tissue, which does not give early clinical symptoms but within 3–5 years it will become the focus of epilepsy.[11] Although the head injury is less severe, the chance of having an epileptic seizure is higher in children than in adults.[12]

Bivariate analysis found that subjects with a history of neonatal infection had a tendency to experience epilepsy. However, after multivariate analysis, neonatal infection was not statistically significant as a risk factor for epilepsy. This could be due to several risk factors influencing one another in their contribution to the incidence of epilepsy. This effect is further reduced in multivariate analysis. In this study, only 6 subjects were born prematurely.

This research has weaknesses, among others, there are possibilities recall bias because this study used a retrospective case-control design. In addition, there is limited information in medical records and not all respondents had medical records during pregnancy and childbirth.

CONCLUSION

In this study, it was found that the age of the mother during pregnancy, low birth weight, assisted birth, and head trauma at the age of <6 are risk factors for epilepsy

both simultaneously and separately. Therefore prenatal, perinatal and postnatal factors from mother and child together and individually have been proven as risk factors that influence the occurrence of epilepsy.

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