

Risk Factors of Behavioral Problems in Pediatric Epilepsy

Fadhilah Tia Nur¹⁾, Nurul Azmi²⁾, Bulan Kakanita Hermasari²⁾

¹⁾Department of Child Health, Faculty of Medicine, Universitas Sebelas Maret

²⁾Faculty of Medicine, Universitas Sebelas Maret

ABSTRACT

Background: Epilepsy is the most common neurological disorders in children and the number of case for epilepsy still increasing. Epilepsy can affect children and their growth physically, psychologically, and socially, yet the treatment of behavioral problems in pediatric epilepsy is still lacking. This study aimed to investigate the association of frequency of seizure, type of seizure, duration of illness, and use of antiepileptic drug with behavioral disorder in children with epilepsy.

Subjects and Method: This was an analytical observational study with a cross sectional design. The study was conducted at Pediatric Neurology Unit of Dr. Moewardi hospital, Surakarta, from September to October 2016. A sample of 50 pediatric patients with epilepsy was selected for this study. Parents or caregivers completed behavioral problems screening tool Pediatric Symptom Checklist-17 (PSC-17) and were interviewed about frequency of seizure, type of seizure, duration of illness, and

use of antiepileptic drug. The data were analyzed by a multiple logistic regression.

Results: Frequent seizure (OR= 3.09; 95% CI= 0.89 to 10.59; p= 0.068) increased behavioral problem. Being treated with ≥ 1 anti-epileptic drugs (OR= 1.58; 95% CI= 0.44 to 5.71; p= 0.521) increased behavioral problem, but it was statistically non-significant. Type of seizure (OR= 1.01; 95% CI= 0.32 to 3.20; p= 0.991) and duration of illness ≥ 1 year (OR= 1.03; 95% CI= 0.22 to 4.89; p= 1.000) were not associated with behavioural problem.

Conclusion: Frequent seizure increase behavioral problem

Keywords: epilepsy, behavioral problems, pediatrics

Correspondence:

Fadhilah Tia Nur. Department of Child Health, Faculty of Medicine, Universitas Sebelas Maret. Jl. Ir. Sutami 36 A, Surakarta 57126, Central Java. Email: fadhilah.harris@gmail.com

Cite this as:

Nur FT, Azmi N, Hermasari BK (2020). Risk Factors of Behavioral Problems in Pediatric Epilepsy. *Indones J Med.* 05(02): 162-169. <https://doi.org/10.26911/theijmed.2020.05.02.11>



Indonesian Journal of Medicine is licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License.

BACKGROUND

Every year, an estimated 2.4 million people are diagnosed with epilepsy. Recently, epilepsy cases in developed countries are around 30-60 per 100,000, while in developing countries the cases have doubled (World Health Organization, 2016). Most epilepsy cases commence in childhood particularly 40-50% of cases (Purba et al., 2008; PERDOSSI, 2012). The highest incidence of epilepsy was in the first 20 years of life, then decreased to the age of 50 years,

and again increased in the elderly (Ikawati, 2011; Pinzon, 2006).

Epilepsy also has an impact on children's growth including physical, mental and social development (de Boer, 2008). Behavioral disorders in people with epilepsy can be caused by demographic factors, neurological dysfunction, variables related to seizures, and the effects of anti-seizure drugs (Cornaggia, 2006).

Behavioral disorders in epilepsy can be grouped into several types in the form of

total behavioral disorders, internalization, externalization and attention (Freilinger, 2006). Of epilepsy sufferers of children with behavioral disorders, it turns out that only 33% get adequate management (Datta, 2005).

Study on children with epilepsy who experience behavioral problems has been carried out in Europe and America. In Indonesia, similar study is only conducted in Jakarta. In Surakarta, especially in the Dr. Moewardi hospital, there is still rare study on pediatric epilepsy associated with behavioral disorders. Therefore, the author examined the prevalence and risk factors for behavioral disorders in epilepsy patients of children aged 3-17 years.

SUBJECTS AND METHOD

1. Study Design

This was an analytic observational study with a cross sectional design. The study was conducted at the pediatric neurology clinic, Dr. Moewardi hospital, Surakarta, from September to October, 2018.

2. Population dan Sample

A total of 50 epilepsy patients aged 3-17 years was selected by purposive sampling.

3. Study Variables

The dependent variable was behavioral problem. The independent variables were seizure frequency, type of seizure, duration of epilepsy and treatment of epilepsy.

4. Operational Definition of Variables

Behavioral problems are categorized into three accordingly with research tools to detect behavioral disorders in the form Pediatric Symptom Checklist-17, namely: internalization disorders, disorders externalization, and attention disturbances. A child is called having behavioral disorders if from the internalization subscale score ≥ 5 , externalization score ≥ 7 , attention score ≥ 7 or the third number of subscales ≥ 15 (Manning, 2012).

Seizure frequency is the number of seizures in a period of time certain. In this study the frequency of seizures was divided into two groups, namely the frequency < 1 time per month in the last 12 months or no seizures for the past 12 months.

Type of seizure was broadly divided into two, namely: partial seizures and generalized seizures (ILAE, 1981).

Duration of epilepsy are broadly divided into two, namely: < 1 year and ≥ 1 year.

Treatment of epilepsy were broadly divided into two, namely: monotherapy and polytherapy.

5. Study Instruments

Parents or guardians of patients fill out informed consent and a behavioral disorder detection questionnaire in the form of Pediatric Symptom Checklist-17, and are interviewed about risk factors related to seizures.

The 17th Pediatric Symptom Checklist (PSC-17) has a high level of validity with a specificity of 0.68 and sensitivity of 0.95. The reliability of the PSC-17 is between 0.84 - 0.91. As time goes by, the classification of case or not cases ranged from 83% - 87% (Jellinek, 1998; Murphy, 1996). Questions on PSC-17 are categorized into internalization subscales consisting of five questions, the externalization subscale consisting of seven questions, and the attention subscale consisting of five questions. Each question has a score of 0 (never), 1 (sometimes), and 2 (often). The score for each subscale is summed, and in turn becomes the total score. The interpretation of PSC-17 is as follows, a child has a behavioral disorder when he gets scores ≥ 5 on the internalization subscale, scores ≥ 7 on the externalization subscale, ≥ 7 on the subscale of attention or total score ≥ 15 (Manning, 2012).

6. Data Analysis

The data were analyzed by bivariate by Chi-square to determine correlation between each independent variables on dependent variable.

7. Research Ethic

The research ethics include inside informed consent, identity confidentiality, and ethical clearance carried out in the Dr. Moewardi hospital, Surakarta.

RESULTS

There were 50 children with the youngest age of 3 years and the oldest 17 years. The average age of subjects was 10 years. Number of male and female proportion was equal. The most of parents had highest education as senior high school education (44%), followed by primary education or elementary - junior high school 30% and tertiary education 26%.

From 50 children, there were more subjects who did not have seizures during

the last 12 months or controlled seizures, as many as 18 patients (36%) compared to subjects with seizure frequency <1 times per month and ≥1 times per month for the last 12 months, each of 16 patients (32%).

Based on the type of seizure, subjects with general seizure types were 29 patients (58%) while the partial seizure types were 21 patients (42%). Subjects diagnosed with epilepsy more than one year ago from the time of the study were carried out far more, namely 42 patients (84%) compared to those diagnosed less than one year, namely 8 patients (16%). When subjects were viewed from pharmacological therapy, those with monotherapy amounted to 37 patients (74%) while polytherapy amounted to 17 patients (26%).

Bivariate analysis of seizure frequency, type of seizure, duration of epilepsy, and antiepileptic drugs correlated with behavioral disorders were described in Table 1.

Table 1. Bivariate analysis of seizure frequency, type of seizure, duration of epilepsy, and antiepileptic drugs correlated with behavioral disorders

Independent Variable	PSC positive		PSC negative		OR	95% CI		p
	n	%	n	%		Lower limit	Upper limit	
Seizure frequency								
Seizure ≥1 time per month (last 12 months)	9	56.3	7	43.8	3.09	0.90	10.59	0.068
No seizure in last 12 month	10	29.4	24	70.6				
Type of seizure								
Partial	8	38.1	13	61.9	1.01	0.32	3.20	0.991
General	11	5.3	18	94.7				
Duration of epilepsy								
≥ 1 year	16	38.1	26	61.9	1.03	0.22	4.89	1.000
<1 year	3	37.5	5	62.5				
Antiepileptic drugs								
Polytherapy	6	46.2	7	53.8	1.58	0.44	5.71	0.521
Monotherapy	13	35.1	24	64.9				

Table 1 showed that seizure ≥1 time per month in the last 12 months increased the risk of PSC 3 times higher than no

seizure in the last 12 months (OR= 3.09; 95% CI= 0.90 to 10.59; p= 0.068).

Table 1 showed that there was no difference of type of seizure on PSC (OR= 1.01 ; 95% CI= 0.32 to 3.20; p= 0.991).

Table 1 showed that there was no difference of duration of epilepsy on PSC (OR= 1.03; 95% CI= 0.22 to 4.89; p= 1.000).

Polytherapy antiepileptic drugs increased PSC, but it was statistically non-significant (OR= 1.58; 95% CI= 0.44 to 5.71; p= 0.521).

DISCUSSION

The frequency of seizures often became a very influential factor in the occurrence of behavioral disorders in children with epilepsy. This study had subjects with high controlled seizures of 18 patients (36%) and rarely or <1 times a month in seizure frequency and frequency frequently or ≥ 1 times a month during the last 12 months, i.e. 16 patients (32%). In bivariate analysis, the author used the rare frequency of seizures and controlled seizures to be a variable (OR= 3.09; p= 0.068). The risk of behavioral disorders 3.09 times greater in children with frequent seizures compared to children with infrequent seizure frequency and controlled seizures.

The insignificant results in seizure frequency are often in line with previous studies conducted by Rodenburg (2006) and Caplan (2004), which were carried out by behavior disorder screening tools in the form of the Child Behavior Checklist (CBCL). Most of the studies on seizure frequency associated with behavioral disorders in pediatric epilepsy patients have not been significant according to a systematic review of the journal 30 years back by Austin and Caplan (Austin, 2007). This could be because seizures actually did not cause behavioral disturbances, but the presence of neurological abnormalities could cause seizures and behavioral dis-

orders (Dunn, 2003). In contrast, a study conducted by Lavina et al. (2015), found a correlation between frequent seizures and behavioral disorders but with simpler operational definitions and subjects with small behavioral disorders.

Types of seizures are divided into two major groups, namely general seizures and partial seizures. General seizures in the data of this study were 29 subjects (58%) and partial seizures as many as 21 subjects (42%). This study found no association between the type of partial seizure and behavioral disorders and there was no difference in the risk of behavioral disorders in the type of partial or general seizures.

Study on the type of seizure had inconsistent results. Some studies suggested that partial or focal seizures were associated with behavioral disorders in pediatric epilepsy patients (Austin, 2007; Oostrom, 2005). A study in Indonesia, the same was stated by Novriska, Sutomo and Setyati (Novriska, 2014). In contrast, Ott et al. stated that there were no differences in behavioral disorders on Central Partial Seizures (CPS) with Primary Generalized Epilepsy (PGE) (Otto, 2003). Patients with CPS had a tendency to have psychiatric disorders in the form of depression, while PGE patients tend to have psychiatric disorders in the form of anxiety (Caplan, 2005).

Inconsistent results in this type of seizure were caused by several things. First, there were weaknesses in the study including a small number of samples with various types of seizures. Second, it was suspected that demographic factors, namely the last education of parents who were low and middle, caused a bias of subjectivity. Actually in this study, efforts had been made to minimize bias by excluding patients with mental retardation, develop-

mental delay and behavioral disorders before seizures were diagnosed.

The duration of the seizure in this study was mostly 42 patients (84%) ≥ 1 years, while 8 patients (16%) had < 1 year epilepsy. There was no relationship between the duration of seizures and the disruption of behavior in pediatric epilepsy patients. OR= 1.03 means that there was no difference in the risk of behavioral disturbances in patients with long-standing seizures ≥ 1 year with < 1 year.

The relationship between duration of suffering from a longer seizure and a behavioral disorder was insignificant in accordance with previous studies (Lavina, 2015; Novriska, 2014). Long duration of epilepsy affected low IQ, poor learning ability and linguistic limitations, but had no effect on behavioral disorders (Adewuya, 2006; Buelow, 2003; Caplan, 2006).

However, Datta et al (2005) found the opposite. This could be due to the operational definition of the variable, where the definition of Datta et al regarding the duration of seizures was < 3 years and ≥ 3 years (Datta, 2005). The author suspected that the longer time span could affect the results to be significant.

Epilepsy treatment factors influenced the occurrence of behavioral disorders in pediatric epilepsy patients. Treatment of epilepsy using more than one type of drug or polytherapy was thought to be a factor in the occurrence of behavioral disorders. In this study, there were 17 patients (34%) with polytherapy while the rest were monotherapy. There was no relationship between treatment of polytherapy and behavioral disorders. Besides that, patients with polytherapy treatment had a risk of experiencing behavioral disorders 1,582 times compared to patients with monotherapy.

Polytherapy treatment with behavioral disorders had no significant relationship

according to previous study conducted by Novriska, Sutomo and Setyati (Novriska, 2014). However, previous studies conducted by Lavina et al. (2015) and Oostrom et al. (2003). A retrospective study found that many antiepileptic drug exposures were associated with the occurrence of cognitive and behavioral disorders (Harbord, 2000). Polytherapy treatment was associated with cognitive and linguistic disorders, thought to be indirectly related to behavioral disorders (Caplan, 2006; Austin, 2007). Anti-epileptic drugs that could cause behavioral disorders were still debated due to the influence of many other factors, namely cerebral lesions, seizure age, seizure etiology, seizure frequency and duration of epilepsy (Bourgeois, 2004)

Based on the results of this study, it can conclude that there was no significant relationship between seizure frequency, type of seizure, duration of epilepsy and treatment of epilepsy with behavioral disorders. The frequent seizure frequencies had a risk of 3.086 times greater behavioral problems than those who were rarely or controlled seizures. Polytherapy treatment had a risk of 1.58 times greater behavior disorder than monotherapy.

AUTHOR CONTRIBUTION

Fadhilah Tia Nur, Nurul Azmi, and Bulan Kakanita Hermasari collected the data, measured resistin level, examined clinical changes, did data analysis, and wrote the manuscript.

CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

FUNDING AND SPONSORSHIP

No external funding and sponsorship

ACKNOWLEDGEMENT

We would like to thank to Dr. Moewardi Hospital that give permission to collect the data.

REFERENCE

- Adewuya AO, Oseni SBA, Okeniyi JAO (2006). School performance of Nigerian adolescents with epilepsy. *Epilepsia*, 47(2):415-20. <https://doi.org/10.1111/j.1528-1167.2006.00437.x>
- Austin J, Caplan R (2007). Behavioral and psychiatric comorbidities in pediatric epilepsy: Toward an integrative model. *Epilepsia*, 48(9): 1639-1651. <https://doi.org/10.1111/j.1528-1167.2007.01154.x>
- Bourgeois BFD (2004). Determining the effects of antiepileptic drugs on cognitive function in pediatric patient with epilepsy. *J Child Neurol*. 19(1): 15-42. <https://doi.org/10.1177/088307380401900103>
- Buelow JM, Austin JK, Perkins S, Shen J, Dunn D, Fastenau P (2003). Behavior and mental health problems in children with epilepsy and low IQ. *Dev Med Child Neurol*. 45(1): 683 – 692. <https://doi.org/10.1017/s0012162203001270>
- Caplan R, Siddarth P, Gurbani S, Oh D, Sankar R, Shields WD (2004). Psychopathology and pediatri complex partial seizures: seizure-related, cognitive, linguistic, variables. *Epilepsia*, 45(10): 1273-1286. <https://doi.org/10.1111/j.0013-9580.2004.58703.x>
- Caplan R, Siddarth P, Gurbani S, Hanson R, Sankar R, Shields WD (2005). Depression and anxiety disorders in pediatric epilepsy. *Epilepsia*. 246(5): 720 – 730. <https://doi.org/10.1111/j.1528-1167.2005.43604.x>
- Caplan R, Siddarth P, Gurbani S, Lanphier E, Koh S, Sankar R (2006). Thought disorder: a developmental disability in pediatric epilepsy. *Epilepsy behave*. 8(4): 726 – 735. <https://doi.org/10.1016/j.yebeh.2006.03.009>
- Cornaggia CM, Beghi M, Provenzi M, Beghi E (2006). Correlation between cognition and behavior in epilepsy. *Epilepsia*, 47(2): 34 – 9. <https://doi.org/10.1111/j.1528-1167.2006.00685.x>
- Datta S, Premkumar T, Chandy S, Kumar S, Kirubakaran C, Gnanamuthu C, Cherian A (2005). Behaviour problems in children and adolescents with seizure disorder: associations and risk factors. *Seizure*, 14(3): 190-197. <https://doi.org/10.1016/j.seizure.2005.01.007>
- deBoer HM, Mula M, Sander JW (2008). The global burden and stigma of epilepsy. *Epilepsy Behav*. 12(4):540-6. <https://doi.org/10.1016/j.yebeh.2007.12.019>
- Dunn D, Austin J, Caffrey H, Perkins S (2003). A prospective study of teachers' ratings of behavior problems in children with new onset seizures. *Epilepsy Behav*, 4(1): 26 – 35. [https://doi.org/10.1016/s1525-5050\(02\)00642-x](https://doi.org/10.1016/s1525-5050(02)00642-x)
- Freilinger M, Reisel B, Reiter E, Zelonko M, Hauser E, Seidl R (2006). Behavioral and emotional problems in children with epilepsy. *J Child Neurol*. 21(11): 939 – 45. <https://doi.org/10.1177/08830738060210110501>
- Harbord MG (2000). Significant anticonvulsant side-effects in children and adolescent. *J Clin Neurosci*, 7(3): 213 – 216. <https://doi.org/10.1054/jocn.1999.0190>
- Ikawati Z (2011). *Epilepsi, Dalam Farmakoterapi Penyakit Sistem Saraf Pusat*. Yogyakarta: Bursa Ilmu.
- Jellinek MS, Murphy JM, Robinson J, Feins A, Lamb S, Fenton T (1988). *Pediatric*

- symptom checklist: Screening school-age children for psychosocial dysfunction. *112*(2):201-9. [https://doi.org/10.1016/s0022-3476\(88\)80056-8](https://doi.org/10.1016/s0022-3476(88)80056-8)
- Lavina A, Widodo DP, Nurdadi S, Tridjaja B (2015). Faktor faktor yang mempengaruhi gangguan perilaku pada anak epilepsi. *Sari Pediatri*, *16*(6): 410-4. <https://dx.doi.org/10.14238/s-p16.6.2015.409-15>
- Manning AR (2012). Screening, Improving the Utility of the Pediatric Symptom Checklist for Mental Health. Charleston: BiblioBazaar.
- Murphy JM, Ichinose C, Hicks RC, Kingdon D, Crist-WhitzeL J, Jordan P, Feldman G and Jellinek MS (1996). Utility of the Pediatric Symptom Checklist as a psychosocial screen to meet the federal Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) standards: A pilot study. *J Pediatr*. *129*(6): 864-9. [https://doi.org/10.1016/s0022-3476\(96\)70030-6](https://doi.org/10.1016/s0022-3476(96)70030-6)
- Novriskita D, Sutomo R, Setyati S (2014). Behavioral problems in children with epilepsy. *Pediatrica Indonesian*, *54*(2): 326. <https://doi.org/10.14238/pi54.6.2014.324-9>
- Oostrom KJ, Smeets-Schouten A, Kruitwagen CLJJ, Peters ACB, Jennekens-Schinkel A, Dutch Study Group of Epilepsy in Childhood (2003). Not only a matter of epilepsy: early problems of cognition and behavior in children with “epilepsy only” a prospective, longitudinal, controlled study starting at diagnosis. *Pediatrics*. *112*(6 Pt 1): 1338-44. <https://doi.org/10.1542/peds.112.6.1338>
- Otto D, Siddarth P, Gurbani S, Koh S, Tournay A, Shields W, Caplan R (2003). Behavioral disorders in pediatric epilepsy: Unmet psychiatric need. *Epilepsia*, *44*(4): 591-597. <https://doi.org/10.1046/j.1528-1157.2003.25002.x>.
- Perhimpunan Dokter Spesialis Saraf Indonesia (2012). Penegakan Diagnosis pada Penderita Epilepsi. Jakarta: PERDOSSI.
- Pinzon R (2006). Karakteristik Epidemiologi Onset Anak-Anak; Telaah Pustaka Terkini. Jakarta: Dexa Media.
- Purba J, S Wahyuni, M Nasution, W Daulay (2008). Asuhan Keperawatan pada Klien dengan Masalah Psikososial dan Gangguan Jiwa. Medan: USU Press.
- Rodenburg R, Meijer A, Decovic M, Aldencamp A (2006). Famili predictors of psychopathology in children with epilepsy. *Epilepsia*, *47*(3): 601-614. <https://doi.org/10.1111/j.1528-1167.2006.00475.x>
- World Health Organization (2016). Epilepsy. 2016. Retrieved from: <http://www.who.int/mediacentre/factsheets/fs999/en/>