

Study of the Determinant Factors in Seizure Following Gastroenteritis in Children Admitted in Tabriz Children's Hospital during 2001 to 2016

Iman Vafaei¹, Mohammadamin Rezazadehsaatlou², *Babak Abdinia¹, Mohamad Khaneshi³, Reshad Hasanpour³, Farshad Panje³, Zakieh Ebadi¹

¹Pediatric Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

²Tuberculosis and Lung Disease Research Center, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Eastern Azerbaijan, Iran.

³Medical Faculty, Tabriz University of Medical Sciences, Tabriz, Iran.

Abstract

Background: One of the common side effects of gastroenteritis in children is seizure, which is one of the causes of fever, electrolyte disturbances, and meningitis. This study was aimed to investigate the determinant factors in seizure in children with gastroenteritis and seizure admitted in Tabriz Children's Hospital from 2001 to 2016.

Materials and Methods: This is a descriptive study. The study population included all children admitted with diagnosis of gastroenteritis and seizure in Tabriz Children's Hospital during the years 2001 to 2016. The data of admitted patients including electrolyte disturbances, age, gender, blood-venous analysis, Blood urine nitrogen (BUN), and creatinine tests were extracted from hospital records by a resident and intern of this hospital using a questionnaire designed for this research.

Results: A total of 84 patients were included in the study. The patients included 44 males (52.4%) and 40 females (47.6%). The mean age of the patients was 9.31 ± 7.13 years. Forty-six (55.42%) patients suffered from electrolyte impairment, 24 of which (52.2%) were male and 22 (47.8%) were female; and hyponatremia was the most common disorder (24.10%). Accordingly, only BUN of has proven to be a strong predictor of the likelihood of seizure; also despite of non-significant p-value of PH, it had a potentially strong association with seizure.

Conclusion

According to the results of this study, electrolyte impairment is fairly common in children with acute gastroenteritis. Education about the management of children with seizure to is an important factor in this regard.

Key Words: Children, Gastroenteritis, Seizure.

*Please cite this article as: Vafaei I, Rezazadehsaatlou M, Abdinia B, Khaneshi M, Hasanpour R, Panje F, et al. Study of the Determinant Factors in Seizure Following Gastroenteritis in Children Admitted in Tabriz Children's Hospital during 2001 to 2016. *Int J Pediatr* 2017; 5(12): 6439-46. DOI: **10.22038/ijp.2017.26753.2305**

*Corresponding Author:

Dr. Babak Abdinia, Associate Professor, Pediatric Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran. Tel: 0098-41-35262280.

Email: babdinia@yahoo.com

Received date: Aug.14, 2017; Accepted date: Sep.12, 2017

1- INTRODUCTION

Gastroenteritis is a digestive tract infection that can be due to the viral and bacterial factors, the most common symptoms include diarrhea and vomiting, which can be accompanied by fever and abdominal pain (1-3). Diarrhea has a high contribution to the death of infants (9%), which accounts for about 71% of the million deaths per year in the world (4, 5). An average of 1.66 billion deaths occurred in 2014 in infants below the age of 5 years old in developed countries, of which about 80% were in Africa, South Asia, and Middle East (6). Gastroenteritis can be found in healthy infants without any association with diseases such as meningitis, encephalitis, and encephalopathy (7). Mostly Gastroenteritis occur in the winter and early spring, and the most common cause for this is rotavirus (8).

In children, the daily water exchange rate is much higher than adults, as well as the incomplete kidney development in children, which results in more extracellular fluid, so water and electrolyte disturbances in children are more dangerous than adults (5, 8, 9). The most important complication of gastroenteritis in children is seizure, which is one of the causes of fever, electrolyte disturbances, meningitis and sometimes toxins (4, 9). Electrolyte disturbances such as hyponatremia, hypernatremia and hypocalcemia are the major cause of seizures in these children (9-11). However, in many cases, seizures followed by gastroenteritis without electrolyte disturbances and abnormalities in Electroencephalogram (EEG) (12). In some cases, seizures followed by gastroenteritis without fever which is not necessarily febrile seizure due to the gastroenteritis (12, 13). Various spectrums of benign convulsions or epileptic syndromes may develop in infants and pediatrics (12, 13). Seizure is one of the

most common problems in children and occurs due to various factors that are common in the ages of 9 months old to 5 years old, but it mainly occurs at the age of 14 months to 18 months, and often can be associated with fever and seizures which is related with good prognosis (11, 13-15). The most common causes of fever in this type of seizure can be: acute infections of the respiratory tract, acute otitis media, and gastrointestinal tract infections and urinary tract infections (5, 8, 15). On the other hand, in children having seizures without fever the assessments to carry out in order to find the causes of such metabolic diseases and infectious and cerebral anomalies, which can be used to evaluate patient's prognosis (2, 11, 14, 16).

Considering the high prevalence of gastroenteritis in children (4), the complications caused by this disease (6), which is involved in the morbidity and morbidity of the disease, especially the seizure following gastroenteritis, is very important. One of the most important measures is to determine the prevalence of these complications for planning preventive measures. The aim of this study was to investigate the determinant factors in seizure in children with gastroenteritis and seizure admitted in Tabriz Children's Hospital from 2001 to 2016.

2- MATERIALS AND METHODS

2-1. Method

The study is an epidemiological descriptive-analytic epidemiologic study based on hospital records. The study population included all children admitted with diagnosis of gastroenteritis and seizure in Tabriz Children's Hospital during the years 2001 to 2016. This study was approved by local Medical Ethical Committee of Tabriz University of Medical Sciences which was in compliance with Helsinki declaration. Also, all patients' information remained confidential.

Exclusion criteria were: the presence of underlying illness or the use of drugs that can cause electrolyte impairment (including kidney, endocrine, heart disease, diuretic use and, and absence of seizure, etc.). Since, Dehydration caused by diarrhea usually is mild and laboratory tests have no derangement in electrolyte levels. Consequently, initial laboratory tests such as serum glucose, blood urea nitrogen, creatinine, and electrolytes, are required in order to assess the degree of dehydration and to differentiate the convulsion with mild gastroenteritis from other type of seizures; accordingly (6), type of electrolyte disturbances (Na, K, BUN, Cr, VBG, BS, Ca, CBC, CRP), age, gender, seizure, and mortality, were recorded from patients hospital records using a designed questionnaire.

2-2. Statistical analysis

Quantitative data were presented as mean \pm standard deviation (SD), and qualitative data were demonstrated as frequency and percent. To analyze the data for the analysis of descriptive statistical methods including frequency distribution tables, graphs and numerical indices were used to describe the variables in question. Statistical analysis was performed using the version 22.0 of SPSSTM statistical software (SPSS Inc., Chicago, IL, USA). In this study $P < 0.05$ was considered statistically significant.

3- RESULTS

A total of 100 children with diagnosis of gastroenteritis associated with seizure were

admitted to Tabriz Children's Hospital during the 2001 to 2016 was studied. Sixteen cases were excluded based on exclusion criteria and 84 patients were enrolled in the study. The patients consisted of 44 boys (52.4%), and 40 girls (47.6%). The mean age of study was 9.31 ± 7.13 years. The mean weight was 11.64 ± 5.33 kg. Forty-six (55.42%) patients suffered from electrolyte impairment, 24 of which (52.2%) were male and 22 (47.8%) were female. Hyponatremia was the most common disorder (24.10%), and the frequencies of other problems were hypernatremia in 9 (10.44%) cases, hyperkalemia, in 16 (19.28%) cases, hypocellular in 1 (1.20%) cases. Acidosis and alkalosis were found in 25 patients (37.88%), and 7 (10.61%) patients, respectively (**Table.1**).

The mean incidence of epilepsy was 0.14 ± 0.35 . The mean of sodium was 136.74 ± 4.20 (mmol/L) and the mean of potassium was 4.44 ± 0.50 (mmol/L); also the mean of calcium was 4.63 ± 4.60 (mg/dL). Mean of creatinine in patients was $0.58 \pm 0/14$ (mg/dL). Mean BUN was 25.28 ± 8.08 (mmol/L). The mean PH was 7.36 ± 0.74 .

Using the regression logistic statistical test, among the examined biomarkers and electrolytes, only BUN has proven to be a strong predictor of the likelihood of seizure ($p = 0.02$, Odds Ratio: 1.31, Z-value: 1.31) (**Figures.1, 2**); although PH had a non-specific p-value, but it had a strong association with seizure (P-value: 0.19, Odds Ratio: 0.85, Z-value: -2.29) (**Figures.1, 3**).

Table-1: Frequency of electrolytes impairment

| Electrolytes impairment | Percent |
|-------------------------|---------|
| Hypokalaemia | 1.20 |
| Hyperkalemia | 19.28 |
| Hypnotherapy | 24.10 |
| Hypernatremia | 10.84 |
| Acidosis | 37.88 |
| Alkalosis | 10.61 |

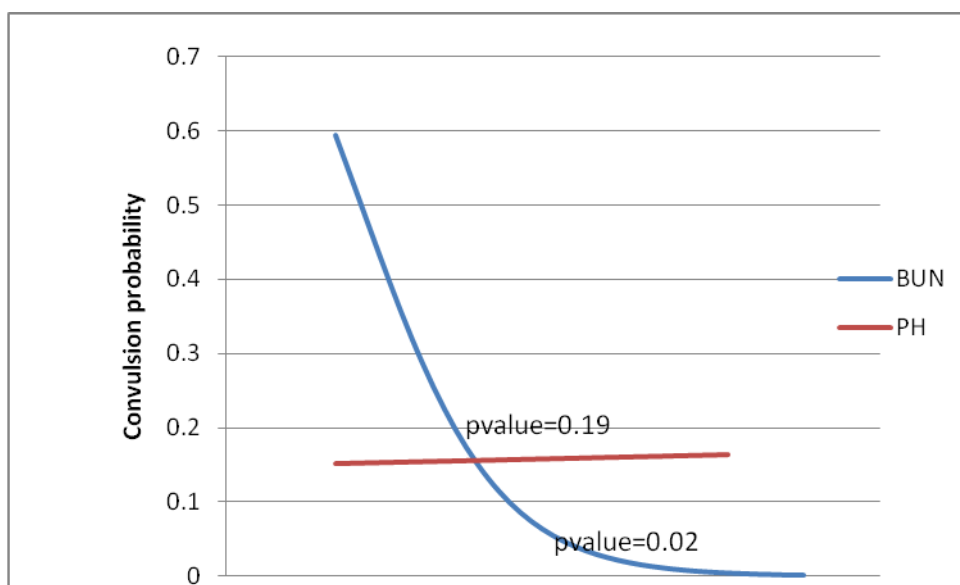


Fig.1: predicting the likelihood of seizure using serum BUN and PH.

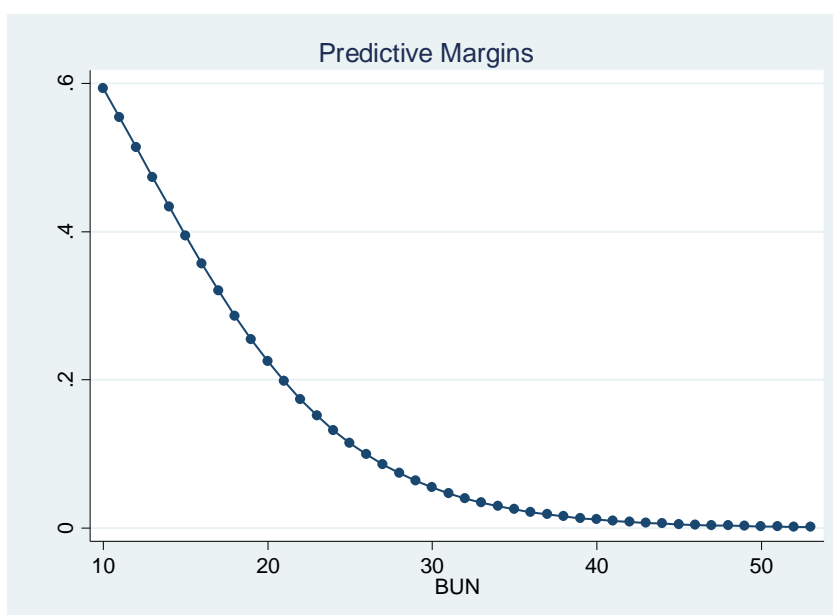


Fig.2: Predicting the likelihood of seizure using serum BUN.

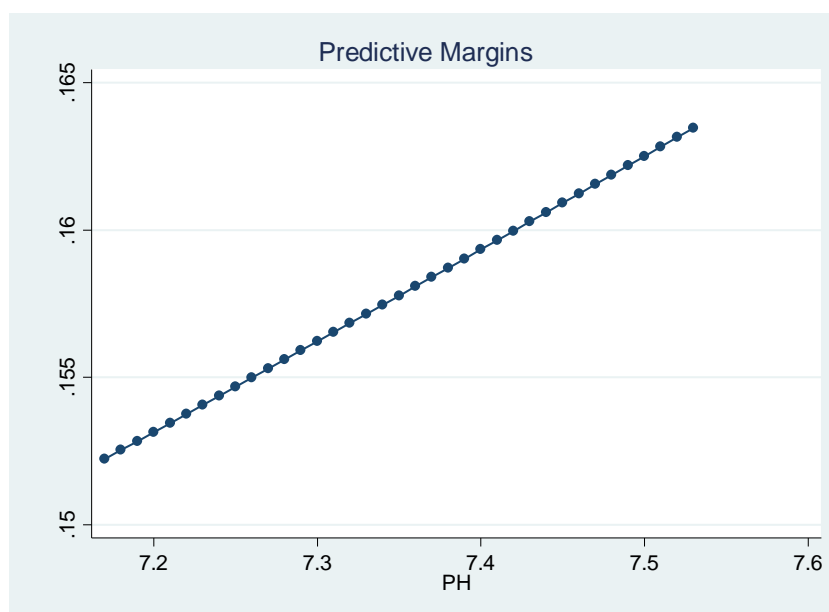


Fig.3: predicting the likelihood of seizure using serum PH.

4- DISCUSSION

The benign infancy seizure is described as no known etiology, has normal EEG, occurs in infants less than 2 years of age, and occurs in infants who have family history of seizure and neurological disease with impaired development. The type of seizure is tonic-generalized clonic is the most common type (15, 16, 18-20). Motoyama et al. also reported a clinical pattern that the mild gastroenteritis caused a clinical condition that the seizure was a febrile seizure at the age of 6 months to 3 years, which was a tonic-generalized clone following days (7). The first to fifth occurs after infection with gastroenteritis. Laboratory tests that contain B1 and liquid serum electrolytes are all normal (13, 20).

Several studies have been carried out after the above-mentioned study (7), which has been described as case report, which has been reported in Japan (2), Hong Kong (13), Taiwan (12), and most recently in Europe (21); all of which indicate the association between gastroenteritis and seizure. A study by Zerr et al. (15), and

Lee et al. (19), have shown that feverless seizures that are repeatedly associated with gastroenteritis are far more likely to occur than the type of FC followed by GE. Rotavirus has been reported in more than 50% of fecal examination among these patients in previous researches, which performed EEG these patients, indicating a focal source with or without secondary generalization of rotavirus (20, 22-25). As previously mentioned gastroenteritis is defined as:

- 1) The age of 6 months to 3 years old as generalized tonic-clonic,
- 2) Mild degree degradation,
- 3) Repetition of seizures on multiple repetitive days,
- 4) The EEG taken during seizure does not contain seizure discharges,
- 5) The presence of rotavirus in SE,
- 6) Good prognosis, and
- 7) Normality (8, 11, 15, 26-28).

In recent years, several reports and studies have been provided from East Asia, including Japan (2), Korea (20, 28), Taiwan (12), and even Western countries (21, 29, 30) about seizures and gastroenteritis (1, 28, 31-33). Gastroenteritis occurs in healthy infants from all walks of life, without any

association with meningitis, encephalitis, and encephalopathy (5, 7). It occurs more often in the winter and early spring, and the most common cause for this is rotavirus (10, 16, 25, 28). In studies, the prevalence of seizure and gastroenteritis is more common in females than males. The prevalence of males/females is 1/1.5-1.8 (9, 19, 31, 33, 34), which in our study this ratio was in favor of male and males / females ratio was 52.4% / 47.6%. Family history in these people is usually negative (35). The most common form of seizure was generalized and the second common form was partial complex form with consciousness impairment (5, 11, 16, 19, 36), in which 13-65% of the studied cases were partial complex form of seizure. On the other hand, gastroenteritis and seizure are classified according to the number of seizures, which are as follows: 1-8 episodes in a 24-hour period. Considering the patients age, gastroenteritis is more common in ages older than 2 years, and also the number of seizures are more common in ages older than 2 years (1, 8, 24, 34).

4-1. Limitations of the study

The limitation in this study was the small sample size. Also, this study was retrospective based on the completion of a questionnaire and in some cases the exact number of seizures was not recorded.

5- CONCLUSION

According to the results of this study, electrolyte impairment is fairly common in children with acute gastroenteritis. Education about the management of children with seizure can be an important factor in this regard.

6- ABBREVIATION

Na: Sodium,

K: Potassium,

BUN: Blood Urea Nitrogen,

Cr: creatinine,

VBG: Venous Blood Gas,

BS: Blood Sugar,

Ca: Calcium,

CBC: Complete Blood Count,

CRP: C - reactive protein.

7- CONFLICT OF INTEREST: None.

8- REFERENCES

1. Millichap JG, Millichap JJ. Role of viral infections in the etiology of febrile seizures. *Pediatr Neurol* 2006 Sep;35(3):165-72.
2. Uemura N, Okumura A, Negoro T, Watanabe K. Clinical features of benign convulsions with mild gastroenteritis. *Brain Dev* 2002; 24(8):745-9.
3. Kianifar H, Ahanchian H, Grover Z, Jafari S, Noorbakhsh Z, Khakshour A, et al. Synbiotic in the management of infantile colic: A randomised controlled trial. *Journal of Paediatrics and Child Health* 2014; 50(10):801-5.
4. Cusmai R, Jovic-Jakubi B, Cantonetti L, Japaridze N, Vigevano F. Convulsions associated with gastroenteritis in the spectrum of benign focal epilepsies in infancy: 30 cases including four cases with ictal EEG recording. *Epileptic Disord* 2010; 12(4):255-61.
5. Okumura A, Uemura N, Negoro T, Watanabe K. Efficacy of antiepileptic drugs in patients with benign convulsions with mild gastroenteritis. *Brain Dev* 2004; 26(3):164-7.
6. Kang B, Kwon YS. Benign convulsion with mild gastroenteritis. *Korean J Pediatr* 2014 Jul;57(7):304-9.
7. Motoyama M, Ichiyama T, Matsushige T, Kajimoto M, Shiraishi M, Furukawa S. Clinical characteristics of benign convulsions with rotavirus gastroenteritis. *J Child Neurol* 2009; 24(5):557-61.
8. Verrotti A, Tocco AM, Coppola GG, Altobelli E, Chiarelli F. Afebrile benign convulsions with mild gastroenteritis: a new entity? *Acta Neurol Scand* 2009; 120(2):73-9.

9. Maruyama K, Okumura A, Sofue A, Ishihara N, Watanabe K. Ictal EEG in patients with convulsions with mild gastroenteritis. *Brain Dev* 2007; 29(1):43-6.
10. Chalouhi C, Barnerias C, Abadie V. [Afebrile seizures in gastroenteritis: a Japanese peculiarity]. *Arch Pediatr* 2006; 13(3):266-8.
11. Li T, Hong S, Peng X, Cheng M, Jiang L. Benign infantile convulsions associated with mild gastroenteritis: an electroclinical study of 34 patients. *Seizure* 2014; 23(1):16-9.
12. Narchi H. Benign afebrile cluster convulsions with gastroenteritis: an observational study. *BMC Pediatr* 2004;4: 2.
13. Wang YF, Zhou ZS. Clinical features of benign convulsions with mild gastroenteritis in Chinese infants. *World J Pediatr* 2013; 9(1):73-5.
14. Marti I, Cilla G, Gomariz M, Eizaguirre J, Garcia-Pardos C, Perez-Yarza EG. [Rotavirus and seizures. A well-defined uncommon association]. *An Pediatr (Barc)* 2010; 73(2):70-3.
15. Zerr DM, Blume HK, Berg AT, Del Beccaro MA, Gospe SM, Jr., Allpress AL, et al. Nonfebrile illness seizures: a unique seizure category? *Epilepsia* 2005; 46(6):952-5.
16. Berg AT, Darefsky AS, Holford TR, Shinnar S. Seizures with fever after unprovoked seizures: an analysis in children followed from the time of a first febrile seizure. *Epilepsia* 1998; 39(1):77-80.
17. Natsume J, Naiki M, Yokotsuka T, Sofue A, Ikuta T, Kondo Y, et al. Transient splenic lesions in children with "benign convulsions with gastroenteritis". *Brain Dev* 2007; 29(8):519-21.
18. Nypaver MM, Reynolds SL, Tanz RR, Davis AT. Emergency department laboratory evaluation of children with seizures: dogma or dilemma? *Pediatr Emerg Care* 1992; 8(1):13-6.
19. Lee WL, Ong HT. Afebrile seizures associated with minor infections: comparison with febrile seizures and unprovoked seizures. *Pediatr Neurol* 2004; 31(3):157-64.
20. Kimia A, Ben-Joseph EP, Rudloe T, Capraro A, Sarco D, Hummel D, et al. Yield of lumbar puncture among children who present with their first complex febrile seizure. *Pediatrics* 2010; 126(1):62-9.
21. Kim GH, Byeon JH, Lee DY, Jeong HJ, Eun BL. Norovirus in benign convulsions with mild gastroenteritis. *Ital J Pediatr*. 2016; 42(1):94.
22. Mustafic N, Tahirovic H, Trnovcevic J, Kapidzic A. [Clinical characteristics at onset of first febrile convulsions]. *Acta Med Croatica* 2008; 62(5):511-5.
23. Gordon KE, Camfield PR, Camfield CS, Dooley JM, Bethune P. Children with febrile seizures do not consume excess health care resources. *Arch Pediatr Adolesc Med* 2000; 154(6):594-7.
24. Berg AT, Shinnar S. Unprovoked seizures in children with febrile seizures: short-term outcome. *Neurology* 1996; 47(2):562-8.
25. Hamiwka LD, Singh N, Niosi J, Wirrell EC. Diagnostic inaccuracy in children referred with "first seizure": role for a first seizure clinic. *Epilepsia* 2007; 48(6):1062-66.
26. Cancho-Candela R, Pena-Valenceja A, Alcalde-Martin C, Ayuso-Fernandez M, Medrano-Sanchez O, Ochoa-Sangrador C. [Benign convulsions with mild rotavirus gastroenteritis]. *Rev Neurol* 2009; 49(5):230-3.
27. Hartfield DS, Tan J, Yager JY, Rosychuk RJ, Spady D, Haines C, et al. The association between iron deficiency and febrile seizures in childhood. *Clin Pediatr (Phila)* 2009;48(4):420-6.
28. Berg AT, Shinnar S, Shapiro ED, Salomon ME, Crain EF, Hauser WA. Risk factors for a first febrile seizure: a matched case-control study. *Epilepsia* 1995; 36(4):334-41.
29. Payne DC, Baggs J, Zerr DM, Klein NP, Yih K, Glanz J, et al. Protective Association Between Rotavirus Vaccination and Childhood Seizures in the Year Following Vaccination in US Children. *Clin Infect Dis* 2014; 58(2):173-7.
30. Freedman SB, Williamson-Urquhart S, Schuh S, Sherman PM, Farion KJ, Gouin S, et al. Impact of emergency department probiotic treatment of pediatric gastroenteritis: study

protocol for the PROGUT (Probiotic Regimen for Outpatient Gastroenteritis Utility of Treatment) randomized controlled trial. *Trials* 2014;15:170.

31. Scarfone RJ, Pond K, Thompson K, Fall I. Utility of laboratory testing for infants with seizures. *Pediatr Emerg Care* 2000; 16(5):309-12.

32. Berg AT, Shinnar S. Complex febrile seizures. *Epilepsia* 1996; 37(2):126-33.

33. Kikuchi K, Hamano S, Higurashi N, Matsuura R, Suzuki K, Tanaka M, et al. Difficulty of Early Diagnosis and Requirement of Long-Term Follow-Up in Benign Infantile Seizures. *Pediatr Neurol* 2015; 53(2):157-62.

34. Weng WC, Hirose S, Lee WT. Benign convulsions with mild gastroenteritis: is it associated with sodium channel gene SCN1A mutation? *J Child Neurol* 2010; 25(12):1521-24.

35. Kawano G, Oshige K, Syutou S, Koteda Y, Yokoyama T, Kim BG, et al. Benign infantile convulsions associated with mild gastroenteritis: a retrospective study of 39 cases including virological tests and efficacy of anticonvulsants. *Brain Dev* 2007; 29(10):617-22.

36. Caraballo RH, Ganez L, Santos CL, Espeche A, Cersosimo R, Fejerman N. Benign infantile seizures with mild gastroenteritis: study of 22 patients. *Seizure* 2009; 18(10):686-9.