Mashhad University of Medical Sciences (MUMS)

Reviews in Clinical Medicine

Clinical Research Development Center Ghaem Hospital

Pathological EEG Findings in the Patients with the First Seizure Admitted to the Emergency Department

Mohsen Ebrahimi (MD)[1], Mohammadreza Shirzadeh (MD)[1], Mohsen Foroughipour (MD)[2], Hamid Zamani Moghadam (MD)[1], Mona Najaf Najafi (MD)[3], Mahdi Foroughian (MD)[1]*

[1]*Department of Emergency Medicine, Faculty of Medicine, Mashhad University of Medical sciences, Mashhad, Iran.*
[2]*Department of Neurology, Faculty of Medicine, Mashhad University of Medical sciences, Mashhad, Iran.*
[3]*Clinical Research Unit, Mashhad University of Medical sciences, Mashhad, Iran.*

ARTICLE INFO

Article type
Original article

Article history
Received: 8 Jul 2019
Revised: 2 Sep 2019
Accepted: 12 Sep 2019

Keywords
Electroencephalography
Pathological
Seizure

ABSTRACT

Introduction: Statistics suggest that a minimum of 4% of the general population experience one or more nonfebrile seizures in their lifetime. Continuous electroencephalography (cEEG) monitoring is an effective diagnostic tool for seizure detection. The present study aimed to investigate the EEG findings in the patients with the first seizure referring to the emergency department (ED).

Methods: This cross-sectional study was conducted on 80 patients with the first seizure admitted to the ED who were selected via convenience sampling. The inclusion criteria were age of more than 17 years, first seizure, and providing written informed consent to participate, and the exclusion criterion was the cases in which seizure was not confirmed by a neurologist. EEG was performed in the ED on the patients within 24 hours after the first attack, and the frequency of pathological changes in the EEG findings was determined. Data analysis was performed in SPSS using descriptive statistics (measures of central tendency and dispersion, frequency distribution) and inferential statistics.

Results: In total, the sample population consisted of 35 male patients (43.8%) and 45 female patients (56.2%). The mean age of the patients was 52.54±19.33 years (median: 53 years). Among the patients, 46 cases (57.5%) had normal EEG findings, while 34 cases (42.5%) had abnormal (pathological) EEG findings.

Conclusion: According to the results, 42.5% of the patients had abnormal EEG findings. However, accurate examinations in this regard may require other diagnostic tools along with EEG in order to confirm the diagnosis of epilepsy and seizure in these patients.

Please cite this paper as:
Ebrahimi M, Shirzadeh M, Foroughipour M, Zamani Moghadam H, Najaf Najafi M, Foroughian M. Pathological EEG Findings in the Patients with the First Seizure Admitted to the Emergency Department. Rev Clin Med. 2019;6(3):98-103.

Introduction

Seizures are defined as the transient physiological disorders of the brain, which occur due to aberrant and abnormal electrical discharges in a group of cortical neurons (1). Seizures impose a significant burden on the patients and healthcare system, accounting for 1.2% of the referrals to the emergency department (ED), with 24% of these cases often confirmed as first-time seizures (2). Epileptic seizures are another common cause of referral to the ED. Several studies have indicated that approximately 45% of new-onset seizures (NOSs) have no known etiology, and 40-50% of these patients eventually receive an epilepsy diagnosis in their ED consultation (3). Although the exact etiology of epileptic seizures remains unclear, dominant MRI findings have shown the presence

***Corresponding author:** Mahdi Foroughian.
Department of Emergency Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
***E-mail:** foroughianmh@mums.ac.ir*
***Tel:** 989151240686*

of T2-hyperintense lesions in the subcortical and periventricular white matter, particularly in the external capsule and anterior temporal lobes, often involving these centers compared to the scattered forms of cerebral small vessel diseases (4).

Neurologists are often concerned that the incidence of NOSs could be the primary sign of chronic epilepsy or non-epileptic events, such as syncope, transient ischemic attacks, and psychogenic non-epileptic seizures. Another issue in this regard for physicians is the cause of the seizure, which may either be direct, in which case the elimination of this contributing factor prevents seizure recurrence, or there may be an unidentified seizure with the risk of recurrence (approximately 40%) within two years (5-8).

Continuous electroencephalography (cEEG) monitoring is an effective diagnostic tool for the detection of seizures and other disorders in patients with critical conditions. The periodic and rhythmic patterns that are often observed in these patients are associated with seizures in some cases (9-16). Early EEG has been reported to exhibit higher efficacy in epilepsy (51%) compared to delayed EEG (34%) (17). Conflicting findings have been proposed regarding the minimum time required for EEG. EEG is considered crucial due to the thermal management protocols that are used for seizure relaxation, which may conceal the clinical symptoms of seizure activity, only providing electrical diagnosis. Moreover, EEG could be effective in the differential diagnosis of seizure activity from shivering to other non-epileptic movements (18, 19).

To date, no EEG studies have been performed on the patients referring to the ED with the first seizure. The present study aimed to investigate the EEG findings in the patients with the first seizure referring to the ED of Ghaem Hospital in Mashhad, Iran in order for the rapid diagnosis of epilepsy, reducing the associated complications, and provide timely and effective treatment for these patients.

Methods

This cross-sectional study was conducted on the patients with the first seizure referring to the ED of Ghaem Hospital in Mashhad, Iran in January 2018. Before sampling, the study protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences (IR.MUMS.MEDICAL.REC.1397.008). The research objectives and methodology were explained to the patients and their caregivers, and written informed consent was obtained prior to enrollment.

The participants were selected via convenience sampling, and eligible patients were enrolled in the study until achieving the required sample size. The inclusion criteria were age of more than 17 years, first seizure attack, and providing written informed consent to participate. The exclusion criteria were the cases in which seizure diagnosis was not confirmed by a neurologist (e.g., pseudoseizure, seizure during pregnancy, and febrile seizures), history of using seizure-inducing medications, and presence of metabolic disorders as reported in the medication history and tests of the patients.

After stabilizing the conditions of the patients, data were collected using a demographic form containing data on age, gender, and comorbidities, which was completed by the researcher. Following that, EEG was performed on the patients in the ED within 24 hours after the first attack. Changes in the EEG were examined by two neurologists, and antiepileptic medications were prescribed to the patients based on the EEG findings (epileptic changes). Finally, the frequency of pathological changes in the EEG findings was determined in the patients.

Data analysis was performed in SPSS version 18 using descriptive statistics (measures of central tendency and dispersion, frequency distribution) in the form of tables and charts. In the intergroup comparison of quantitative variables (e.g., genders), independent t-test was used for the data with normal distribution, and Mann-Whitney U test was utilized for the data with non-normal distribution. In addition, the intergroup comparison of qualitative variables (e.g., genders) was carried out using Chi-square and Fisher's exact test if necessary. In all the statistical analyses, the significance level was considered to be 0.05.

Results

In total, the sample population consisted of 35 male patients (43.8%) and 45 female patients (56.2%) (Table 1).

Table 1. Frequency of Patients in Terms of Gender.

Gender	N	%
Male	35	43.8
Female	45	56.2
Total	80	100

Among the studied patients, five cases (6.3%) were aged ≤20 years, 18 cases (22.5%) were aged 21-40 years, 27 cases (33.8%) were aged 41-60 years, 23 cases (28.8%) were aged 61-80 years, and seven cases (8.8%) were aged ≥81 years. It is notable that the minimum and maximum age of the patients were 18 and 90 years, respectively. The mean age of the patients was 52.54±19.33 years (median: 53 years).

In terms of education level, 58 patients (72.5%)

had secondary education, and 22 cases (27.5%) had higher education levels than high school. No family history of seizures was reported in 75 patients (93.8%), while five cases (6.2%) had a family history of seizures. On the same note, 67 patients (83.8%) had no disease history, while six cases (7.5%) had a history of diabetes, three cases (3.8%) had a history of hypertension, and four patients (5%) had a history of stroke (Table 2).

Table 2. Frequency of Patients in Terms of Medical History of Diseases.

Disease History	N	%
None	67	83.8
Diabetes	6	7.5
Hypertension	3	3.8
Stroke	4	5
Total	80	100

According to the results, 68 patients (85%) were referred to the ED by family members, and 12 cases (15%) were referred by emergency medical services to the ED of Ghaem Hospital in Mashhad. The other findings indicated that 71 patients (88.8%) were non-smokers, while nine cases (11.2%) were smokers. In addition, 46 patients (57.5%) had normal EEG findings with no epileptic discharge, whereas 34 cases (42.5%) had abnormal EEG findings (pathological with epileptic discharge) (Table 3).

Table 3. Frequency of Patients in Terms of EEG Findings.

EEG Findings	N	%
Normal	46	57.5
Abnormal (pathological discharge)	34	42.5
Total	80	100

In the present study, Pearson's Chi-squared test was used to examine the correlation between the EEG findings and gender of the patients referring to the ED of the hospital, and the obtained results indicated no significant correlation between the gender of the patients and their EEG findings ($\chi2=0.159$; df=1; P>0.05) (Tables 4 & 5).

Table 4. Contingency Table of Gender and EEG Findings of Patients.

EEG Findings		Gender		Total
		Male	Female	
Normal	**N**	21	25	4
	%	60	55.6	57.5
Abnormal	**N**	14	20	34
	%	40	44.4	42.5
Total	**N**	35	45	80
	%	100	100	100

Moreover, Yates' continuity correction yielded a similar result in this regard. Therefore, it could be concluded that the ratio of the normal and pathological EEG findings had no significant difference between the male and female patients.

Table 5. Pearson's Chi-squared Test Results Regarding Correlation of Gender and EEG Findings in Patients.

Test	Chi-square	Degree of Freedom	P-value
Pearson's Chi-squared Test	0.159	1	0.690
Yates' Continuity Correction	0.029	1	0.864

Pearson's chi-squared test was also used to examine the correlation between the EEG findings and age of the patients referring to the ED of the hospital, and the obtained results showed no significant correlation between the age of the patients and their EEG findings ($\chi2=2.456$; df=4; P>0.05). Therefore, it could be concluded that the ratio of the normal and pathological EEG findings had no significant difference between the patients in various age ranges.

In the current research, Pearson's chi-squared test was employed to examine the correlation between the EEG findings and family history of epilepsy in the patients referring to the ED of the hospital, and the obtained results demonstrated no significant correlation between the family history of epilepsy in the patients and their EEG findings ($\chi2=0.668$; df=1; P>0.05). Furthermore, Yates' continuity correction yielded a similar result in this regard. Therefore, it could be concluded that the ratio of the normal and pathological EEG findings had no significant difference between the patients with and without the family history of epilepsy (tables 6 & 7).

Table 6. Contingency Table Regarding Family History of Epilepsy and EEG Findings.

EEG Findings		Family History of Epilepsy		Total
		No	Yes	
Normal	**N**	44	2	46
	%	58.7	40	57.7
Abnormal	**N**	31	3	34
	%	41.3	60	42.5
Total	**N**	75	5	80
	%	100	100	100

Table 7. Pearson's Chi-squared Test Regarding Correlation of Family History of Epilepsy and EEG Findings.

Test	Chi-square	Degree of Freedom	P-value
Pearson's Chi-squared Test	0.668	1	0.414
Yates' Continuity Correction	0.123	1	0.726

Pearson's chi-squared test was also used to assess the correlation between the EEG findings and medical disease history of the patients referring to the ED of the hospital, and the obtained results indicated no significant correlation between the history of medical diseases and EEG findings ($\chi 2=0.953$; df=3; P>0.05). Therefore, it could be concluded that the ratio of the normal and pathological EEG findings had no significant difference between the patients with variable medical records (Tables 8 & 9).

Table 8. Contingency Table Regarding Medical Disease History and EEG Findings.

EEG Findings		Medical Disease History				Total
		None	Diabetes	Hypertension	Stroke	
Normal	N	37	4	2	3	46
	%	55.2	66.7	66.7	75	57.7
Abnormal	N	30	2	1	1	34
	%	44.8	33.3	33.3	25	42.5
Total	N	67	6	3	4	80
	%	100	100	100	100	100

Table 9. Pearson's Chi-squared Test Regarding Correlation of Medical Disease History and EEG Findings.

Test	Chi-square	Degree of Freedom	P-value
Pearson's Chi-squared Test	0.953	1	0.813

Discussion

The first seizure is an unexpected, horrifying event to the patient, as well as the observers and family members. The detection of seizures is common in routine clinical practice. Statistics suggest that a minimum of 4% of the general population experience one or more nonfebrile seizures in their lifetime (20,21). The sensitivity of conventional EEG in seizure detection has been estimated at 25-56%, and its specificity has been reported to be 70-90% (22). The present study aimed to investigate the EEG findings in the patients with the first seizure referring to the ED of Ghaem Hospital in Mashhad (Iran) so as to enable the rapid diagnosis of epilepsy, reduce the associated complications, and provide rapid and effective treatment. This cross-sectional study was conducted on 80 patients with the first seizure, including 35 males (43.8%) and 45 females (56.2%). The mean age of the patients was 52.54±19.33 years. Overall, 46 patients (57.5%) had normal EEG findings, while 34 cases (42.5%) had abnormal (pathological) EEG findings.

In a prospective study in this regard, Paliwal et al. (2015) examined all the patients who were diagnosed with the first seizure referring to the hospital during 2008-2011. In the mentioned research, early EEG was carried out at the ED before discharge, and specialized examinations were also performed by a neurologist within the first two weeks. In addition, a neurologist was responsible for the clinical decision-making. Seizure recurrence was evaluated within a follow-up period of nine months to three years. Among 136 studied patients, 92 were male and 44 were female, and the mean age of the patients was 32 years (range: 16-73 years). According to the obtained results, 40 patients had abnormal EEG, and the patients with abnormal EEG (51% versus 11%) and abnormal MRI (53% versus 28%) were more likely to be allocated to the medication therapy group. Furthermore, the findings of the study indicated that abnormal MRI was independently associated with the higher risk of recurrence, and EEG contributed to the medical decision-making in the patients with abnormal MRI (23). In the present study, 42.5% of the patients were observed to have abnormal EEG findings.

Wyman et al. (2016) conducted a first-time seizure ED EEG study on 71 patients receiving EEG. In the mentioned study, all the EEGs were performed within 11 hours following the seizure (average: 3.85 hours). In addition, 24% of the patients (95% confidence interval of 15-36%) were diagnosed with epilepsy and prescribed with antiepileptic medications at the ED. Among 34 patients who were followed-up by an epileptologist, nine cases were diagnosed with epilepsy at the ED, and none of these patients discontinued their antiepileptic medication in their initial follow-up. Finally, it was concluded that the EEG function at the ED in the adults who had the first seizure yielded significant results for the epilepsy diagnosis, which also contributed to the immediate onset of antiepileptic medication (24).

In the current research, 34 patients (42.5%) referring to the ED had abnormal (pathological) EEG findings. In a prospective study entitled "EEG as Part of the Decision-making Process in the Emergency Department", Yigit et al. (2013) examined 110 patients with seizure or seizure-mimicking symptoms, and EEG was reported to be normal in 56% of the patients with the first seizure (25).

In the present study, 57.5% of the patients had normal EEG findings, and the positive predictive value of EEG was observed to be higher than 80% after the first seizure. It has been well documented that the detection of abnormal signs in EEG is associated with the increased risk of seizure recurrence (26). In a research in this regard, King et al. evaluated the detection of epilepsy based on first-time seizure reports in 300 patients with seizure, and generalized or focal epilepsy syndrome was clinically diagnosed in 141 cases

(47%). Moreover, the EEG findings resulted in the diagnosis of epilepsy syndrome in 232 patients (77%). The EEGs were observed to be more effective in the detection of epilepsy within 24 hours after the diagnosis of epilepsy as opposed to later EEGs (51% versus 34%) (17).

In the present study, EEG was obtained within 24 hours after the first seizure at the ED, which was reported to be pathological in 42.5% of the studied patients.

In this regard, Schreiner et al. conducted a prospective study on 157 patients with unknown first-time seizures, reporting that seizures were observed in 13.3% of the EEG cases without the diagnosis of various types of epilepsy (27). Therefore, it must be borne in mind that normal EEGs might also be associated with errors, and continuous follow-up of the patient and using a combination of imaging tools could predispose the diagnosis of epilepsy.

Based on the results of the present study and correlations between the outcomes and history of the risk factors for epilepsy (based on the EEG findings), it could be inferred that the ratio of normal and pathological EEG findings had no significant difference in terms of the demographic data of the patients (age, gender, family history of epilepsy, smoking habits, medical disease history, and mode of referral to the ED). Nevertheless, some studies have denoted that positive family history may increase the risk of epilepsy 2-3 times (28,29). For instance, Bhalla et al. stated that family history is a key risk factor for focal epilepsy (30). Furthermore, Ottman et al. reported that the risk of seizure increases in the individuals with the family history of seizures (31), while no significant associations were observed between the family history of epilepsy and normal and pathological EEG findings in the current research.

Limitations of the Study and Research Implications

The main limitations of the study were the small sample size and lack of patient follow-up. Therefore, it is recommended that similar investigations be conducted on larger sample sizes, and patient follow-up is also suggested in the next steps.

Conclusion

According to the results, 42.5% of the patients with the first seizure had abnormal (pathological) EEG findings. However, it seems that the accurate examination of these patients may require the use of other diagnostic tools along with EEG in order to achieve the definitive diagnosis of epilepsy and seizure.

Acknowledgements

This study was derived from thesis of Mohammadreza shirzadeh registered in Mashhad University of Medical Sciences (960494). The authors would like to thank and appreciate the material aid and spiritual support of the Research Deputy of Mashhad University of Medical Sciences and the patients participating in the project. We also thank the Clinical Research Development Unit of Peymanieh Educational and Research and Therapeutic Center of Jahrom University of Medical Sciences for revising the manuscript.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Victor M, Ropper AH. Adams and victors' principles of neurology. 17th ed. New York: Mcgraw hill; 2000.
2. Huff JS, Morris DL, Kothari RU, et al. Emergency department management of patients with seizures: a multicenter study. Acad Emerg Med. 2001;8:622-628.
3. Krumholz A, Wiebe S, Gronseth GS, et al. Evidence-based guideline: Management of an unprovoked firstseizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology. 2015;84:1705-1713.
4. O'Sullivan M, Jarosz JM, Martin RJ, et al. MRI hyperintensities of the temporal lobe and external capsule in patients with CADASIL. Neurology. 2001;56:628-634.
5. Hauser WA, Beghi E. First seizure definitions worldwide incidence mortality. Epilepsia. 2008; 49: 8-12.
6. Berg AT, Shinnar S. The risk of seizure recurrence following a first unprovoked seizure: a quantitative review. Neurology. 1991;41:965-972.
7. Hui AC, Tang A, Wong KS, et al. Recurrence after a first untreated seizure in the Hong Kong Chinese population. Epilepsia. 2001;42:94-97.
8. Bora I, Seçkin B, Zarifoglu M, et al. Risk of recurrence after first unprovoked tonic-clonic seizure in adults. J Neurol. 1995;242:157-163.
9. Gaspard N, Manganas L, Rampal N, et al. Similarity of lateralized rhythmic delta activity to periodic lateralized epileptiform discharges in critically ill patients. JAMA Neurol. 2013;70:1288-1295.
10. Claassen J, Mayer SA, Kowalski RG, et al. Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. Neurology. 2004;62:1743-1748.
11. Foreman B, Claassen J, Abou Khaled K, et al. Generalized periodic discharges in the critically ill: a case-control study of 200 patients. Neurology. 2012;79:1951-1960.
12. Chong DJ, Hirsch LJ. Which EEG patterns warrant treatment in the critically ill? reviewing the evidence for treatment of periodic epileptiform discharges and related patterns. J Clin Neurophysiol. 2005;22:79-91.
13. García-Morales I, García MT, Galán-Dávila L,, et al. Periodic lateralized epileptiform discharges: etiology, clinical aspects, seizures, and evolution in 130 patients. J Clin Neurophysiol. 2002;19:172-177.
14. Fitzpatrick W, Lowry N. clinical correlates. Can J Neurol Sci. 2007;34:443-450.
15. Pohlmann-Eden B, Hoch DB, Cochius JI, et al. Periodic lateralized epileptiform discharges: a critical review. J Clin Neurophysiol. 1996;13: 519-530.
16. CHATRIAN GE, SHAW CM, LEFFMAN H. The significance of periodic lateralized epileptiform discharges in EEG: an electrographic, clinical and pathological study. Electroencephalogr Clin Neurophysiol. 1964;17:177-193.
17. King MA, Newton MR, Jackson GD, et al. Epileptology of the firstseizure presentation: a clinical, electroencephalograph-

ic, and magnetic resonance imaging study of 300 consecutive patients. Lancet. 1998;352:1007-1011.
18. Venkatesan A, Frucht S. Movement disorders after resuscitation from cardiac arrest. Neurol Clin. 2006;24:123-132.
19. Benbadis SR, Chen S, Melo M. What's shaking in the ICU? The differential diagnosis of seizures in the intensive care setting. Epilepsia. 2010;51:2338-2340.
20. Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota; 1935–1984. Epilepsia. 1993;34:453-468.
21. Forsgren L, Bucht G, Eriksson S, et al. Incidence characterization of unprovoked seizures in adults: a prospective population-based study. Epilepsia. 1996;37:224-229.
22. Mohan KK, Markand ON, Salanova V. Diagnostic utility of video EEG monitoring in paroxysmal events. Acta Neurol Scand. 1996;94:320-325.
23. Paliwal P, Wakerley BR, Yeo LL, et al. Early electroencephalography in patients with Emergency Room diagnoses of suspected new-onset seizures: Diagnostic yield and impact on clinical decision-making. Seizure. 2015;31:22-26.
24. Wyman AJ, Mayes BN, Hernandez-Nino J, et al. The First-Time Seizure Emergency Department Electroencephalogram Study. Ann Emerg Med. 2017;69:184-191.
25. Yigit O, Eray O, Mihci E. EEG as a part of the decision-making process in the emergency department. Eur J Emerg Med. 2013;20:402-427.
26. van Donselaar CA, Schimsheimer RJ, Geerts AT, et al. Value of the lectroencephalogram in adult patients with untreated idiopathic first seizures. Arch Neurol. 1992;49:231-237.
27. Schreiner A, Pohlmann-Eden B. Value of the early electroencephalogram after a first unprovoked seizure. Clin Electroencephalogr. 2003 ;34:140-144.
28. Anderson VE, Hauser WA, Rich SS. Rich SS Genetic heterogeneity in the epilepsies. Adv Neurol. 1986;44:59-75.
29. Anderson VE, Hauser WA. The genetics of epilepsy. Prog Med Genet. 1985;6:9-52.
30. Bhalla D, Chea K, Hun C, et al. Population-based study of epilepsy in Cambodia associated factors, measures of impact, stigma, quality of life, knowledge-attitude-practice, and treatment gap. PLoS One. 2012;7:e46296.
31. Ottman R, Hirose S, Jain S, et al. Genetic testing in the epilepsies-- report of the ILAE Genetics Commission. Epilepsia. 2010;51:655-670.