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The relationship between patient characteristics, laboratory findings and outcomes of the patients presenting with seizures to the emergency department

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ABSTRACT

Aims: Most patients with epilepsy have recurrent admissions to the emergency department (ED) during the disease. Insufficient information about this patient population causes a mismatch between patients' needs and health care delivery. For this reason, there is a need for objective methods that can be used to monitor seizure patients in EDs and to determine the need for hospitalization. This study aimed to develop management recommendations for patients with active seizures or a history of seizures prior to admission and contribute to the determination of the criteria for the ED follow-up period.
Methods: This study was designed as a single-center, prospective, and observational study and included patients over 18 who presented to the ED for seizures. After the patients were included in the study, demographic and laboratory findings were recorded, and patients were followed up for 30 days for mortality and recurrent seizures.

Results: Seventy-one patients were included in the study. The most known seizure causes were drug incompatibility (15.49%) and infection (9.86%). The most common comorbidities were Hypertension (16.90%), Diabetes Mellitus (12.68%), and cerebrovascular diseases (9.86%). The mortality rate was higher in patients who were hospitalized, had an active infection, and had a high CRP value.

Conclusion: The 30-day mortality is higher in patients presenting to the ED with epileptic seizures; in the advanced age group, patients with active infection have an elevated C-reactive protein in laboratory parameters.

Keywords: Emergency medicine, epilepsy, seizure

INTRODUCTION

Epilepsy is defined as recurrent unprovoked seizures caused by a genetic predisposition or an acquired brain disorder. Approximately more than 10% of the population has a seizure at least once in their lifetime, and yet only 3% are diagnosed with epilepsy.[1] A small number of studies have shown that 15% to 35% of epilepsy patients present to the emergency department (ED) for seizures. Inadequate information regarding this patient population results in a mismatch between patients' needs and healthcare delivery. In particular, inadequate coordination between ED and clinical branches leads to unnecessary hospitalizations.[2] Additionally, significant differences were found in the care received by seizure patients in the hospital, both for those who were followed up in the ED and for those who were later admitted.[3] Therefore, there is a need for objective methods that can be used to monitor epileptic patients in the ED and determine the need for hospitalization.

This study aimed to examine the relationship between clinical characteristics, laboratory findings, and patient outcomes who were admitted to the ED with seizures.

METHODS

This study received approval from the Institutional Ethics Committee of the Kocaeli Derince Training and Research Hospital (Date:01.09.2020 , Decision No: 01.07.2021). This study was designed as single-center, prospective, and observational.

Pregnant women, patients under 18 years of age, presenting with their first seizure, seizure activity not longer than 5 minutes, status epilepticus, refractory status epilepticus, and seizures due to secondary causes (i.e., mass lesion, head trauma,graphic and clinical characteristic data, laboratory findings, and hospitalization information were recorded, and enrolled patients were followed up. Mortality information of the patients who were followed up and whether they had a seizure within 30 days were questioned by phone.

Statistical Analysis

All analyses were performed in SPSS v21 (SPSS Inc., Chicago, IL, USA). Compliance of quantitative variables with normal distribution was checked with the Shapiro-Wilk test. Quantitative variables were summarized as mean ± standard deviation and median (minimum value - maximum value), while qualitative variables were summarized as frequency (percentage). Quantitative variables that assumed normal distribution were analyzed with t-test in independent samples. Quantitative variables that did not meet the assumption of normal distribution were analyzed with the Mann-Whitney U test or Kruskal Wallis test according to the number of groups. Qualitative variables were analyzed with the chi-square test or Fisher's exact test. Spearman correlation coefficient was used to evaluate the relationships between quantitative and ordinal variables. P values <0.05 were considered statistically significant.

RESULTS

Seventy-one patients who applied to the ED due to seizures within the study date range were included in our study. The average age of the patients included in the study was 42.66±18.22. Gender distribution was calculated as 46 males (64.78%) and 25 females (35.21%).

The seizure timeframe of 47.14% of the patients before admission to ED was between 10 and 30 minutes. There was a history of head trauma in 10 (14.08%) patients and aura in 19 (26.76%). The most common seizure type was generalized tonic-clonic seizures in 64 patients, 5 patients had complex partial seizures while 1 patient had absence and 1 patient had simple partial seizure. The most known causes of seizures were medication incompatibility (15.49%) and the patient's infection (9.86%). The possible cause of seizures could not be determined in 47 patients (66.20%).

Sixty-four patients (90.14%) were using anti-epileptic drugs (AEDs). The most frequently used drugs were levetiracetam (54.93%), valproic acid (28.17%), and carbamazepine (16.90%). A total of 20 (28.17%) patients had additional chronic diseases. The most frequently observed additional diseases were determined as Hypertension (16.90%), Diabetes Mellitus (12.68%), and cerebrovascular diseases (9.86%). Except for lactate levels, the average ED admission parameters of the patients were within the normal range. ED admission laboratory parameters of the patients are summarized in Table 1.

Twenty patients (28.17%) had a seizure during ED follow-up. Levatiracetam (21.13%) and diazepam (19.72%) were most frequently administered to these patients as treatment in the ED. The average follow-up time of the patients in ED was 367.77 minutes (70-1230, min-max). While 6 (8.45%) patients were admitted to the ward and 2 (2.82%) to the intensive care unit, 63 (88.73%) patients were discharged. 24 (33.80%) patients had a seizure again within 30 days, and 4 (5.63%) patients died.

Table 1. Laboratory parameters of patients

Laboratory parameters	Mean ± SD
WBC (x1000/mm^3)	8.39±3.79
Lymphocyte (%)	31.05±11.96
Neutrophil (%)	59.49±13.58
pH	7.30±0.14
Lactate (mmol/L)	5.30±4.19
HCO3 (mEq/L)	21.96±5.25
BE (mmol/L)	-4.36±6.97
Glucose (mg/dL)	126.85±48.53
CRP (mg/L)	7.31±12.91
Potassium (mmol/L)	4.20±0.50
Calcium (mg/dL)	8.82 ± 0.56
Sodium (mmol/L)	139.34±3.53

WBC: White blood cells, BE: Base excess, CRP: C reactive protein, SD: Standard deviation

No statistical difference was detected in terms of age, systolic and diastolic blood pressure and ED follow-up period between patients who were alive one month after discharge from the ED and those who died within one month Table 2.

Table 2. Comparison of 30-day mortality and age, blood pressures and ED lenght of stay

	30 day Mortality	Mean ± SD	p value
Age	Survivor	41.99 ± 17.89	0.312
	Non- survivor	54.00 ± 22.82	
SBP	Survivor	116.12 ± 20.52	0.494
	Non- survivor	120.00 ± 16.33	
DBP	Survivor	70.45 ± 10.93	0.927
	Non- survivor	70.00 ± 8.16	
LOS	Survivor	363.46 ± 183.14	0.162
	Non- survivor	440.00 ± 109.32	

ED: Emergency department, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, LOS: lenght of stay

While the most common cause of seizures was unknown in 46 (68.66%) patients who were alive after a month, the most common cause of seizures in patients who died within a month was infection (50.00%) (p=0.018). 30-day mortality and clinical characteristics have been compared and summarized in Table 3.

The mortality rate was higher in hospitalized patients than in others (p<0.001)—no statistical difference in seizure rates within one month between hospitalized and non-hospitalized patients Table 4.

No statistical difference was detected between patients who had a seizure again within 30 days in terms of laboratory findings; furthermore, CRP values were higher in patients with 30-day mortality (p=0.004), while no statistical difference was found in other laboratory values Table 5.

Table 3. Comparison of 30-day mortality and patients' characteristic and vital parameters

	30 day Mortality		
	Survivor	Non- survivor	p value
Gender			
Male	43 (%64.18)	3 (%75.00)	
Female	24 (%35.82)	1 (%25.00)	
Body Temperature			
Normal	64 (%95.52)	3 (%75.00)	0.211
>37,8	3 (%4.48)	1 (%25.00)	
Time of seizure prior to the admission			
<5 min	4 (%6.06)	1 (%25.00)	
5-10 min	9 (%13.64)	0 (%0.00)	
10-20 min	20 (%30.3)	1 (%25.00)	0.466
20-30 min	12 (%18.18)	0 (%0.00)	
>30 min	21 (%31.82)	2 (%50.00)	
Aura			
Not present	48 (%71.64)	4 (%100.00)	0.568
Present	19 (%28.36)	0 (%0.00)	
Reason of seizure			
Unknown	46 (%68.66)	1 (%25.00)	
Drug incompatibility	11 (%16.42)	0 (%0.00)	0.018
Infection	5 (%7.46)	2 (%50.00)	
Other	5 (%7.46)	1 (%25.00)	
Comorbidities			
Not present	58 (%86.57)	4 (%100.00)	0.065
Present	9 (%13.43)	0 (%0.00)	
Prior admission within 30 days			
Not present	58 (%86.57)	4 (%100.00)	1.000
Present	9 (%13.43)	0 (%0.00)	
Seizure in the ED			
Not present	47 (%70.15)	4 (%100.00)	0.571
Present	20 (%29.85)	0 (%0.00)	

Min: Minute, ED: Emergency department

Table 4. Comparison of re-seizure within 30 days, mortality and hospitalization

	Hospitalization		
	No	Yes	p
Re-Seizure			
Not present	37(%62.71)	1 (%33.33)	0.554
Present	22 (%37.29)	2 (%66.67)	
Mortality			
Survivor	63 (%100.00)	4 (%50.00)	<0.001
Non survivor	0 (%0.00)	4 (%50.00)	

Table 5. Comparison of laboratory parameters of 30-day mortality and re-seizures within 30 days

	Re-seizure	Mean ± SD	p	Mortality	Mean ± SD	p
WBC (x1000)	Not present	8.73 ± 3.92	0.248	Survivor	8.27 ± 3.58	0.636
	Present	7.64 ± 3.24		Non survivor	10.45 ± 6.78	
Lymphocyte (%)	Not present	30.66 ± 12.52	0.355	Survivor	31.60 ± 11.91	0.105
	Present	33.63 ± 11.74		Non survivor	21.85 ± 9.75	
Neutrophil (%)	Not present	60.56 ± 14.03	0.171	Survivor	58.81 ± 13.54	0.061
	Present	55.58 ± 13.37		Non survivor	70.93 ± 9.43	
pH	Not present	7.31 ± 0.11	0.414	Survivor	7.30 ± 0.14	0.186
	Present	7.26 ± 0.17		Non survivor	7.38 ± 0.06	
Lactate (mmol/L)	Not present	5.60 ± 4.42	0.573	Survivor	5.36 ± 4.28	0.871
	Present	5.18 ± 4.27		Non survivor	4.23 ± 2.31	
HCO3 (mmol/L)	Not present	21.32 ± 5.18	0.465	Survivor	21.81 ± 5.28	0.439
	Present	22.43 ± 5.59		Non survivor	24.53 ± 4.56	
BE (mmol/L)	Not present	-4.73 ± 6.79	0.707	Survivor	-4.60 ± 7.02	0.396
	Present	-4.71 ± 7.73		Non survivor	-0.37 ± 5.14	
Glucose (mg/dl)	Not present	125.66 ± 29.90	0.084	Survivor	123.27 ± 37.43	0.765
	Present	119.33 ± 49.00		Non survivor	186.75 ±138.07	
CRP (mg/L)	Not present	5.82 ± 7.29	0.527	Survivor	5.25 ± 6.58	0.004
	Present	4.13 ± 5.48		Non survivor	41.78 ± 35.42	
Potassium (mmol/L)	Not present	4.17 ± 0.54	0.390	Survivor	4.19 ± 0.50	0.832
	Present	4.28 ± 0.42		Non survivor	4.30 ± 0.56	
Calcium (mg/dl)	Survivor	8.78 ± 0.56	0.564	Yok	8.82 ± 0.55	0.960
	Non survivor	8.86 ± 0.54		Var	8.85 ± 0.81	
Sodium (m/mol)	Survivor	139.24 ± 3.48	0.942	Yok	139.19 ± 3.38	0.304
	Non survivor	139.75 ± 3.18			141.75 ± 5.56	

WBC: White blood cells, BE: Base excess, CRP: C reactive protein, Min: Minute, ED: Emergency department

DISCUSSION

The average age of the patients included in our study was 42.66. Considering the incidence of seizures, which rises and plateaus in adulthood and increases even more in the group over 60 years of age, it was observed that 21.1% of the present study's patients were over 60 years of age, which was found to be similar to the literature.[4] Likewise, considering that epilepsy is more common in males in the literature, there was a similar gender distribution in our study.[5]

Although there was no statistically significant difference between the age factor and ED follow-up period, seizurerecurrence, and mortality, the average age of the deceased patients was found to be higher in our study. In an observational study conducted by Quintana et al.,[6] a high age factor was found to be associated with higher mortality in the epileptic patient group.[6]

14.08% of the patients included in our study had a history of head trauma during the seizure. Due to loss of consciousness, which is the main feature of complex seizures seen in epilepsy patients, the head trauma history of the patients was obtained through the seizure-related anamnesis taken from their relatives and the patient's head trauma examination findings. Although there was no statistically significant difference in the hospitalization and re-seizure risk within 1 month of patients with a history of head trauma, the average ED follow-up time was observed to be higher.

When the seizure types of the patients were examined according to the epilepsy classification, the most common seizure type was generalized tonic-clonic (90.14%). In a retrospective, cross-sectional study conducted by Bozali et al.,[7] the characteristics of patients presenting to ED with seizures and the factors affecting the frequency of admission, generalized tonic-clonic seizures were found to be the most common seizure type.[7] In various prevalence studies, it has been observed that focal seizures vary between 33-65% and generalized tonic-clonic seizures vary between 17-60% .[8] The low number of focal seizures in our study may be because our study included only patients presenting with ED. Epilepsy patients with focal seizures may have fewer ED presentations. Although the correct classification of seizure types is important in terms of helping clinical communication

between the patient and the clinician and guiding the correct treatments, the high rate of 90.14% of generalized tonic-clonic seizures in our study in terms of ED admissions can be explained by several factors. These factors also explain the small number of patients in our study, with changes in patients' habits of using EDs due to the COVID-19 pandemic, which was during the study, and the fact that the study only included the adult age group.

The evaluation of non-epileptic chronic diseases of the patients included in our study revealed that the most common were HT DM. Similar to our study, a review study by Gasparini et al. stated that epilepsy and HT are both common chronic conditions with high prevalence in older age groups and that HT may have both a direct and indirect role in epileptogenesis.[9] In a study conducted by Shlobin et al.[10] examining the relationship between Type 2 DM and epilepsy, relationship and biological mechanisms found that mitochondrial dysfunction and adiponectin deficiency were common for epilepsy and Type 2 DM.

88.73% of the patients included in our study were discharged home after their ED follow-up period ended. 6 patients (8.45%) were admitted to the ward, and 2 patients (2.82%) were admitted to the intensive care unit. In a study conducted by Cordato et al.[11] on the number of patients presenting to ED with seizures, it was found that 58% of patients with seizures were discharged from ED.

The patients included in the study were called by phone 30 days after leaving the ED, and their health status and whether they had re-seizures were questioned. 24 (33.80%) patients had a seizure again within 30 days, and 4 (5.63%) patients died. Similar to the data we obtained in our study, in a study on epilepsy epidemiology in Europe conducted by Forsgren et al.,[8] approximately 20-30% of the epilepsy population may have more than one seizure per month.In the study conducted by Avilés et al.,[12] 16.2% of the patients had a seizure again within 30 days after ED discharge. The same study reported the mortality rate from any cause within 30 days as 1.4%.[12] Our study's relatively high mortality rate may be due to the small number of patients included in the study and the fact that the study was conducted during the COVID-19 pandemic.

In our study, CRP values were found to be higher in patients who died within the 30-day follow-up period after leaving ED than in other patients ($p = 0.004$). Based on a review of the literature, CRP was previously considered an inflammatory marker but has subsequently been extensively studied in many non-inflammatory neurological conditions. However, studies on CRP in the context of seizures or epilepsy are limited. Alapirtti et al. [13] reported in their study that there was a significant increase in CRP levels in generalized tonic-clonic seizures.Fujii et al.[14] found that the CRP level did not increase significantly in acute encephalopathy seen with biphasic seizures and late reduced diffusion in the pre-seizure period. However, the increase in procalcitonin levels was significant.Since procalcitonin is not a routine test in patients with seizures, this parameter could not be evaluated in our study. Sohn et al.[15] investigated the frequency and severity of inflammation-like responses in patients presenting with ED with seizures, associated clinical factors, and whether transient responses caused by seizures could be distinguished from responses caused by concurrent infection. In a meta-analysis in 2019, CRP levels in peripheral blood in epileptic patients increased significantly compared to healthy controls, and there was a significant relationship between inflammation and epilepsy. However, it was added that further studies should be conducted to evaluate the etiology of epilepsy, age of epilepsy onset, seizure frequency, and the effect of AED use on CRP levels in epilepsy. In our study, the fact that CRP levels were found to be higher in patients who died within the 30-day follow-up. period than in other patients suggests that CRP levels should be carefully monitored in patients presnting to ED with seizures.

Finally, the data curation of this study conducted during COVID-19 pandemic which makes our data unique. Pandemic period resulted in fewer ED admissions for epileptic patients.[16] Delaying admissions in the fear of nosocomial cross-infection of COVID-19 might have changed outcomes, especially for the infected patients. Understanding the multifactorial concept of help-seeking behavior requires further studies with the data from the pandemic period.

Limitations

This study was conducted in a single center; therefore, the results can not be generalized. The change in patients' ED admission habits due to the COVID-19 pandemic may have affected the number of patients applying to ED and their outcomes. Although the EEG could have been utilized for further re-seizure data due to its application to all patients in the ED, it is not feasible in our institution. Lastly in our institution we did not had the capacity to measure blood drug levels. Measuring the drug levels would have include more insight to the patients conditions.

CONCLUSION

Among patients presenting to ED with epileptic seizures, the 30-day mortality is higher in patients who are elderly, have active infection, and have elevated CRP in their laboratory parameters. These patient groups should be followed up closely for a longer period.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ethical Committe of Faculty of Kocaeli Derince Training and Research Hospital (Date:01.09.2020 , Decision No: 01.07.2021).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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