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Evaluation of the Impact of Epileptic Seizures on Cardiac Electrical Activity Through Postictal Electrocardiography (ECG): an Observational Prospective Study

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ABSTRACT

Objective: Epileptic seizures affecting higher autonomic control centers may disrupt parasympathetic-sympathetic balance, contributing to cardiovascular dysfunction and increased morbidity and mortality. This study aimed to evaluate the impact of epileptic seizures on cardiac electrical activity using post-ictal electrocardiography (ECG).

Methods: This prospective cohort study evaluated patients presenting to the emergency department with epileptic seizures. Demographic data, laboratory results, and ECG parameters (heart rate, rhythm, wave durations, and morphologies) were recorded. Patients were categorized as newly diagnosed or known epilepsy cases, with further classification based on antiepileptic drug use. The frequency of ECG abnormalities was analyzed, comparing conduction disturbances between groups.

Results: This study included 205 cases of epileptic seizures. Among the patients, 35 (17.1%) were newly diagnosed. Sinus tachycardia was observed in 24.4%, T wave inversion in 30.2%, and first-degree atrioventricular block in 4.9%. PR interval abnormalities were detected in 7.8% and corrected QT interval (QTc) abnormalities in 10.7%. Prolonged PR interval was more common in newly diagnosed patients (14.3% vs. 2.9%, p=0.036), while the mean QTc interval was shorter in these patients compared to controls (p=0.040). No significant differences were found in tachycardia/bradycardia (p=0.403), ST segment changes (p=0.680), QRS duration (p=0.204), or ECG parameters based on antiepileptic drug use. Intensive care unit (ICU) patients had higher leukocyte (p=0.036) and neutrophil counts (p=0.009), with lower pH (p=0.004) and bicarbonate levels (p=0.009).

Conclusion: Sinus tachycardia is the most prevalent ECG abnormality in epileptic seizures. Elevated lactate and decreased bicarbonate levels may predict seizure duration and ICU admission. No significant association was found among epilepsy, anti-epileptic drugs, and severe arrhythmias.

Keywords: Electrocardiography, anti-epileptics, epileptic seizure, autonomic dysfunction, cardiac conduction abnormalities

INTRODUCTION

Epilepsy is a complex neurological condition involving abnormal, hypersynchronous neuronal activity. It manifests with a wide range of symptoms, including involuntary motor movements such as muscle contractions, automatisms like chewing and swallowing, autonomic disturbances, and varying degrees of altered consciousness (1). Although different theories have been proposed, it is thought to occur due to an imbalance in the excitation-inhibition dynamics of neurons (2). Epileptic seizures cause transient disruption of brain functions and can lead to severe complications by impacting multiple physiological systems simultaneously. In this regard, epileptic seizures represent a potentially life-threatening and prevalent public health concern.

Various mechanisms have been proposed for the pathophysiology of epileptic seizures. However, the cellular mechanisms are not fully understood. Among the most widely accepted mechanisms are the inhibition of Gamma-aminobutyric acid (GABA) ergic interneurons and ion channel mutations (3). Ion channel mutations disrupt excitatory-inhibitory balance, leading to increased neuronal excitability. One of the systems most directly associated with ion channels is the cardiac conduction system. This relationship is a key point that suggests a potential link between epilepsy, epileptic seizures, and cardiac arrhythmias.

Epileptic discharges involving higher autonomic control centers may disrupt the balance between parasympathetic and sympathetic activity. This can lead to autonomic dysfunction and

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result in various cardiovascular abnormalities during seizures (4). Cardiovascular abnormalities are often characterized by alterations in heart rate and rhythm. These effects are linked to an increased risk of early mortality and morbidity, primarily due to their association with cardiovascular disease (4).

The primary aim of this study is to evaluate the effect of epileptic seizures on the electrical activity of the heart through electrocardiography (ECG) obtained during the post-ictal period. Additionally, it aims to investigate the association between anti-epileptic drugs and ECG abnormalities in patients with known epilepsy. The secondary aim of our study is to identify key parameters, such as vital signs, ECG findings, and laboratory results, that can help determine the need for admission and assess the requirement for intensive care unit admission in patients with epileptic seizures.

METHODS

Ethical committee approval for the study was obtained from Haydarpaşa Numune Training and Research Hospital, Clinical Research Ethics Committee, University of Health Sciences (approval no: HNEAH-KAEK 2022/KK/117, date:13.06.2022). This study was conducted in accordance with the Declaration of Helsinki. Informed written consent was obtained from all subjects or their relatives.

Case Selection

This study was conducted on patients admitted to the Emergency Medicine Clinic of Haydarpaşa Numune Training and Research Hospital, University of Health Sciences Türkiye, between July 13, 2022, and January 13, 2023, with active epileptic seizures or in the postictal period. Inclusion criteria were age over 18 years, a known or newly diagnosed epilepsy, and presentation either with an active seizure or during the postictal period. Exclusion criteria included pregnancy, seizures secondary to increased intracranial pressure (e.g., hemorrhagic or ischemic stroke, mass lesions, or traumatic hemorrhage), unconfirmed epileptic seizure diagnosis during follow-up, and a history of cardiac arrhythmia or coronary artery disease.

Case Classification

Patients diagnosed with epilepsy for the first time in the emergency department were categorized as "newly diagnosed"; while those with a known history of epilepsy were categorized as "known epilepsy". Patients receiving a single anti-epileptic drug were classified under monotherapy, while those receiving more than one anti-epileptic drug were classified under polytherapy. The cases were further categorized based on the type of epileptic seizure as partial (focal) or generalized.

Electrocardiogram Recording

Electrocardiogram (ECG) was performed in the post-ictal period to assess the effects of epileptic seizures on cardiac electrophysiology. The heart rate, rhythm, wave durations, and wave morphologies were individually recorded for each patient. Thus, the frequency of ECG abnormalities and the relationship between epilepsy and cardiac conduction disturbances were examined. ECG parameters were compared between the "newly diagnosed" and "known epilepsy" groups, as well as among "known epilepsy" patients based on the type and number of anti-epileptic drugs used. Thus, ECG findings potentially associated with anti-epileptic drug use and those that could help distinguish known epilepsy cases from newly diagnosed ones were investigated. Additionally, ECG findings related to discharge-admission decisions were identified and analyzed.

Diagnostic Tests

The patients' characteristics, including age, gender, history of known epilepsy or newly diagnosed, and medications, were recorded. Age, gender, comorbidities, hemogram, blood urea nitrogen, creatinine, sodium, potassium, calcium, magnesium, phosphorus, chloride, creatine kinase, albumin, high-sensitive troponin tests, and venous blood gas (lactate, bicarbonate level, pH) were compared between the newly diagnosed and known epilepsy patient groups. Additionally, cerebral imaging tests (computed tomography, magnetic resonance imaging) were used for etiology and differential diagnosis.

Statistical Analysis

Descriptive statistics were expressed as frequency (n), percentage (%), mean, standard deviation, median, and interquartile range [interquartile range (IQR) 25-75 percentiles]. The relationship between categorical variables was examined using Pearson's chi-square and Fisher Exact tests. The normality of the data was tested using the Shapiro-Wilk test. Differences in continuous variables between independent groups were assessed using the Mann-Whitney U test and Kruskal-Wallis test, when the data did not follow a normal distribution, and the independent t-test and one-way analysis of variance when the data followed a normal distribution. In non-parametric comparisons of three or more groups, the Bonferroni correction was applied for post hoc tests, while the Türkiye hypermobility spectrum disorder test was used for parametric comparisons. The data analysis was performed using IBM Statistical Package for the Social Sciences 23.0 software (IBM Corp., Armonk, NY), and p-values less than 0.05 were considered statistically significant.

RESULTS

Our study included 205 patients. The mean age was 33 years (IQR: 24-41). Among the patients, 117 (57.1%) were male and 88 (42.9%) were female. The majority of the patients had a known diagnosis of epilepsy, while 35 patients (17.1%) were newly diagnosed. A significant proportion of the patients (90.7%) were discharged following treatment and follow-up in the emergency department, while 7 patients (3.4%) were admitted to the neurology ward, and 12 patients (5.9%) were transferred to the intensive care unit for further management. The age (p=0.081) and gender (p=0.993) distributions between patients with newly diagnosed and known epilepsy were similar. The demographic characteristics, vital

parameters, laboratory findings, and admission-discharge status of patients with known epilepsy and newly diagnosed epilepsy are shown in Table 1.

ECG analysis revealed that 88.3% of the patients had normal sinus rhythm, 24.4% had sinus tachycardia, 30.2% exhibited T wave inversion, and 4.9% had first-degree atrioventricular (AV) block. ST segment changes were absent in 199 patients (97.1%). PR interval abnormalities were observed in 16 patients (7.8%), while corrected QT (QTc) interval abnormalities were detected in 22 patients (10.7%). The overall mean PR interval duration was 154.29±23.58 ms, the mean QTc interval duration was 417.61±27.68 ms, and the mean QRS complex duration was 90.83±11.09 ms.

The baseline rhythm characteristic, (p=0.269), the presence of tachycardia or bradycardia, (p=0.403), ST segment changes, (p=0.680), PR interval abnormalities, (p=0.255), QTc interval abnormalities, (p=0.619), and QRS complex duration (p=0.204) were comparable between the newly diagnosed and known epilepsy groups. Although the rate of T wave negativity was higher in patients with known epilepsy, this difference was not statistically significant (p=0.064). The rate of first-degree AV block was significantly higher in the newly diagnosed group compared to, the known epilepsy group (14.3% vs. 2.9%, p=0.015). The proportion of prolonged PR interval was significantly higher in the newly diagnosed group compared to the known epilepsy group (14.3% vs. 2.9%, p=0.036). Additionally, the mean QTc interval duration was observed to be shorter in the newly diagnosed group (p=0.040). The ECG findings of patients in the newly diagnosed and known epilepsy groups are shown in Table 2.

Table 1. Comparison of demographics, laboratory parameters, and admission status

Parameters	All patients	Newly diagnosed	Known epilepsy	p-value
Number of patients, (%)	205	35 (17.1)	170 (82.9)	-
Age (year)	33 (24-41)	39 (26-51)	32 (24-41)	0.081
Gender				
Male	117 (57.1)	20 (57.1)	97 (57.1)	0.993
Female	88 (42.9)	15 (42.9)	73 (42.9)	
Blood sugar (mg/dL)	113 (97-130)	121 (108-140)	110 (96-127)	**0.014**
Body temperature (°C)	36.6 (36.4-36.8)	36.6 (36.5-36.8)	36.5 (36.4-36.8)	0.254
Heart rate (atım/dk)	86 (73-98)	83 (69-94)	86 (74-99)	0.185
SBP (mmHg)	123 (110-134)	123 (111-142)	122 (110-132)	0.216
Leukocyte (/uL)	8270 (6760-10860)	8300 (7040-12480)	8100 (6720-10840)	0.253
Neutrophil (/uL)	5290 (3690-7090)	5400 (4030-7020)	5285 (3660-7110)	0.416
Lymphocyte (/uL)	2220 (1600-3210)	2500 (1590-3740)	2165 (1600-3050)	0.260
Hemoglobin (g/dL)	13.52±1.88	13.5±1.85	13.53±1.89	0.942
Hct (%)	40.82±5.26	40.79±5.44	40.82±5.24	0.973
Platelets (103/uL)	256 (209-297)	285000 (208-323)	252 (209-291)	0.254
CRP (mg/dL)	1.63 (0.63-4.75)	3.17 (0.7-7.56)	1.51 (0.59-4.09)	0.189
Urea (mg/dL)	24.4 (19.3-30.2)	27 (18.8-33)	24.05 (19.3-29.3)	0.126
BUN (mg/dL)	11.4 (9.01-14.11)	12.62 (8.79-15.42)	11.24 (9.01-13.69)	0.123
Creatinine (mg/dL)	0.76 (0.65-0.93)	0.75 (0.65-0.98)	0.76 (0.65-0.93)	0.518
Sodium (mEq/L)	138 (136-140)	138 (135.1-140.4)	138 (136.2-139.9)	0.872
Chloride (mEq/L)	102.2 (99.9-103.9)	101.3 (99.1-103.5)	102.25 (99.9-104)	0.280
Na-Cl	35.88±3.05	36.06±3.32	35.84±3	0.704
HS-troponin (ng/L)	3.46 (3-5.89)	4 (3-5.51)	3.44 (3-6)	0.605
pH	7.35 (7.31-7.38)	7.35 (7.3-7.37)	7.35 (7.31-7.38)	0.716
Bicarbonate (mEq/L)	22.4 (20-24)	21.6 (17.8-23)	22.6 (20.2-24.2)	**0.013**
Lactate (mmol/L)	2.4 (1.51-5.12)	4.41 (2.3-8.16)	2.25 (1.46-4.85)	**0.001**
Admission status				
Discharged	186 (90.7)	30 (85.7)	156 (91.8)	0.265
Ward	7 (3.4)	1 (2.9)	6 (3.5)	
ICU	12 (5.9)	4 (11.4)	8 (4.7)	

The results are presented as mean±SD, median (IQR), or n (%). Independent t-test, Mann-Whitney U test, Pearson Chi-square test, Fisher's Exact test
BUN: Blood urea nitrogen, Na-Cl: Sodium chloride, CRP: C-reactive protein, Hct: Hematocrit, HS: High sensitive, ICU: Intensive care unit, SBP: Systolic blood pressure, IQR: Inpatient quality reporting, SD: Standard deviation

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In our study, we determined that 186 patients were discharged after emergency department follow-up, 7 patients were admitted to the neurology ward for further observation, and 12 patients were transferred to the ICU. No statistically significant relationship was found between patients' baseline rhythm characteristics (p=0.217), ST segment abnormalities (p=0.156), PR interval duration (p=0.225), QTc interval abnormalities (p=0.707), QTc interval duration (p=0.337), and their admission status. The rates of tachycardia and T wave negativity (p=0.108 and p=0.355), as well as the average QRS complex duration (p=0.090), were higher in patients with status epilepticus admitted to the ICU, although the differences were not statistically significant. The frequency of P-wave absent rhythm (8.3%) was significantly higher in patients followed in the ICU compared to those admitted to the ward (0%) (p=0.027). The ECG findings based on the patients' admission status are presented in Table 3.

In terms of vital parameters, the heart rate was higher in the ICU group compared than the other groups; however, this difference was not statistically significant. Among patients followed in the ICU, leukocyte (p=0.036) and neutrophil (p=0.009) counts were significantly higher, while pH (p=0.004) and bicarbonate (p=0.009) levels were notably lower compared to the other groups. There were no significant differences in other laboratory findings based on admission status (p>0.05). Vital parameters and laboratory

Table 2. Comparison of ECG parameters based on new diagnosis vs. known epilepsy

ECG parameters	All patients (n=205)	Newly diagnosed (n=35)	Known epilepsy (n=170)	p-value
Basic rhythm				
Sinus rhythm	181 (88.3)	29 (82.9)	152 (89.4)	0.269
RBBB	4 (2)	2 (5.7)	2 (1.2)	
AF	1 (0.5)	0 (0)	1 (0.6)	
Sinus arrhythmia	19 (9.3)	4 (11.4)	15 (8.8)	
Heart rate				
Tachycardia	50 (24.4)	6 (17.1)	44 (25.9)	0.403
Bradycardia	11 (5.4)	3 (8.6)	8 (4.7)	
Normal	144 (70.2)	26 (74.3)	118 (69.4)	
T wave abnormality				
Absent	143 (69.8)	29 (82.9)	114 (67.1)	0.064
T wave negativity	62 (30.2)	6 (17.1)	56 (32.9)	
ST segment abnormality				
Absent	199 (97.1)	34 (97.1)	165 (97.1)	0.680
ST elevation	3 (1.5)	1 (2.9)	2 (1.2)	
ST depression	3 (1.5)	0 (0)	3 (1.8)	
AV block				
Absent	195 (95.1)	30 (85.7)	165 (97.1)	**0.015**
First-degree	10 (4.9)	5 (14.3)	5 (2.9)	
PR interval				
Normal duration	189 (92.2)	29 (82.9)[a]	160 (94.1)[b]	**0.036**
Short PR	5 (2.4)	1 (2.9)[a]	4 (2.4)[a]	
Long PR	10 (4.9)	5 (14.3)[a]	5 (2.9)[b]	
P wave absent rhythm	1 (0.5)	0 (0)[a]	1 (0.6)[a]	
PR interval (msn)	154.29±23.58	158.43±30.46	153.43±21.9	0.255
QTc interval				
Normal duration	183 (89.3)	33 (94.3)	150 (88.2)	0.619
Short QT	1 (0.5)	0 (0)	1 (0.6)	
Long QT	21 (10.2)	2 (5.7)	19 (11.2)	
QTc interval (msn)	417.61±27.68	408.86±28.33	419.42±27.28	**0.040**
QRS complex (msn)	90.83±11.09	93±11.52	90.38±10.99	0.204

The results are presented as mean±SD or n (%). Independent t-test, Pearson Chi-square test, Fisher's Exact test. The same lowercase letters in a row indicate no significant difference between the groups
AF: Atrial fibrillation, RBBB: Right bundle branch block, AV: Atrioventricular, SD: Standard deviation, ECG: Electrocardiography

findings according to patients' discharge and admission status between admission and discharge are shown in Table 4.

In our study, patients were divided into two groups based on the number of seizures before admission: single-seizure and multiple seizure patients. No statistically significant differences were found between single seizure and multiple-seizure patients regarding ECG rhythm characteristics.

Patients with multiple seizures before admission, had significantly higher systolic blood pressure (p=0.042), neutrophil count (p=0.028), bicarbonate (p=0.043), and neutrophil-to-lymphocyte ratio (p=0.002); while lymphocyte count (p=0.023) was significantly lower. Although high-sensitivity troponin and platelet-lymphocyte ratio were higher in the multiple seizure group, the differences were not statistically significant (p=0.063 and p=0.080). Lactate levels were lower in the multiple seizure group, but the difference was not significant (p=0.053). The other laboratory findings were similar between the two groups (p>0.05). The comparison of vital signs and laboratory findings based on the number of epileptic seizures is presented in Table 5.

In our study, it was found that 114 out of 170 patients with known epilepsy received monotherapy, while 56 received polytherapy. There were no statistically significant differences between the monotherapy and polytherapy groups in terms of baseline rhythm (p=0.189), presence of tachycardia/bradycardia (p=0.426),

Table 3. Comparison of ECG parameters based on hospitalization status

ECG parameters	Discharged (n=186)	Ward (n=7)	Intensive care unit (n=12)	p-value
Basic rhythm				
Sinus rhythm	164 (88.2)	7 (100)	10 (83.3)	0.217
RBBB	4 (2.2)	0 (0)	0 (0)	
AF	0 (0)	0 (0)	1 (8.3)	
Sinus arrhythmia	18 (9.7)	0 (0)	1 (8.3)	
Heart rate				
Tachycardia	41 (22)	2 (28.6)	7 (58.3)	0.108
Bradycardia	11 (5.9)	0 (0)	0 (0)	
Normal	134 (72)	5 (71.4)	5 (41.7)	
T wave abnormality				
Absent	132 (71)	5 (71.4)	6 (50)	0.355
T wave negativity	54 (29)	2 (28.6)	6 (50)	
ST segment abnormality				
Absent	181 (97.3)	7 (100)	11 (91.7)	0.156
ST elevation	3 (1.6)	0 (0)	0 (0)	
ST depression	2 (1.1)	0 (0)	1 (8.3)	
AV block				
Absent	176 (94.6)	7 (100)	12 (100)	0.999
First-degree	10 (5.4)	0 (0)	0 (0)	
PR interval				
Normal duration	173 (93)[a]	6 (85.7)[a]	10 (83.3)[a]	**0.027**
Short PR	3 (1.6)[a]	1 (14.3)[a]	1 (8.3)[a]	
Long PR	10 (5.4)[a]	0 (0)[a]	0 (0)[a]	
P wave absent rhythm	0 (0)[a]	0 (0)[a]	1 (8.3)[b]	
PR interval (msn)	150 (140-170)	140 (140-160)	140 (130-160)	0.225
QTc interval				
Normal duration	166 (89.2)	7 (100)	10 (83.3)	0.707
Short QT	1 (0.5)	0 (0)	0 (0)	
Long QT	19 (10.2)	0 (0)	2 (16.7)	
QTc interval (msn)	420 (400-435)	412 (399-428)	432 (399.5-447.5)	0.337
QRS complex (msn)	90 (80-100)	80 (80-90)	95 (90-102.5)	0.090

Findings are presented as median (IQR) or n (%), Kruskal-Wallis test, Fisher's Exact test, The same lowercase letters in a row indicate no significant difference between groups.
AF: Atrial fibrillation, ICU: Intensive care unit, RBBB: Rright bundle branch block, AV: Atrioventricular

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T wave abnormalities (p=0.231), ST segment abnormalities (p=0.999), AV block (p=0.333), PR interval pathology (p=0.599), PR interval (p=0.381), QTc interval (p=0.173), and QRS complex duration (p=0.346). In our study, 95 patients used levetiracetam, 52 carbamazepine, 51 valproate, and 25 lamotrigine. There was no statistically significant relationship between the use of anti-epileptic agents and heart rate, rhythm, wave durations, wave morphologies, segments, or intervals.

DISCUSSION

In our study, sinus tachycardia was the most common ECG abnormality in patients with epileptic seizures. Additionally, we observed a higher frequency of prolonged QT intervals. In patients admitted to the ICU with status epilepticus, serum lactate levels were elevated, while bicarbonate levels were significantly lower compared to other patients. However, no significant relationship was found between the type or number of anti-epileptic drugs (monotherapy vs. polytherapy) and ECG parameters. In our study, sinus arrhythmia was detected in 9% of the cases, and tachycardia was detected in 24%. Additionally, in patients with epileptic seizures, abnormalities were observed in all ECG waveforms, segments, and intervals. Specifically, T wave inversion was present in 30% of the cases, QT interval abnormalities (both shortened and prolonged) in 11%, PR interval abnormalities (both shortened and prolonged) in 7%, and ST segment abnormalities (depression and elevation) in 3%. Furthermore, first-degree AV block was identified in 5% of the cases.

One of the mechanisms implicated in the development of epileptic seizures is an ion channel mutation. This association is a potential cause for the severe cardiac conduction system abnormalities observed during seizures. In patients with epileptic seizures, the hyperadrenergic state induced by the release of epinephrine and norepinephrine into systemic circulation within the first 30 minutes leads to an increase in heart rate and cardiac output. This response also enhances the utilization of glucose and oxygen throughout the body (5). These mechanisms can result in tachycardia in some patients. Zijlmans et al. (6) reported that 59.6% of patients with epileptic seizures developed tachycardia,

Table 4. Comparison of vitals and laboratory findings based on hospitalization status

Parameters	Discharged (n=186)	Ward (n=7)	Intensive care unit (n=12)	p-value
Blood sugar (mg/dL)	112.5 (98-130)[a]	94 (78-99)[b]	123 (105-151.5)[a]	**0.009**
Body temperature (°C)	36.5 (36.4-36.8)	36.5 (36.5-36.7)	36.7 (36.6-37.05)	0.159
Heart rate (heartbeat/dk)	85 (72-96)	85 (78-101)	105.5 (79.5-134.5)	0.095
SBP (mmHg)	123 (111-133)	126 (115-142)	120.5 (94.5-144)	0.786
Leukocyte (/uL)	8185 (6720-10780)[a]	7250 (5900-10380)[a]	11590 (7905-15360)[b]	**0.036**
Neutrophil (/uL)	5155 (3680-7020)[a]	4480 (3550-6770)[a]	7275 (5655-9230)[b]	**0.009**
Lymphocyte (/uL)	2225 (1590-3070)	2280 (1230-3420)	2105 (1645-5030)	0.792
Hemoglobin (g/dL)	13.4 (12.3-14.8)	13.7 (11.8-15.2)	13.9 (11.7-14.75)	0.943
Hct (%)	40.55 (37.4-44.3)	42.1 (35.4-44.2)	42.45 (36.6-45.6)	0.912
Platelets (10^3/uL)	255.5 (209-295)	372 (193-386)	233 (199-340)	0.180
CRP (mg/dL)	1.67 (0.65-4.77)[a]	0.4 (0.34-1.31)[b]	3.66 (0.96-7.32)[a]	**0.037**
Urea (mg/dL)	24.25 (19.3-29.3)	32.2 (23.7-44.8)	22.05 (16.2-34.05)	0.135
BUN (mg/dL)	11.33 (9.02-13.69)	15.04 (11.07-20.93)	10.3 (7.57-15.91)	0.135
Creatinine (mg/dL)	0.76 (0.65-0.93)	1 (0.6-1.07)	0.75 (0.54-1.02)	0.596
Sodium (mEq/L)	138 (136-139.9)	137.3 (136-141.7)	138.95 (137.55-141.5)	0.440
Chloride (mEq/L)	102.15 (99.9-103.9)	101.3 (99.4-103.9)	102.25 (96.05-105.05)	0.844
Albumin (gr/L)	44.68 (42.56-47.07)	44.14 (40.73-46.49)	42.85 (41.05-46.01)	0.333
Na-Cl	35.6 (34.1-37.3)	37.8 (33.7-43.3)	35.8 (34.05-40.85)	0.295
HS-troponin (ng/L)	3.46 (3-5.89)	3.88 (3-5)	4.07 (3-47.69)	0.678
pH	7.35 (7.32-7.38)[a]	7.34 (7.23-7.36)[a,b]	7.27 (7.07-7.34)[b]	**0.004**
Bicarbonate (mEq/L)	22.4 (20.2-24.1)[a]	22.8 (15.4-24.6)[a]	18.25 (14.3-20.85)[b]	**0.009**
Lactate (mmol/L)	2.35 (1.5-4.9)	2.2 (1.2-14.2)	5.56 (3.21-12.67)	0.062
NLR	2.01 (1.4-3.33)	1.96 (1.63-2.61)	3.53 (2.55-4.72)	0.181
PLR	108.15 (76.08-155.71)	160.34 (95.32-203.33)	95.35 (60.31-141.9)	0.185
CRP/albumin	35.98 (14.62-102.69)[a]	8.8 (6.88-29.68)[b]	86.82 (21.36-166.1)[a]	**0.037**

The results are presented as median IQR: Kruskal-Wallis test, The same lowercase letters in a row indicate no significant difference between groups
BUN: Blood urea nitrogen, Na-Cl: Sodium chloride, CRP: C-reactive protein, Hct: Hematocrit, HS: High sensitive, ICU: Intensive care unit, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, SBP: Systolic blood pressure

with 93% of these patients showing a heart rate increase of 10 beats, 80% a 20-beat increase, and 15% a decrease of 10 beats. In the same study, sinus arrhythmia was observed in 18.3% of the patients, atrial extrasystole in 11.5%, ventricular extrasystole in 7%, and sinus arrest in 6%. In our study, tachycardia was observed in a quarter of the patients, while the majority (70%) had a normal heart rate, and only 5% exhibited bradycardia. In our study, the majority of cases (88%) had sinus rhythm, 9% had sinus arrhythmia, and 2% had right bundle branch block. Only one case exhibited atrial fibrillation as the baseline rhythm. The main reason for the difference in tachycardia frequency compared to the literature is that in our study, the heart rhythm was assessed using an ECG obtained during the postictal period, rather than during the epileptic seizure itself.

In cases of prolonged seizure duration, cerebral autoregulation is impaired due to decompensation, leading to a decrease in cardiac output, the development of hypotension, and widespread hypoperfusion. This cascade of events results in diminished cellular energy metabolism, mitochondrial dysfunction, and an increased reliance on anaerobic metabolism. A study by Wijdicks and Hubmayr (7) demonstrated that metabolic and lactic acidosis developed in cases with status epilepticus. In a study conducted by Kılıc et al. (8) in the emergency department, it was found that a pH below 7.24, a bicarbonate level below 17 mmol/L, and a lactate level above 7.65 mmol/L increased the risk of recurrent seizures. In our study, in cases admitted to the ICU with status epilepticus, the average pH value was 7.27 (p=0.004) and the average bicarbonate level was 18.25 mmol/L (p=0.009). This suggests that metabolic acidosis is an important finding that can be used to predict prolonged seizure activity and the need for ICU in patients presenting with epileptic seizures. Similar to prolonged seizure activity, metabolic acidosis may be observed in cases with multiple seizures. However, in our study, no significant differences were observed in pH, bicarbonate, and lactate levels between the groups with multiple seizures and a single seizure. One of the main reasons for the lack of similar statistical results may be the variability in seizure duration and factors such as the

Table 5. Comparison of vitals and laboratory findings based on number of epileptic seizures

Parameters	Single seizure (n=159)	Multiple seizures (n=46)	p-value
Blood sugar (mg/dL)	112 (96-127)	117 (101-138)	0.203
Body temperature (°C)	36.5 (36.4-36.8)	36.6 (36.4-36.8)	0.422
Heart rate (heartbeat/dk)	86 (74-98)	84.5 (71-105)	0.896
SBP (mmHg)	121 (110-131)	131 (109-142)	**0.042**
Leukocyte (/uL)	8080 (6720-10780)	8535 (7200-11960)	0.191
Neutrophil (/uL)	5060 (3660-6880)	6110 (3880-8210)	**0.028**
Lymphocyte (/uL)	2290 (1680-3240)	1865 (1290-2720)	**0.023**
Hemoglobin (g/dL)	13.52±1.86	13.53±1.97	0.976
Hct (%)	40.75±5.09	41.06±5.87	0.726
Platelets (10^3/uL)	259 (208-302)	242.5 (213-297)	0.572
CRP (mg/dL)	1.63 (0.63-4.2)	1.72 (0.59-6.43)	0.436
Urea (mg/dL)	24.9 (20-30.2)	22.75 (17.4-30.3)	0.206
BUN (mg/dL)	11.63 (9.34-14.11)	10.63 (8.13-14.15)	0.204
Creatinine (mg/dL)	0.77 (0.65-0.94)	0.71 (0.62-0.93)	0.232
Sodium (mEq/L)	138 (136.5-139.8)	137.65 (136-140)	0.681
Chloride (mEq/L)	102.2 (99.7-103.9)	102.15 (100-104.6)	0.624
Albumin (gr/L)	44.73±3.58	43.93±4.64	0.214
Na-Cl	35.96±2.91	35.58±3.51	0.450
HS-troponin (ng/L)	3.42 (3-5.08)	4.93 (3-8.36)	0.063
pH	7.35 (7.31-7.37)	7.36 (7.33-7.39)	0.159
Bicarbonate (mEq/L)	22.1 (19.8-23.7)	22.75 (21-25)	**0.043**
Lactate (mmol/L)	2.5 (1.53-6.1)	1.84 (1.43-3.6)	0.053
NLR	1.96 (1.33-3.31)	2.85 (1.94-5.01)	**0.002**
PLR	104.33 (75.67-144.89)	139.05 (78.55-205.45)	0.080
CRP/albumin	35.65 (14.15-91.23)	38.43 (14.16-136.49)	0.489

The results are presented as median (IQR), independent t-test, Mann-Whitney U test, The same lowercase letters in a row indicate no significant difference between groups
BUN: Blood urea nitrogen, Na-Cl: Sodium chloride, CRP: C-reactive protein, Hct: Hematocrit; HS: High sensitive, ICU: Intensive care unit, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, SBP: Systolic blood pressure

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time to hospital arrival in cases with multiple seizures. In addition, there were no significant differences in ECG parameters between the two groups.

Anti-epileptic drugs exert their effects by enhancing GABA receptor activation, blocking N-methyl-D-aspartate receptors, and altering the permeability of ion channels such as sodium, potassium, and calcium, which are crucial for neuronal transmission. This condition causes antiepileptic drugs to affect not only the neuronal transmission system but the entire body as well, leading to abnormalities in laboratory parameters. Numerous antiepileptic drugs have been reported to be associated with hematological disorders, ranging from mild thrombocytopenia and neutropenia to anemia, aplastic anemia, and bone marrow failure (9). Beyond the use of antiepileptic drugs, it is suggested that drug interactions in patients undergoing polytherapy may result in hematological and biochemical abnormalities, osteomalacia, and liver failure (10). In our study, the lymphocyte count, hemoglobin level, hematocrit percentage, and lactate level were found to be lower in the polytherapy group compared to the monotherapy group.

The interactions of antiepileptic drugs can induce abnormalities in the cardiac conduction system, leading to abnormal ECG findings. It has been shown that frequent generalized seizures can trigger cardiac pathologies, and that polytherapy with anti-epileptic drugs can lead to cardiac involvement in patients (11). Krishnan and Krishnamurthy (12) reported that the average QT interval duration was shorter in patients with polytherapy for epilepsy compared to those on monotherapy. The same study reported no significant difference in PR interval duration between the two groups. We found that 19 patients (11.2%) using anti-epileptic drugs had QT interval pathology (either prolonged or shortened). Only one of these patients was receiving polytherapy, while the others were receiving monotherapy. Our findings indicate that QT interval prolongation was observed in the monotherapy group. However, neither the type nor the number of anti-epileptic drugs appeared to have an impact on QT interval duration.

Various anti-epileptic drugs and pharmacological agents, with off-label use, are often preferred in the treatment of epilepsy. We found that the most commonly used agents in patients with epilepsy were levetiracetam (55.9%), carbamazepine (30.6%), valproate (29.4%), and lamotrigine (14.7%).

There are numerous studies in the literature that have found a relationship between antiepileptic drugs and cardiac conduction abnormalities (13-15). Aydin and Korkut (13) reported no significant changes in any ECG parameters before and after levetiracetam therapy. Siniscalchi et al. (14) reported an approximately 25 ms increase in QTc in patients treated with levetiracetam. Levetiracetam is a widely preferred anti-epileptic drug that exerts its effects primarily through calcium channel inhibition. In the literature, there are case-based reports suggesting an association between levetiracetam and long QT syndrome, as well as torsades de pointes (15). However, Hulhoven et al. (16) reported no statistical relationship between the increase in levetiracetam dosage and QTc prolongation. In our study, we did not observe significant pathological changes related to levetiracetam in the ECG.

The majority of studies investigating antiepileptic–cardiovascular interactions have concentrated on carbamazepine. In our study, carbamazepine was the second most commonly used drug after levetiracetam, with a frequency of 30.6%. Apfelbaum et al. (17) reported that carbamazepine overdose did not lead to a statistically significant change in heart rate in their case series of carbamazepine intoxication. It has been reported that carbamazepine can cause negative chronotropy (18). Hojer et al. (19) reported that sinus tachycardia is the most common side effect of carbamazepine; additionally, at toxic doses, sinus bradycardia, AV blocks, and junctional escape rhythms may be observed. The effect of carbamazepine on heart rate remains unclear in the literature. Nonetheless, it is widely accepted that its cardiovascular impact differs between therapeutic and toxic concentrations. Surges et al. (20) have reported an association between carbamazepine and a short QTc interval. In our study, the mean QTc interval was significantly shorter in patients receiving carbamazepine. However, the observed values did not fall within the pathological range defined as "short QT".

Study Limitations

The limitations of this study include its single-center design, which may limit the generalizability of the findings to other populations. Additionally, the relatively small sample size may have reduced the statistical power to detect subtle differences between groups. The study only included patients presenting to the emergency department with active seizures or in the post-ictal period, potentially leading to selection bias by excluding individuals with well-controlled epilepsy or those who did not seek emergency care. Another limitation is the reliance on post-ictal ECG recordings rather than continuous ECG monitoring, which may have missed transient arrhythmias occurring during the ictal phase. Lastly, the study did not account for potential confounding factors such as medication adherence and seizure triggers, that might have influenced ECG findings. Future research involving larger, multi-center cohorts and continuous ECG monitoring during seizures would offer more comprehensive insights.

CONCLUSION

Our study indicates that sinus tachycardia is the most common ECG abnormality in patients with epileptic seizure. The frequency of a prolonged QT interval increases in patients with epileptic seizures. Furthermore, our study suggests that elevated serum lactate and decreased bicarbonate levels may serve as predictors of seizure duration and the need for ICU admission. We did not find a significant relationship among epileptic seizures, status epilepticus, the use and number of antiepileptic drugs, and serious cardiac arrhythmias. Large-scale prospective studies are required to investigate the relationship between the types of antiepileptic drugs, the number of drugs (monotherapy/polytherapy), and ECG abnormalities in patients with epileptic seizures.

Ethics

Ethics Committee Approval: Ethical committee approval for the study was obtained from Haydarpaşa Numune Training and Research Hospital, Clinical Research Ethics Committee, University of Health Sciences Türkiye, (approval no: HNEAH-KAEK 2022/KK/117, date:13.06.2022).

Informed Consent: Informed written consent was obtained from all subjects or their relatives.

Footnotes

Author Contributions: Concept – A.Ş., K.Y.; Design – A.Ş., İ.A., K.Y., S.D., B.G.Y.; Data Collection and/or Processing -A.Ş., S.D., B.G.Y.; Analysis and/or Interpretation - İ.A., K.Y., S.D.; Literature Search -B.G.Y.; Writing - A.Ş., İ.A.

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