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Corrected QT interval and QT dispersion in temporal lobe epilepsy in children and adolescent

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ABSTRACT

Aim: The purpose of this research was to contrast (heart-rate corrected QT interval) QTc, and (QT dispersion) QTd intervals in individuals with (temporal lobe epilepsy) TLE and those without TLE using a standard 12-lead electrocardiogram.

Patients & methods: This cross-sectional research was undertaken on 100 cases aged 10 to 20 diagnosed with epilepsy in accordance with 2017 ILAE criteria. The patients' informed written permission was acquired. In our study, we included 100 cases: 50 with TLE and 50 with non-TLE verified by seizure semiology. All patients were subjected to a comprehensive history, clinical examination (heart rate, pulse, and blood pressure), and clinical evaluation, which included a comprehensive epilepsy history. On the basis of neurology service documents or the initial publication of the international classification of diseases, 9th revision (ICD9) diagnostic or 10th revision (ICD10) codes for epilepsy, diagnostic age for epilepsy was calculated.

Results: The mean QT interval in group I was 418.30±25.48 ms while that of group II was 406.20±27.63 ms, the mean QTc of group I was 513.60±61.94 ms and was 488.70±50.65 in group II. The calculated QTd was with a mean of 57.60±25.05 ms while that of group II was 43.60±31.89 ms. It means that the QT interval, QTc, and QTd values were considerably greater in the group I (temporal epilepsy) contrasted with group II (non-temporal epilepsy); (p=0.025, 0.030, and 0.016, respectively). The mean QT, QTc, and QTd values for FE were 409.20±20.80, 500.70±55.60, and 52.60±29.70 ms, respectively. QT, QTc, and QTd mean values for patients with widespread epilepsy were 412.00±25.60, 505.00±68.60, and 46.20±28.70 ms. QT, QTc, and QTd interval were insignificantly different between focal and generalized epilepsy. The longer an illness progresses, the longer the QT and QTc intervals, as there was a substantial positive correlation among illness's course and QT interval (r=0.391, p<0.001) and QTc interval (r=0.289, p=0.011), but there was no noticeable impact on QTd due to the illness's duration, as we found an insignificant correlation among duration of illness and QTC and QTd.

Conclusions: Our findings indicate that; QTc interval and QTd are longer in epilepsy cases more among TLE cases contrasted with non-TLE. Since there was no distinction among different epilepsy types (focal and generalized).

Keywords: corrected QT interval, QT dispersion, temporal lobe epilepsy

INTRODUCTION

Sudden unexpected death in epilepsy (SUDEP) is a potentially fatal complication of seizures that occurs in people with epilepsy who have no history of trauma or drowning and whose epilepsy is extensively documented yet who die suddenly and unexpectedly [1]. Autonomic and respiratory degradation are regarded as the primary pathophysiologic processes driving SUDEP, with cardiac abnormalities constituting a substantial proportion of the autonomic aspect [2].

Several studies indicated that persons with epilepsy had a two- to three-fold greater incidence of sudden cardiac arrest (SCA), regardless of conventional cardiac hazard factors for SCA. 10.0%-50.0% of deaths in people with persistent

refractory epilepsy are caused by SUDEP [3, 4]. Those between the ages of 20 and 40 are most frequently affected. Despite strong efforts to understand the pathophysiology of SUDEP today, it is still not completely comprehended [5].

Comorbidities of FE include cardiac autonomic impairment and irregular heart rhythms, particularly TLE, due to the amygdala's crucial role in regulating cardiovascular autonomic activity and the transmission of seizure activity through the insular cortex [6]. Many investigations focusing on rhythm anomalies and their predictions [7, 8] have been conducted on this patient population. Unfortunately, there are very few studies that focus on people with generalized epilepsy (GE). This is feasible for clinical investigations since the relevant cohorts consist mostly of in-hospital candidates for TLE surgery who have undergone at least a preliminary cardiac evaluation (ECG) [9, 10]. Abnormal cardiac repolarization is reflected on the ECG as a shorter or prolonged QT interval and high QT dispersion (QTd) [11]. The QT interval is the period that passes between when the ventricles depolarize and repolarize [12]. Ventricular arrhythmias [13] are potentially fatal and are associated with prolonged ventricular repolarization [8]. Interictal ECG lengthening of the corrected QT interval (QTc) was more common in adults with epilepsy than in those without epilepsy, and it was also detected in certain pediatric patients two hours after generalized seizures [14]. During prolonged, unobserved night-time seizures with associated hypoxia, in [15], it was theorized that some persons are more prone to develop a cardiac arrhythmia due to the effects of QT hysteresis and more persistent or exacerbated prolongation of the QTc. Autonomic dysfunction is commonly disrupted by both partial and generalized seizures [16]. While convulsive status epilepticus is a frequent neurological disorder in children, it remains unstudied whether protracted seizures in healthy children might result in chronic ventricular depolarization–repolarization abnormalities. Investigations of children with epilepsy, nevertheless, have shown that short-term seizures are associated with lengthening QTc intervals and higher spatial variability, as well as considerable heart rate (HR) oscillations and premature ventricular beats [17, 18]. In children, like in adults, epileptic episodes can be followed by ventricular instability due to abnormal ventricular depolarization-repolarization [19]. Convulsive status epilepticus is a frequent juvenile neurological disorder; however, it has not yet been determined whether protracted seizures in otherwise healthy children might result in chronic ventricular depolarization-repolarization abnormalities [20]. In order to evaluate if there is a distinction in QTc or QTd among TLE and non-TLE, we designed this research to assess QTc and QTd in epileptic cases using a standard 12-lead ECG and to determine whether there is a variation in QTc or QTd among TLE and non-TLE.

PATIENTS & METHODS

This cross-sectional investigation was done on 100 cases in Al-Hussein Hospital, and Sayed Galal Hospital, Al-Azhar University. Participants' written informed consent was acquired. The research was done after approval from the Ethical Committee of Al-Azhar University, Al-Hussein, and Sayed Galal Hospitals, from January 2022 to February 2023.

Inclusion Criteria

Our included patients aged 10-20 years old and above, diagnosed with epilepsy in respect to 2017 ILAE criteria [21].

Exlusion Criteria

Exclusion criteria were epileptic cases on medication that is associated with extended QT interval (chlorpromazine; haloperidol; droperidol; quetiapine; olanzapine; amisulpride; thioridazine; types of IA, IC, and III antiarrhythmic; tricyclic antidepressants; antihistamines; chloroquine; hydroxychloroquine; quinine; and macrolides) in addition to epileptic cases who suffer hypokalemia, cardiac, hepatic, or renal illnesses, pregnancy and lactation.

In our research, we enrolled 100 cases: 50 with TLE and 50 with non-TLE confirmed by seizure semiology. All patients were treated to a comprehensive history, clinical examination (HR, pulse, and blood pressure), and clinical evaluation, which included a comprehensive epilepsy history.

The age at diagnosis of epilepsy was established founded on neurology service documents or the 1st manifestation of ICD, 9th revision (ICD-9) diagnostic or 10th revision (ICD-10) codes for epilepsy. Based on the neurology service's data, as an operational definition, refractory epilepsy was defined as the inability to control seizures while trying two different, effective ASMs [22].

TLE was identified based on seizure semiology, magnetic resonance imaging (MRI), and electroencephalogram (EEG) findings. ECG recordings were performed on every patient in the research (CM 300 A, Comen, China). In leads with stable isoelectric lines, QT interval was recorded from the start of the QRS until the end of the T wave. In the company of U waves, QT interval was determined by going to the lowest point on the graph among the T and U waves and computed manually [23]. Bazett's formula, $QT/(RR)^{1/2}$, was used to calculate QTc. The variance among the highest and minimum QT intervals was calculated to estimate the QTd [24]. A cardiologist evaluated every ECG. QT interval value was determined in accordance with the criteria of European Society of Cardiology [25], which define a prolonged QT interval as more than 470 ms in females and more than 450 ms in men. It was defined prolonged QTd as a value greater than 50 ms [23].

Statistical Analysis

The statistical analysis was done using SPSS v27 (IBM, Armonk, NY, USA). To assess the normality of the data distribution, the Shapiro-Wilks test and histograms were employed. Parametric quantitative data were given as the mean and standard deviation (SD) and analyzed using the unpaired student t-test. Non-parametric quantitative data were provided as the median and interquartile range and analyzed using Mann Whitney-test. Where applicable, Chi-square test or Fisher's exact test was used to analyze qualitative variables provided as frequency and percentage (%). Pearson correlation was used to measure the correlation between two quantitative variables. A two-tailed p-value of 0.050 was regarded as statistically substantial.

RESULTS

The mean age was 15.60±3.250 years in group I and 15.90±3.04 in group II. There were 58.0% males and 42.0%

Table 1. Basic descriptive data of researched groups

		Group I (n=50)	Group II (n=50)	p-value
Age (years)		15.60±3.25	15.90±3.04	0.527
Sex	Male	29 (58.0%)	27 (54.0%)	0.687
	Female	21 (42.0%)	23 (46.0%)	
Weight (kg)		46.90±11.47	48.50±10.36	0.471
Height (m)		1.50±0.06	1.51±0.07	0.695
BMI(kg/m^2)		20.70±5.10	21.50±5.20	0.437
Duration of illness (years)		6.10±1.48	5.90±1.34	0.724
Types of epilepsy	Focal	33 (66.0%)	36 (72.0%)	0.665
	Generalized	17 (34.0%)	14 (28.0%)	
Focal epilepsy	Temporal	25 (75.8%)	-	-
	Extra temporal	8 (24.2%)	-	-
Seizure attack duration (s)		63 (36.7-93.7)	76.5 (50.2-98.7)	0.373

Table 2. Vital signs & ECG data between researched groups

	Group I (n=50)	Group II (n=50)	p-value
Vital signs			
HR (beats/min)	85.20±8.70	84.40±9.23	0.665
SBP (mmHg)	133.20±12.36	129.00±13.13	0.103
DBP (mmHg)	85.00±15.68	87.40±14.11	0.423
ECG			
EF (%)	57.00±4.91	56.20±4.56	0.425
LVEDD (cm)	4.14±0.15	4.08±0.14	**0.029***
LVESD (cm)	2.40±0.22	2.50±0.19	0.596
p-max (ms)	151.70±14.11	147.30±12.54	0.106
p-min (ms)	121.40±10.93	119.70±12.61	0.478
p-wave dispersion (ms)	33.40±11.03	29.60±8.82	0.063

females in group I and 54.0% males and 46.0% females in group II. The mean weight was 46.90±11.47 kg in group I and 48.50±10.36 kg in in group II. The mean height was 1.50±0.06 m in group I and 1.51±0.07 m in group II. The mean BMI was 20.70±5.10 kg/m^2 in group I and 21.50±5.20 kg/m^2 in group II. The cases had been afflicted with the illness for a mean of 6.10±1.48 years in group I and for a mean of 5.90±1.34 in group II. 66.0% of group I had focal epilepsy and 34.0% had generalized type, whereas 72.0% of group II had focal epilepsy and 28.0% had generalized type. In patients with focal epilepsy in group I, 75.8% cases were temporal and 24.2% were extratemporal. The median duration of seizure attack was 63.0 (36.7-93.7) in group I and 76.5 (50.2-98.7) in group II.

Basic descriptive data (age, sex, weight, height, BMI, period of illness, types of epilepsy, and duration of seizure attack) were insignificantly different between the studied groups (**Table 1**).

Regarding the vital signs, the mean HR was 85.2±8.7 beats/min in group I and 84.40±9.230 beats/min in group II. The mean SBP was 133.20±12.36 mmHg in group I and 129.00±13.13 mmHg in group II. The mean DBP was 85.00±15.68 mmHg in group I and 87.40±14.11 mmHg in group II. On ECG data, EF was with a mean of 57.00±4.91% in group I and 56.20±4.56% in group II. LVEDD was with a mean of 4.140±0.15 cm in group I and 4.08±0.14 cm in group II.

LVESD was with a mean of 2.4±0.22 cm in group I and 2.5±0.19 cm in group II. p-max was with a mean of 151.70±14.11 ms in group I and 147.30±12.54 ms in group II. p-min was with a mean of 121.40±10.93 ms in group I and 119.70±12.61 ms in group II. p-wave dispersion was with a mean of 33.40±11.03 ms in group I and 29.60±8.82 ms in group II. Vital signs (HR, SBP, and DBP) were not distinguishable amongst two groups. ECG data had no discernible effect on either group. Except LVEDD was considerably greater in group I contrasted with group II (p=0.029; **Table 2**).

Table 3. Contrast between researched groups as regard QT, QTc, & QTd intervals

	Group I (n=50)	Group II (n=50)	p-value
QT interval (ms)	418.30±25.48	406.20±27.63	**0.025***
QTc interval (ms)	513.60±61.94	488.70±50.65	**0.030***
QTd interval (ms)	57.60±25.05	43.60±31.89	**0.016***

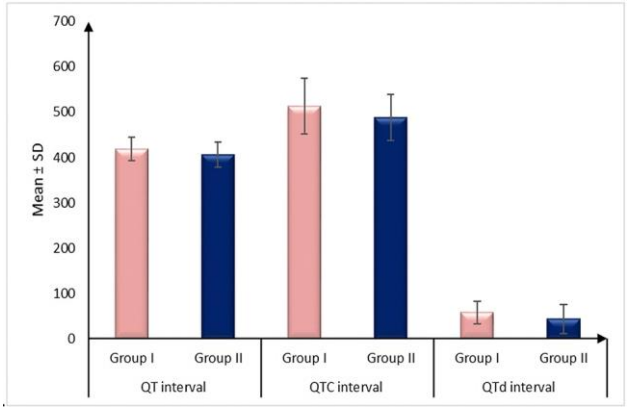

Figure 1. Contrast between researched groups as regard QT, QTc, & QTd intervals (Source: Authors' own elaboration)

Table 4. Comparison of QT according to focal & generalized epilepsy & relation between sex & QT data of studied patients

	Focal epliepsy (n=50)	Genralized epilepsy (n=50)	p-value
QT interval (ms)	409.20±20.80	412.00±25.60	0.586
QTc interval (ms)	500.70±55.60	505.00±68.60	0.738
QTd interval (ms)	52.60±29.70	46.20±28.70	0.314
	Male (n=56)	**Female (n=44)**	**p-value**
QT interval (ms)	411.20±22.70	408.60±21.90	0.569

Patients were screened using a 12-lead electrocardiogram for comparability purposes of the QT interval, QTc, and QTd among the studied groups. The mean QT interval in group I was 418.30±25.48 ms while that of group II was 406.20±27.63 ms, the mean QTc of group I was 513.60±61.94 ms and was 488.70±50.65 in group II. The calculated QTd was with a mean of 57.60±25.05 ms while that of group II was 43.60±31.89 ms. It means that the QT interval, QTc and QTd values were considerably greater in the group I (temporal epilepsy) contrasted with group II (non-temporal epilepsy); (p=0.025, 0.030, and 0.016, respectively; **Table 3**; **Figure 1**).

In our research, 69.0% of our cases had focal seizures, and 31.0% had generalized seizures. The mean QT, QTc, and QTd values for FE were 409.2±20.8, 500.7±55.6, and 52.6±29.7 ms, respectively, QT, QTc, and QTd mean values for patients with widespread epilepsy were 412.00±25.60, 505.00±68.60, and 46.20±28.70 ms. QT, QTc, and QTd interval were insignificantly different amongst focal and GE.

Among the studied patients, 12 cases exhibited MRI pathology, including 10 cases with signs of temporal sclerosis, two cases with cortical dysplasia in the right TLE and one case with a low-grade glioma in the right upper parietal area.

There was an insignificant relation between sex and QT as There was no discernible gender difference in QT (**Table 4**). The period of sickness had a substantial effect on the QT interval and QTc. The longer an illness progresses, the longer the QT and QTc intervals, as there was a substantial positive correlation among illness's course and QT interval (r=0.391,

Table 5. Correlation between duration of illness & different QT data of studied patients

	Duration of ilness	
	Correlation coefficient	**p-value**
QT interval (ms)	0.391	**<0.001***
QTc interval (ms)	0.289	**0.011***
QTd interval (ms)	0.059	0.560

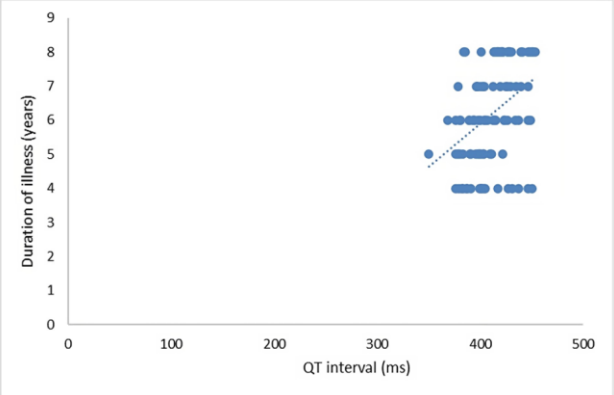

Figure 2. Significant positive correlation between QT interval & duration of illness (Source: Authors' own elaboration)

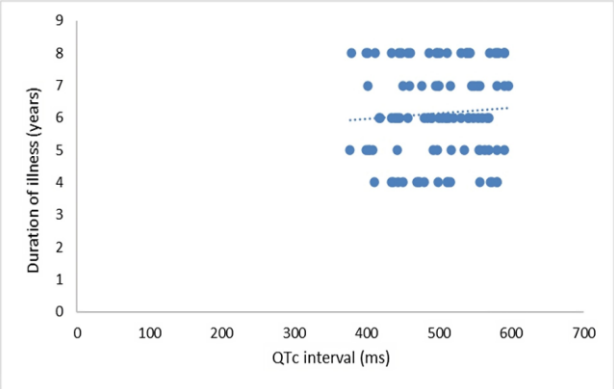

Figure 3. Significant positive correlation between QTc interval & duration of illness (Source: Authors' own elaboration)

p<0.001) and QTc interval (r=0.289, p=0.011), but there was no noticeable impact on QTd due to the illness's duration, as we found an insignificant correlation among duration of illness and QTC and QTd (**Table 5**; **Figure 2**, and **Figure 3**).

DISCUSSION

Epilepsy is a chronic condition that causes central autonomic dysfunction, which can lead to cardiac electrophysiological remodeling [26]. Autonomic function is frequently affected during partial and generalized seizures, in addition to during the interictal and postictal phases [27]. During most seizures, whether temporal or extra-temporal in origin, sympathetic reactions predominate, resulting in tachycardia, tachypnea, elevated BP, pupillary dilatation, diaphoresis, and facial flushing [28].

Much research indicate lateralization of cardiovascular autonomic regulation on the hemispheres. The right hemisphere regulates sympathetic tone more than parasympathetic tone [29, 30]. After temporal seizures, tachycardia can be more prevalent [31]. Although epileptic seizures raise the hazard of cardiac arrhythmias, we intended to better understand the pathophysiology of SUDEP by evaluating cardiac repolarization indices in interictal epileptic cases, particularly those with TLE, versus non-TLE cases using a regular 12-lead surface ECG. In fact, it is simpler to examine indicators of cardiac repolarization using a 12-lead surface ECG [32] even if Holter monitoring could properly monitor QTc and QTd with additional data on temporal distinction in QTc and QTd as opposed to merely spatial variation detected by ECG.

Heart electrical alterations and observed ECG abnormalities in children with epilepsy have yet to be fully characterized for their clinical importance. To completely define the cardiac electrical changes represented by the minor ECG variations and to assess their likely long-term effect on the overall pediatric epilepsy population, more prospective studies are needed [12, 33].

The results of our research showed that epileptic patients had a significantly longer QT interval, which increased their hazard of ventricular arrhythmia, particularly in the company of cardiac structural changes such as ischemic heart disease, heart failure, ventricular hypertrophy, or autonomic nervous system dysfunction, and could even lead to sudden death.

Previous research has shown that epileptic patients have prolonged repolarization indices compared to healthy controls. For example, in [19], it was researched cases with generalized tonic-clonic seizures during the interictal period and discovered that epileptic patients had a prolonged QTd in comparison to the healthy group. Interictal QT prolongation and QTc prolongation were also observed in epileptic patients [34].

Moreover, in [35], it was discovered that QTc considerably increased in epileptic patients during convulsions across all types of epilepsy. Animal studies demonstrating altered heart representation of various Na, K, Ca, and cationic channels may provide an explanation for the increased arrhythmic hazard and potential for sudden death seen in epileptic individuals due to abnormalities in ventricular repolarization [36].

The correlation among epilepsy severity and ECG alterations has been established, and this correlation might be due to a number of causes. The presence of inotropes, irregular electrolytes, and chronic seizure types were all shown in univariant analysis to be linked with ECG changes [37]. In their research of 127 children, it was observed that the longer children had epilepsy, the higher the risk of an irregular ECG [38]. QT interval and QTc were shown to be significantly longer in the current research with increasing illness duration, but QTd was not significantly affected by illness length.

This agreed with the results of [39], which studied 100 people with epilepsy (50 with temporal and 50 with non-temporal forms) and 50 healthy age- and gender-matched controls and discovered a substantially extended QTc with greater illness duration. Similarly, children with Dravet syndrome who have had epilepsy for five years or more had longer QTc intervals and more severe spatial temporal ventricular repolarization heterogeneity [40].

Epilepsy severity and ECG abnormalities may be related in several ways. For instance, changes in HR variability (a metric for sympathy-vagal balance) have been widely reported as a hallmark of epilepsy [41]. Long-term epileptic adults who have sympathetic dominance may experience worse cardiac

function, including increased heart stiffness and reduced exercise tolerance [42].

A similar molecular remodeling of the heart, this time in mice with both newly developed and long-standing epilepsy, has been documented. These results indicate that epilepsy may have negative effects on the heart by causing myocardial remodeling due to abnormal autonomic control. Further research into the mechanism among epilepsy duration and cardiac abnormalities [43, 44] is warranted.

Cases with TLE were discovered to have significantly longer QTc and QTd contrasted with non-TLE cases, which may be accounted for by [45] description of a mechanism termed the lockstep phenomenon, because of a research in which an anesthetized cat received pentylenetetrazol (a substance that, at large amounts, induces convulsions) and the cardiac postganglionic sympathetic and vagal nerve discharges were associated with the onset of convulsions It has been demonstrated that sympathetic activity is altered during an epileptiform discharge, leading to a shift in peripheral efferent output to the heart. Increased autonomic dysregulation seen in epileptic individuals is a possible explanation for this [46].

Autonomic dysregulation is a hallmark of TLE with elevated hazard of SUDEP due to disrupted neuro-respiratory and neuro-cardiac connections caused by sympathetic and parasympathetic overactivation [47]. Increased sympathetic activity has been linked to a prolonged QT interval and this association has been linked to early following depolarization [48]. Uncontrolled sickness is associated with an increase in sympathetic activity due to parasympathetic dysfunction, which decreases once the disease is under control [6]. This may explain why QTc prolongation is more common when the disease is not under control. Further to the arrhythmic hazard, which may be the most well-known cause of sudden cardiac mortality in the elderly, elevated sympathetic activity with TLE is associated with increased myocardial stiffness, atrial volumes and ventricular pressures [42].

Consistent with our findings, it was contrasted TLE and non-TLE groups for QTc and QTd and found that the former were considerably greater in the former (p=0.025 and p=0.038) [39]. In addition, it was studied 80 epileptic cases (40 controlled epileptic cases and 40 refractory epileptic cases) and discovered that controlled and refractory epileptic cases had elevated average QTc and QTD values contrasted with the placebo group [49].

Being a single-center research with a very limited sample size, our research had several limitations. Our research did not have a placebo group. TLE was diagnosed solely on the basis of semiology and interictal EEG; nevertheless, autonomic seizures may result from the activation of extratemporal regions.

CONCLUSIONS

Our findings indicate that the QTc interval and QTd are longer in epilepsy cases with TLE contrasted with those without TLE. As there was no distinction among the distinct forms of epilepsy (focal and GE), QTc prolongation, and QTc dispersion may be the result of epilepsy itself, independent of its cause. More prospective, bigger investigations are required to elucidate the underlying processes and prognostic significance of elevated QTc and QTd in TLE relative to non-TLE. In epileptic cases, a follow-up ECG is advised, as is the use of a QT interval diary, especially for TLE.

Author contributions: AHM, MMMS & HAAM: design, methodology, investigation, data curation, formal analysis, supervision; **MAHA, AHIA, MFF, AMFA & AMH:** investigation, literature review, project administration, supervision; **AIM, AAAA, AAFA, AMZ & AAA:** conceptualization, literature review, project administration, data curaton, investigation; **MME, AIAA, ASIM, AYA, AEAE & EHF:** investigation, writing – original draft, writing – review & editing; **KAR & EIS:** conceptualization, project administration, supervision; & **EIS, MFF & AMZ:** conceptualization, literature review, investigation, supervision. **All authors** provided critical feedback and helped shape the research, data analysis, intellectually review or criticize the content, and final approval of article. **All authors** agreed with the results and conclusions.

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Ethical statement: The authors stated that the study was approved by the Ethical Committee of Al-Azhar University, Al-Hussein, and Sayed Galal Hospitals, from January 2022 to February 2023. Written informed consents were obtained from the participants.

Declaration of interest: No conflict of interest is declared by the authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

REFERENCES

1. Teran FA, Bravo E, Richerson GB. Sudden unexpected death in epilepsy: Respiratory mechanisms. Handb Clin Neurol. 2022;189:153-76. https://doi.org/10.1016/B978-0-323-91532-8.00012-4 PMid:36031303 PMCid:PMC10191258
2. O'Neal TB, Shrestha S, Singh H, et al. Sudden unexpected death in epilepsy. Neurol Int. 2022;14(3):600-13. https://doi.org/10.3390/neurolint14030048 PMid:35893283 PMCid:PMC9326725
3. Wojewodka G, Gulliford MC, Ashworth M, Richardson MP, Ridsdale L. Epilepsy and mortality: A retrospective cohort analysis with a nested case-control study identifying causes and risk factors from primary care and linkage-derived data. BMJ Open. 2021;11(10):e052841. https://doi.org/10.1136/bmjopen-2021-052841 PMid: 34697121 PMCid:PMC8547505
4. Dhaibar H, Gautier NM, Chernyshev OY, Dominic P, Glasscock E. Cardiorespiratory profiling reveals primary breathing dysfunction in Kcna1-null mice: Implications for sudden unexpected death in epilepsy. Neurobiol Dis. 2019; 127:502-11. https://doi.org/10.1016/j.nbd.2019.04.006 PMid:30974168 PMCid:PMC6588471
5. Shlobin NA, Sander JW. Reducing sudden unexpected death in epilepsy: Considering risk factors, pathophysiology and strategies. Curr Treat Options Neurol. 2021;23:38. https://doi.org/10.1007/s11940-021-00691-3
6. Dono F, Evangelista G, Frazzini V, et al. Interictal heart rate variability analysis reveals lateralization of cardiac autonomic control in temporal lobe epilepsy. Front Neurol. 2020;11:842. https://doi.org/10.3389/fneur.2020.00842 PMid:32922353 PMCid:PMC7456848
7. Billeci L, Marino D, Insana L, Vatti G, Varanini M. Patient-specific seizure prediction based on heart rate variability and recurrence quantification analysis. PLoS One. 2018;13(9):e0204339. https://doi.org/10.1371/journal.pone.0204339 PMid:30252915 PMCid:PMC6155519

8. Nass RD, Hampel KG, Elger CE, Surges R. Blood pressure in seizures and epilepsy. Front Neurol. 2019;10:501. https://doi.org/10.3389/fneur.2019.00501 PMid:31139142 PMCid:PMC6527757
9. Tatum WO, Mani J, Jin K, et al. Minimum standards for inpatient long-term video-EEG monitoring: A clinical practice guideline of the international league against epilepsy and international federation of clinical neurophysiology. Clin Neurophysiol. 2022;134:111-28. https://doi.org/10.1016/j.clinph.2021.07.016 PMid:34955428
10. Vorderwülbecke BJ, Wandschneider B, Weber Y, Holtkamp M. Genetic generalized epilepsies in adults–Challenging assumptions and dogmas. Nat Rev Neurol. 2022;18(2):71-83. https://doi.org/10.1038/s41582-021-00583-9 PMid:34837042
11. Shmuely S, van der Lende M, Lamberts RJ, Sander JW, Thijs RD. The heart of epilepsy: Current views and future concepts. Seizure. 2017;44:176-83. https://doi.org/10.1016/j.seizure.2016.10.001 PMid:27843098
12. Suna N, Suna I, Gutmane E, et al. Electrocardiographic abnormalities and mortality in epilepsy patients. Medicina (Kaunas). 2021;57(5):504. https://doi.org/10.3390/medicina57050504 PMid:34065703 PMCid:PMC8156797
13. Mohebi R, Jehan A, Grober A, Froelicher V. Percentile categorization of QT interval as an approach for identifying adult patients at risk for cardiovascular death. Heart Rhythm. 2017;14(8):1210-6. https://doi.org/10.1016/j.hrthm.2017.05.002 PMid:28495651
14. Lamberts RJ, Blom MT, Novy J, et al. Increased prevalence of ECG markers for sudden cardiac arrest in refractory epilepsy. J Neurol Neurosurg Psychiatry. 2015;86(3):309-13. https://doi.org/10.1136/jnnp-2014-307772 PMid:24946773 PMCid:PMC4345521
15. Sadrnia S, Yousefi P, Jalali L. Correlation between seizure in children and prolonged QT interval. ARYA Atheroscler. 2013;9(1):7-10.
16. Faria MT, Rodrigues S, Campelo M, et al. Does the type of seizure influence heart rate variability changes? Epilepsy Behav. 2022;126:108453. https://doi.org/10.1016/j.yebeh.2021.108453 PMid:34864377
17. Ali W, Bubolz BA, Nguyen L, et al. Epilepsy is associated with ventricular alterations following convulsive status epilepticus in children. Epilepsia Open. 2017;2(4):432-40. https://doi.org/10.1002/epi4.12074 PMid:29430560 PMCid:PMC5800777
18. Schreiber JM, Frank LH, Kroner BL, Bumbut A, Ismail MO, Gaillard WD. Children with refractory epilepsy demonstrate alterations in myocardial strain. Epilepsia. 2020;61(10):2234-43. https://doi.org/10.1111/epi.16652 PMid:33053223 PMCid:PMC8191539
19. Asoglu R, Ozdemir M, Aladag N, Asoglu E. Evaluation of cardiac repolarization indices in epilepsy patients treated with carbamazepine and valproic acid. Medicina (Kaunas). 2020;56(1):20. https://doi.org/10.3390/medicina56010020 PMid:31935975 PMCid:PMC7022319
20. Aulická Š. Current management of generalized convulsive status epilepticus in children. Children (Basel). 2022;9(10):1586. https://doi.org/10.3390/children9101586 PMid:36291522 PMCid:PMC9600522
21. Fisher RS, Cross JH, French JA, et al. Operational classification of seizure types by the international league against epilepsy: Position paper of the ILAE commission for classification and terminology. Epilepsia. 2017;58(4):522-30. https://doi.org/10.1111/epi.13670 PMid:28276060
22. Kwan P, Arzimanoglou A, Berg AT, et al. Definition of drug resistant epilepsy: Consensus proposal by the ad hoc task force of the ILAE commission on therapeutic strategies. Epilepsia. 2010;51(6):1069-77. https://doi.org/10.1111/j.1528-1167.2009.02397.x PMid:19889013
23. Christensen PK, Gall MA, Major-Pedersen A, et al. QTc interval length and QT dispersion as predictors of mortality in patients with non-insulin-dependent diabetes. Scand J Clin Lab Invest. 2000;60(4):323-32. https://doi.org/10.1080/003655100750046486 PMid:10943602
24. Li H, Li H, Song Y, et al. High voltage J-waves as a predictor of death in acute ST-segment elevated myocardial infarction in hospital. Cardiol Plus. 2019;4(1):10-4. https://doi.org/10.4103/cp.cp_32_18
25. Asadollahi M, Shahidi M, Ramezani M, Sheibani M. Interictal electrocardiographic alternations in patients with drug-resistant epilepsy. Seizure. 2019;69:7-10. https://doi.org/10.1016/j.seizure.2018.07.002 PMid:30952092
26. Mori S, Hori A, Turker I, et al. Abnormal cardiac repolarization after seizure episodes in structural brain diseases: Cardiac manifestation of electrical remodeling in the brain? J Am Heart Assoc. 2021;10(9):e019778. https://doi.org/10.1161/JAHA.120.019778 PMid:33899505 PMCid:PMC8200721
27. Sevcencu C, Struijk JJ. Autonomic alterations and cardiac changes in epilepsy. Epilepsia. 2010;51(5):725-37. https://doi.org/10.1111/j.1528-1167.2009.02479.x PMid:20067509
28. Ballendine S, Shahab I, Perez-Careta M, et al. Resolution of ictal bradycardia and asystole following temporal lobectomy: A case report, and review of available cases using pacemakers. Epilepsy Behav Rep. 2019;12:100333. https://doi.org/10.1016/j.ebr.2019.100333 PMid:31453568 PMCid:PMC6700408
29. Seyal M, Bateman LM, Li CS. Impact of periictal interventions on respiratory dysfunction, postictal EEG suppression, and postictal immobility. Epilepsia. 2013;54(2):377-82. https://doi.org/10.1111/j.1528-1167.2012.03691.x PMid:23016848 PMCid:PMC3535512
30. Semmelroch M, Elwes RD, Lozsadi DA, Nashef L. Retrospective audit of postictal generalized EEG suppression in telemetry. Epilepsia. 2012;53(2):e21-4. https://doi.org/10.1111/j.1528-1167.2011.03296.x PMid:22050242
31. Mazzola L, Rheims S. Ictal and interictal cardiac manifestations in epilepsy. A review of their relation with an altered central control of autonomic functions and with the risk of SUDEP. Front Neurol. 2021;12:642645. https://doi.org/10.3389/fneur.2021.642645 PMid:33776894 PMCid:PMC7994524
32. Monitillo F, Leone M, Rizzo C, Passantino A, Iacoviello M. Ventricular repolarization measures for arrhythmic risk stratification. World J Cardiol. 2016;8(1):57-73. https://doi.org/10.4330/wjc.v8.i1.57 PMid:26839657 PMCid:PMC4728107

33. Akyuz E, Polat K, Ates S, et al. Investigating cardiac morphological alterations in a pentylenetetrazol-kindling model of epilepsy. Diagnostics (Basel). 2020;10(6):388. https://doi.org/10.3390/diagnostics10060388 PMid: 32526953 PMCid:PMC7344915
34. Dagar S, Emektar E, Corbacioglu SK, Demirci OL, Tandogan M, Cevik Y. Evaluation of electrocardiographic parameters in patients with epileptic seizure. Acta Neurol Belg. 2020; 120(2):321-7. https://doi.org/10.1007/s13760-019-01182-8 PMid:31297670
35. Brotherstone R, Blackhall B, McLellan A. Lengthening of corrected QT during epileptic seizures. Epilepsia. 2010;51(2):221-32. https://doi.org/10.1111/j.1528-1167.2009.02281.x PMid:19732135
36. Li MCH, O'Brien TJ, Todaro M, Powell KL. Acquired cardiac channelopathies in epilepsy: Evidence, mechanisms, and clinical significance. Epilepsia. 2019;60(9):1753-67. https://doi.org/10.1111/epi.16301 PMid:31353444
37. Mańka-Gaca I, Łabuz-Roszak B, Machowska-Majchrzak A, et al. Association between electrocardiographic and electroencephalographic changes in patients with epilepsy. Arch Med Sci. 2020;16(6):1472-3. https://doi.org/10.5114/aoms.2019.87495 PMid:33224352 PMCid: PMC7667441
38. Chan SW, Dervan LA, Watson RS, Anderson AE, Lai YC. Epilepsy duration is an independent factor for electrocardiographic changes in pediatric epilepsy. Epilepsia Open. 2021;6(3):588-96. https://doi.org/10.1002/epi4.12519 PMid:34235879 PMCid:PMC8408606
39. Nasef MS, Gaber AA, Abdelhamid YA, Bastawy I, Abdelhady ST, Wahid El Din MM. Corrected QT interval and QT dispersion in temporal lobe epilepsy. Egypt J Neurol Psychiatry Neurosurg. 2021;57:6. https://doi.org/10.1186/s41983-020-00257-1
40. Lyu SY, Nam SO, Lee YJ, et al. Longitudinal change of cardiac electrical and autonomic function and potential risk factors in children with dravet syndrome. Epilepsy Res. 2019;152:11-7. https://doi.org/10.1016/j.eplepsyres.2019.02.018 PMid:30870727
41. Lotufo PA, Valiengo L, Benseñor IM, Brunoni AR. A systematic review and meta-analysis of heart rate variability in epilepsy and antiepileptic drugs. Epilepsia. 2012;53(2):272-82. https://doi.org/10.1111/j.1528-1167.2011.03361.x PMid:22221253
42. Fialho GL, Wolf P, Walz R, Lin K. Increased cardiac stiffness is associated with autonomic dysfunction in patients with temporal lobe epilepsy. Epilepsia. 2018;59(6):e85-90. https://doi.org/10.1111/epi.14084 PMid:29697139
43. Brewster AL, Marzec K, Hairston A, Ho M, Anderson AE, Lai YC. Early cardiac electrographic and molecular remodeling in a model of status epilepticus and acquired epilepsy. Epilepsia. 2016;57(11):1907-15. https://doi.org/10.1111/epi.13516 PMid:27555091 PMCid:PMC5545890
44. Lai YC, Li N, Lawrence W, et al. Myocardial remodeling and susceptibility to ventricular tachycardia in a model of chronic epilepsy. Epilepsia Open. 2018;3(2):213-23. https://doi.org/10.1002/epi4.12107 PMid:29881800 PMCid: PMC5983128
45. Lathers CM, Schraeder PL, Weiner FL. Synchronization of cardiac autonomic neural discharge with epileptogenic activity: The lockstep phenomenon. Electroencephalogr Clin Neurophysiol. 1987;67(3):247-59. https://doi.org/10.1016/0013-4694(87)90023-X PMid:2441959
46. Thijs RD, Ryvlin P, Surges R. Autonomic manifestations of epilepsy: Emerging pathways to sudden death? Nat Rev Neurol. 2021;17(12):774-88. https://doi.org/10.1038/s41582-021-00574-w PMid:34716432
47. Manolis TA, Manolis AA, Melita H, Manolis AS. Sudden unexpected death in epilepsy: The neuro-cardio-respiratory connection. Seizure. 2019;64:65-73. https://doi.org/10.1016/j.seizure.2018.12.007 PMid: 30566897
48. Wang R, Wang M, He S, Sun G, Sun X. Targeting calcium homeostasis in myocardial ischemia/reperfusion injury: An overview of regulatory mechanisms and therapeutic reagents. Front Pharmacol. 2020;11:872. https://doi.org/10.3389/fphar.2020.00872 PMid:32581817 PMCid: PMC7296066
49. Gurses AA, Genc E, Gurses KM, Altiparmak T, Yildirim I, Genc BO. QT interval alterations in epilepsy: A thorough investigation between epilepsy subtypes. J Clin Neurosci. 2022;104:113-7. https://doi.org/10.1016/j.jocn.2022.08.014 PMid:36027652