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Original Article

Temporal and Seasonal Patterns of Seizure Recurrence and Implications for Antiepileptic Drug Timing in Patients With Epilepsy

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Abstract

Background: Identifying temporal and seasonal patterns may help improve patient management and treatment planning. Accordingly, this study aimed to investigate these patterns in seizure occurrences among patients diagnosed with epilepsy.

Methods: A retrospective, cross-sectional analysis was conducted using medical records from 1,962 epilepsy patients admitted to Imam Reza Hospital, Tabriz, Iran, between 2021 and 2023. Data related to seizure timing (by hour, day of week, and season), patient demographics, clinical characteristics, and adherence to anti-seizure medication were extracted and then analyzed using SPSS 23.

Results: The mean age of all patients was 38.5 years, and 52.3% were male. The highest frequency of seizures was recorded between 23:00 and 23:59 (6.3%), while the lowest frequency was between 07:00 and 07:59 (1.5%). Moreover, weekly analysis revealed that seizures occurred most frequently on Saturdays (15.3%) but least on Mondays (13.3%). In terms of season, autumn and spring had the highest (27.3%) and lowest (23.1%) seizure frequencies, respectively. Ultimately, no statistically significant relationship was found between seizure recurrence and either time of day or season.

Conclusion: Although temporal and seasonal peaks were observed in seizure occurrence, these variations were not statistically meaningful. Nonetheless, these findings highlight the potential for aligning antiepileptic drug prescribing with biological rhythms. It is recommended that future studies use continuous electroencephalography monitoring to validate and expand upon these findings.

Keywords: Epilepsy, Seizures, Circadian rhythm, Seasonality, Temporal pattern

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Introduction

Epilepsy is one of the most prevalent chronic neurological disorders, affecting nearly 50 million people worldwide.[1-3] It is characterized by recurrent, unprovoked seizures and can seriously impair patients' quality of life and functioning. Although the etiology of epilepsy is diverse, ranging from genetic predispositions to structural brain abnormalities, the precise mechanisms underlying seizure initiation remain incompletely understood.[4-6]

Recent research has increasingly focused on the potential influence of biological rhythms and environmental factors on seizure dynamics. Circadian and seasonal patterns, which govern various physiological processes (e.g., hormone release, sleep-wake cycles, and core body temperature), have been proposed as modulators of neuronal excitability.[7-9] Consequently, investigating these temporal variables may yield novel insights into seizure predictability and therapeutic timing. In addition, understanding the chronobiological characteristics of epilepsy is clinically relevant, especially in tailoring medication schedules and anticipating periods of heightened seizure risk. According to some studies, seizures may not occur randomly but instead may follow discernible temporal distributions influenced by both endogenous (e.g., melatonin levels and sleep architecture) and exogenous (e.g., light exposure and temperature fluctuations) factors. Chronopharmacology studies have demonstrated diurnal variations in antiepileptic drug pharmacokinetics, supporting the concept of "Chronotherapy", where dosing schedules are adapted to seizure risk windows.[10-12] Similarly, seasonal variations in antiepileptic drug concentrations have been reported. For instance, oxcarbazepine levels are lower in spring and summer compared to autumn and winter.[13]

Despite these theoretical underpinnings, there are contradictory empirical data on the relationship between seizure occurrence and diurnal or seasonal changes. Some studies have suggested increased seizure incidence during specific times of the day or seasons, while others have reported no significant associations. Moreover, cultural and geographical factors may influence such patterns. Therefore, this study aims to examine the seasonal and temporal distribution of seizure occurrences in a large cohort of patients with confirmed epilepsy by analyzing patterns based on hour, day of the week, and season. It also seeks to clarify whether identifiable trends exist that can support more personalized approaches to epilepsy drug management.

Methods

Study Design and Setting

This retrospective, cross-sectional study was performed at Imam Reza Hospital, a major tertiary referral center for neurological conditions, in Tabriz, Iran.

Study Population

The study analyzed medical records of 1,962 patients with a confirmed diagnosis of epilepsy who were admitted to the hospital between 2021 and 2023. The inclusion criteria included a prior diagnosis of epilepsy and at least one documented seizure event within the study period. On the other hand, patients with seizure events due to fever, metabolic disturbances, brain tumors, or incomplete medical records were excluded from the analysis.

Data Collection

Data were extracted from patient records using a standardized checklist. Collected variables included demographic information (age, gender, marital status, and residence), clinical characteristics (type of epilepsy, seizure type, medication adherence, and family history), and seizure timing (hour of day, day of week, month, and season). Then, medication adherence was evaluated by patient or family recording. Finally, seizure recurrence was defined as any unprovoked seizure following antiepileptic drug withdrawal.

Statistical Analysis

All data were coded and analyzed using SPSS, version 23. Descriptive statistics were used to summarize patient demographics and seizure characteristics. Frequencies and percentages were calculated for categorical variables. Additionally, normality of the continuous variables was assessed using the Shapiro-Wilk test. Chi-square tests were also utilized to evaluate the association between seizure occurrence and time-related variables (hour, weekday, and season).

Ethical Considerations

Patient confidentiality was maintained throughout the study. In addition, ethical approval was obtained from the Research Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC1403.543).

Results

A total of 1,962 patients with epilepsy were included in the study. The mean age was 38.5 years, with an age range of 3–95 years. Furthermore, the study population comprised 52.3% male patients and 47.7% female patients from urban and rural areas, with diverse socioeconomic backgrounds.

Hourly Distribution of Seizures

Analysis of seizure occurrence by hour revealed the highest frequency between 23:00 and 23:59, accounting for 6.3% (n = 123) of all seizures. The lowest frequency occurred between 07:00 and 07:59, with only 1.5% (n = 29) of seizures reported. Other peak times included 22:00–22:59 (5.8%) and 21:00–21:59 (5.3%). Despite these observations, the statistical analysis demonstrated no significant association between time of day and seizure recurrence ($P = 0.27$). Table 1 and Figure 1 present the circadian patterns of seizure incidence among the participants.

Table 1. Circadian Pattern of Seizure Incidence in Participants

Hour Interval		Number (%)
0:00	0:59	102 (5.2)
1:00	1:59	93 (4.7)
2:00	2:59	94 (4.8)
3:00	3:59	69 (3.5)
4:00	4:59	56 (2.9)
5:00	5:59	55 (2.8)
6:00	6:59	36 (1.8)
7:00	7:59	29 (1.5)
8:00	8:59	32 (1.6)
9:00	9:59	55 (2.8)
10:00	10:59	77 (3.9)
11:00	11:59	77 (3.9)
12:00	12:59	93 (4.7)
13:00	13:59	101 (5.1)
14:00	14:59	105 (5.4)
15:00	15:59	86 (4.4)
16:00	16:59	106 (5.4)
17:00	17:59	91 (4.6)
18:00	18:59	85 (4.3)
19:00	19:59	94 (4.8)
20:00	20:59	86 (4.4)
21:00	21:59	103 (5.2)
22:00	22:59	114 (5.8)
23:00	23:59	123 (6.3)
Total		1,962 (100)

Weekly Distribution of Seizures

When analyzed by day of the week, seizures most commonly occurred on Saturdays (15.3%, n = 297), followed closely by Tuesdays (15.0%, n = 295). On the other hand, the least frequent occurrences were on Mondays (13.3%, n = 260) and Sundays (13.45%, n = 267). These variations were not statistically significant (P = 0.57, Table 2).

Seasonal Distribution of Seizures

The seasonal analysis (Table 3) demonstrated that seizures were most frequent in autumn (27.3%, n = 536), followed by summer (25.4%, n = 499), winter (24.0%, n = 472), and spring (23.1%, n = 455). Based on the results, no statistically significant relationship was observed between season and seizure recurrence (P = 0.41).

These results suggest patterns in seizure occurrence across temporal variables, but without statistically significant correlations (Figure 2).

Discussion

This study explored temporal and seasonal patterns in seizure occurrences among a large cohort of Iranian epilepsy patients. Although no statistically significant associations were found between seizure recurrence and time of day or season, the observed frequency trends offer insights that may inform future research and clinical practice. Our results align with those of prior studies, suggesting circadian and seasonal influences on seizures,[9,14-16] although precise mechanisms remain unclear.

The highest seizure occurrence between 23:00 and 23:59 conforms to the findings of other studies, indicating a nocturnal peak in seizure activity, potentially linked to sleep-wake transitions and neurohormonal fluctuations (e.g., melatonin and cortisol secretion). Conversely, the early morning trough (07:00–07:59) may reflect stabilizing neuronal activity following the sleep phase.

Weekday analysis revealed a modest peak on Saturdays and a low one on Mondays, although these variations were not statistically significant. Sociocultural or behavioral factors (e.g., weekend routines and stress levels at the beginning of the workweek) could influence seizure susceptibility, which merits further investigation.

The highest and lowest seizure frequencies were recorded in autumn and spring, respectively. While not statistically significant, such trends may relate to environmental variables, such as daylight duration, ambient temperature, and atmospheric pressure, which all have been implicated in previous studies as modulators of seizure threshold. Notably, autumn in Iran coincides with shorter daylight hours and cooler temperatures, which may affect circadian regulation and neurophysiological stability.[17-19]

These findings may have implications for antiepileptic drug administration. Chronopharmacological studies show diurnal variations in antiepileptic drug absorption and metabolism,[10,11] s seasonal fluctuations in antiepileptic drug concentrations have been reported as well [13]. Therefore, aligning antiepileptic drug dosing schedules with temporal risk periods may represent a promising strategy, although our findings alone are insufficient to guide clinical practices.

Our findings are in line with several other epidemiological investigations that reported temporal clustering of seizures, even in the absence of statistical significance. In our study, the lack of strong associations

Table 2. Weekly Patterns of Seizure Incidence Among the Participants

Day	Number (%)
Saturday	297 (15.32)
Sunday	267 (13.45)
Monday	260 (13.25)
Tuesday	295 (15.03)
Wednesday	287 (14.62)
Thursday	274 (13.96)
Friday	282 (14.37)
Total	1,962 (100)

Table 3. Seasonal Patterns of Seizure Incidence in Participants

Season	2021	2022	2023	Total
Spring	100	140	215	455
Summer	111	167	221	499
Autumn	109	215	212	536
Winter	147	178	147	472
Total	467	795	700	1,962

Figure 1. Circadian Patterns of Seizure Incidence Among the Participants

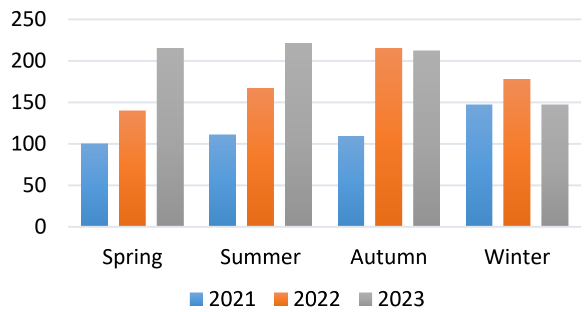

Figure 2. Seasonal Patterns of Seizure Incidence Among the Participants

may be attributed to methodological limitations, including reliance on retrospective data and absence of continuous electroencephalography monitoring, which could miss subclinical or nocturnal events.[20,21]

Despite these limitations, our research contributes to the understanding of seizure temporal dynamics in a Middle Eastern population, a region underrepresented in chronobiological epilepsy research. It indicates the need for prospective studies employing wearable seizure detection technology or long-term video electroencephalography monitoring to capture finer-grained data. Recognizing potential seizure patterns could eventually support anticipatory guidance for patients and personalized treatment scheduling, particularly for those with drug-resistant epilepsy or disrupted sleep cycles.

Conclusion

Our findings revealed distinct patterns, such as increased seizure frequency during late-night hours and in the autumn season, although none of these associations reached statistical significance. However, the observed trends, along with prior chronotherapy research, suggest that tailoring antiepileptic drug administration schedules to biological rhythms warrants further investigation.

The findings highlight the complexity of seizure timing and the multifactorial nature of epilepsy. Although no definitive temporal or seasonal trigger was identified, awareness of potential rhythmic trends may help clinicians optimize treatment plans and counsel patients about seizure risk periods.

To deepen our understanding, future studies should utilize real-time seizure tracking technologies and broader, multi-center datasets in order to validate temporal associations and uncover individualized seizure patterns that may aid in prediction and prevention strategies.

Ethics statement

This study was approved by the Research Ethics Committee of Tabriz University of Medical Sciences under the approval code IR.TBZMED.REC.1403.543. Patient confidentiality was maintained throughout the study.

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Conflict of interests declaration

The authors declare that they have no conflicts of interest.

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Data availability statement

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Author contributions

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Consent for publication

Not applicable.

References

1. Chen Z, Brodie MJ, Ding D, Kwan P. Editorial: Epidemiology of epilepsy and seizures. Front Epidemiol 2023;3:1273163. doi:10.3389/fepid.2023.1273163
2. Beghi E. The Epidemiology of Epilepsy. Neuroepidemiology 2020;54(2):185–91. doi:10.1159/000503831
3. Lawal M, Omobayo H, Lawal K. Epilepsy: pathophysiology, clinical manifestations and treatment options. British Journal of Neuroscience Nursing 2018;14(2):58–72. doi:10.12968/bjnn.2018.14.2.58
4. Engelborghs S, D'Hooge R, De Deyn PP. Pathophysiology of epilepsy. Acta Neurol Belg 2000;100(4):201–13.
5. Henshall DC, Hamer HM, Pasterkamp RJ, Goldstein DB, Kjems J, Prehn JHM, et al. MicroRNAs in epilepsy: pathophysiology and clinical utility. Lancet Neurol 2016;15(13):1368–76. doi:10.1016/s1474-4422(16)30246-0
6. Patel DC, Tewari BP, Chaunsali L, Sontheimer H. Neuron-glia interactions in the pathophysiology of epilepsy. Nat Rev Neurosci 2019;20(5):282–97. doi:10.1038/s41583-019-0126-4
7. Ruan W, Yuan X, Eltzschig HK. Circadian rhythm as a therapeutic target. Nat Rev Drug Discov 2021;20(4):287–307. doi:10.1038/s41573-020-00109-w
8. Jin B, Aung T, Geng Y, Wang S. Epilepsy and Its Interaction With Sleep and Circadian Rhythm. Front Neurol 2020;11:327. doi:10.3389/fneur.2020.00327
9. Smyk MK, van Luijtelaar G. Circadian Rhythms and Epilepsy: A Suitable Case for Absence Epilepsy. Front Neurol 2020;11:245. doi:10.3389/fneur.2020.00245
10. Ramgopal S, Thome-Souza S, Loddenkemper T. Chronopharmacology of anti-convulsive therapy. Curr Neurol Neurosci Rep 2013;13(4):339. doi:10.1007/s11910-013-0339-2
11. Ben-Cherif W, Dridi I, Aouam K, Ben-Attia M, Reinberg A, Boughattas NA. Chronotolerance study of the antiepileptic drug valproic acid in mice. J Circadian Rhythms 2012;10:3. doi:10.1186/1740-3391-10-3
12. Niu R, Guo X, Wang J, Yang X. The hidden rhythms of epilepsy: exploring biological clocks and epileptic seizure dynamics. Acta Epileptol 2025;7(1):1. doi:10.1186/s42494-024-00197-w
13. Chiara F, Allegra S, Brescia I, Arrigo E, De Francia S. Influence of seasonal variation and gender on anti-epileptic drugs pharmacokinetics. The Italian Journal of Gender-Specific Medicine 2022;8(3):127–34. doi:10.1723/3927.39106
14. Loddenkemper T. Chrono-epileptology: time to reconsider seizure timing. Seizure 2012;21(6):411. doi:10.1016/j.

seizure.2012.05.013

15. Liu M, Ding J, Wang X. The interaction between circadian rhythm and epilepsy. Acta Epileptologica 2022;4(1):28. doi:10.1186/s42494-022-00094-0
16. Karoly PJ, Rao VR, Gregg NM, Worrell GA, Bernard C, Cook MJ, et al. Cycles in epilepsy. Nat Rev Neurol 2021;17(5):267–84. doi:10.1038/s41582-021-00464-1
17. Leung AK, Hon KL, Leung TN. Febrile seizures: an overview. Drugs Context 2018;7:212536. doi:10.7573/dic.212536
18. Batra P, Thakur N, Mahajan P, Patel R, Rai N, Trivedi N, et al. An evidence-based approach to evaluation and management of the febrile child in Indian emergency department. Int J Crit Illn Inj Sci 2018;8(2):63–72. doi:10.4103/ijciis.Ijciis_3_18
19. Paksu MS, Aslan K, Kendirli T, Akyildiz BN, Yener N, Yildizdas RD, et al. Neuroinfluenza: evaluation of seasonal influenza associated severe neurological complications in children (a multicenter study). Childs Nerv Syst 2018;34(2):335–47. doi:10.1007/s00381-017-3554-3
20. Gulcebi MI, Bartolini E, Lee O, Lisgaras CP, Onat F, Mifsud J, et al. Climate change and epilepsy: Insights from clinical and basic science studies. Epilepsy Behav 2021;116:107791. doi:10.1016/j.yebeh.2021.107791
21. Altimiras-Roset J, Brunet-Gómez A, Aragonès J, Roura-Poch P. [Influence of meteorological and chronological factors in epilepsy]. Rev Neurol 2014;59(8):345–8.