# PAPER DETAILS

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AUTHORS: Sinan ELIAÇIK, Serdar AYKAÇ

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# HEALTH SCIENCES **MEDICINE**

# Characteristics and effects of headaches on quality of life in individuals with epilepsy in Çorum province of Turkey

# Sinan Eliaçık, Serdar Aykaç

Department of Neurology, Faculty of Medicine, Hitit University, Çorum, Turkey

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#### ABSTRACT

**Aims**: Varying headache prevalence rates have been reported in individuals with epilepsy in the literature. This study was investigate the frequency and types of headaches in individuals with epilepsy, and the impact of headaches on the clinical features and quality of life in this patient group.

**Methods**: 150 individuals with epilepsy, 83 female and 67 male, were included in the study sample by random sampling method. Headaches were primarily defined as pre-ictal, ictal, and post-ictal headaches according to the temporal relationship with seizures. Headaches that were not temporally related to seizures were defined as inter-ictal headaches. Types and features of participants' headaches were evaluated using the headache questionnaire consisting of 35 questions. Individuals' quality of life was evaluated using the Quality of Life in Epilepsy Inventory (QOLIE-10).

**Results**: Of the 150 participants included in the study, 73.33% had generalized, 20% focal, and 6.66% combined generalized focal epilepsy, and 41.33% had accompanying headache complaints. Of the participants with headaches, 35.48% were male and 64.51% were female. Inter-ictal headache, which was detected in 72.58% participants, was the most common type of headache. Tension and migrainous type headaches were more common among participants with inter-ictal headache, whereas migrainous type headaches were more common among participants with inter-ictal headache. There were statistically significant differences in the scores obtained from all three subscales of QOLIE-10 inventory between the participants with and without headache. Accordingly, quality of life was worse in the headache group than in the headache-free group (p<0.05).

**Conclusion**: Although clinicians focus more on diagnosis and treatment in the context of epilepsy, the treatment of comorbidities is also important. In this context, it is likely that accurate diagnosis of headaches in individuals with epilepsy and treating headaches along with epilepsy will significantly reduce the burden of disease in this patient group.

Keywords: Headache, migraine, tension headache, epilepsy, quality of life

# INTRODUCTION

Diverse epidemiological findings have emerged from various studies on the prevalence of headaches among individuals diagnosed with epilepsy. Migraine, a frequent comorbidity of epilepsy, has been the focus of numerous research investigations. We aimed to explore the frequency and classification of headaches among individuals with epilepsy, as well as the impact of headaches on the clinical characteristics and quality of life in this population. This study was conducted in the Çorum Province of Turkey, focusing on patients attending neurology outpatient clinics.

# **METHODS**

This prospective, single-centre study involved patients with epilepsy assessed for headaches at the neurology outpatient clinics of Hitit University Erol Olçok Training and Research Hospital and initiated after Hitit University Faculty of Medicine Clinical Researches Ethics Committee (Date: 16.03.2023, Decision No: 2023-33), and adhered to the ethical guidelines established by the Declaration of Helsinki. All the participants provided informed consent.

The Kolmogorov-Smirnov test assessed the normal distribution of data, while the chi-square test, Pearson's correlation test, and Spearman's correlation rho coefficient were used for statistical analyses. All analyses were two-tailed, with p-values  $\leq 0.05$  indicating statistical significance.

Headache characteristics of patients with epilepsy were evaluated according to the International Headache Classification. Individuals with secondary headaches, symptomatic epilepsy, and intellectual disabilities were

Corresponding Author: Sinan Eliaçık, sinaneliacik@gmail.com



excluded. Ultimately, the sample consisted of 150 epilepsy patients (83 females and 67 males) attending neurology outpatient clinics, who were selected through random sampling. Headaches were categorized as pre-ictal, ictal, and post-ictal based on their temporal relationship with seizures, whereas headaches unrelated to seizures were classified as inter-ictal. Pre-ictal headaches were defined as those commencing within 24 hours before a seizure and lasting until seizure onset. Ictal headaches coincided with other seizure symptoms, and post-ictal headaches developed within 3 hours after a seizure, resolving within 72 hours. Epilepsy diagnoses followed the International League Against Epilepsy classification criteria, while migraine diagnoses followed the International Headache Society criteria.<sup>1-3</sup> Seizure types were determined based on electroencephalographic (EEG) findings and the patient's medical histories. Clinical and demographic data were collected, and headache types and characteristics were assessed using a 35-question headache questionnaire. The Quality of Life in Epilepsy Inventory (QOLIE-10), comprising 10 items, was used to evaluate the participants' quality of life.

The QOLIE-10, which measures the quality of life, features three subscales: effects of epilepsy, mental health, and role functioning. Higher QOLIE-10 scores signify a lower quality of life. Analyses compared the headache and headache-free groups and their respective subgroups.

# RESULTS

A total of 150 participants were included in the study, with 110 (73.33%) having generalized epilepsy, 30 (20%) having focal epilepsy, 10 (6.66%) having generalised focal epilepsy, and 62 (41.33%) reporting concurrent headache complaints. The average age of the sample was  $35.2\pm17.9$  years. The study population comprised 90 (60%) married and 60 (40%) single individuals. The average age of epilepsy onset in the study sample was  $15\pm10.4$  years, while the average duration of epilepsy was  $11.8\pm7.9$  years.

The headache group's mean age was  $32\pm10.3$  years. Among the 62 epilepsy patients with headaches, 22 (35.48%) were male and 40 (64.51%) were female; 14 (22.58%) had focal onset, 45 (72.58%) had generalised, and 3 (4.83%) had combined generalised and focal epilepsy. In the headache group, the mean duration of epilepsy was  $10.8\pm5.1$  years, and the mean age of epilepsy onset was  $14.03\pm10.3$  years. Forty-five (72.58%) patients received monotherapy, while 17 (27.41%) received polytherapy. Levetiracetam was the most commonly prescribed antiseizure medication in the headache group, followed by carbamazepine, valproic acid, lacosamide, topiramate, and zonisamide. In this group, the patients' headaches continued while they were using antiepileptic therapy. None of the patients were receiving prophylactic treatment other than the use of analgesics. Inter-ictal headache was the most prevalent headache type, occurring in 45 (72.58%) participants, followed by post-ictal headache in 11 participants and pre-ictal headache in six participants. No participants reported ictal headaches.

Patients with pre- and post-ictal headaches more frequently experienced migrainous-type headaches. Consequently, migraine headaches were identified in four patients with pre- and five patients with post-ictal headaches. Only three patients with pre-ictal headaches reported visual aura.

In the inter-ictal headache group, 20 (44.44%) patients experienced tension-type headache, 14 (31.11%) had migraine without aura, 5 (11.11%) had migraine with aura, 4 (8.88%) had mixed-type headache, 1 (2.22%) had cluster headache, and 1 (2.22%) had paroxysmal hemicranias headache. No significant differences were found between the subgroups in the headache group in terms of age, epilepsy duration, epilepsy onset age, seizure and epilepsy types, and EEG findings.

The average headache duration in the overall study group was  $5.1\pm4.3$  years. A majority (64.51%) of epilepsy patients with headaches were female. The average number of headache days in the last month in the headache group was  $3.2\pm0.9$  days. Paracetamol was the most commonly used medication for headaches (27.41%). Other simple analgesics used by the patients included naproxen, flurbiprofen, and etodolac.

Thirty patients (48.38%) experienced compressive or heavy headaches, and 28 (45.16%) reported throbbing headaches. Patients typically described migraine headaches as occurring in the frontal region of the head and/or around the eyes, regardless of left or right side. The average visual analog scale score in the headache group was 5±3.8. Twelve (19.35%) patients reported dizziness and unsteadiness during headaches. Nine patients described visual aura, and three patients reported sensory aura. Furthermore, 18 (29.03%) patients described allodynia as the most severe headache, with 12 (66.66%) complaining of mild allodynia. Ten (16.12%) patients believed fasting, 15 (24.19%) attributed stress, and 14 (22.58%) reported poor sleep as triggers for both seizures and headaches.

In the interictal headache group, 15 (33.33%) patients stated that headaches limited at least one day of their school, work, study, or social life; ten (22.22%) patients experienced headaches almost daily; ten (22.22%) patients attempted to sleep of their headaches; and 25 (55.55%) patients used analgesics for headache relief. None of the patients had medication overuse headache.

Factors such as sex, marital status, epilepsy type, and treatment modalities did not significantly affect the quality of life. However, patients with an income at or below the minimum wage level had significantly higher total QOLIE-10 scores than those above the minimum wage, indicating a positive correlation between income and quality of life. Statistically significant differences were observed in the scores obtained from all three QOLIE-10 subscales between patients with and without headaches. Comparing the headache and headache-free groups revealed statistically significant differences in all three dimensions of the QOLIE-10. Consequently, the quality of life was worse in the headache group than in the headache-free group (p<0.05). In the headache group, there was no statistically significant relationship between income level and headache.

In the headache group, no significant difference in quality of life was observed between subgroups with and without a temporal relationship with seizures. However, in cases with inter-ictal headaches, QOLIE-10 scores were higher, albeit not significantly, in the tension headache group than in the migraine group, indicating that the quality of life in tension headache patients was worse among individuals with epilepsy. The findings are summarized in Table 1.

#### DISCUSSION

Epidemiological findings indicate that individuals with epilepsy have an increased propensity for headaches, including migraine. These headaches may manifest before, during, or after a seizure, and seizures and headache episodes are often not simultaneous. The pathophysiological connections between epilepsy and headaches are intricate and remain incompletely understood.<sup>4</sup> A multicenter study conducted in Turkey involving 809 epileptic participants aged 6-40 found that 62.8% experienced headaches.<sup>5</sup> Regarding headache types, interictal headaches and migraines were most prevalent among patients with epilepsy. Headaches, including migraines, are reported in 29.5% of epilepsy patients and are among the most frequent comorbidities after anxiety and mood disorders.<sup>6</sup> In 2018, headaches were detected in 47.6% of epilepsy patients, with tensiontype headaches being the most common, followed by migraines with and without aura, stabbing headaches, cluster headaches, and other primary headaches.<sup>7</sup> Research on genetic and clinical features common to the etiopathogenesis of epilepsy and headaches has emphasised the imbalance of inhibitory and excitatory neurotransmitters.<sup>8-12</sup>

The migraine comorbidity in epilepsy has been extensively examined.<sup>13,14</sup> The prevalence of migraine-like headaches in patients with seizure-related headaches varies among studies.<sup>15,16</sup> A substantial association has been reported between migraine-like headaches and interictal migraines in seizure-related headaches.<sup>17</sup> Consistent with numerous studies in the literature, the present investigation found no significant relationship between sex, age, education level, marital status, epilepsy duration, seizure type, and QOLIE-10 scores. Although some studies, like this one, did not identify a relationship between epilepsy onset and duration and quality of life, others reported a decline in quality of life as the duration of epilepsy increased.<sup>18-20</sup> The negative correlation between low-income levels and quality of life found in this study aligns with the findings of other studies.<sup>21, 22</sup>

Stigmatisation is a factor that influences the quality of life of individuals with epilepsy. A stigmatisation study involving patients with epilepsy in Norway revealed that 56% felt stigmatised, with 70% internalizing or experiencing stigma at least once.<sup>23</sup> While the present study could not examine all factors, it sought to

Table 1. Demographic, clinical characteristics, and quality of life scores in epilepsy patients with and without headache								
		QOLIE-10 average score	Effects of epilepsy	Mental health	Role functioning			
Gender								
n=150	Female	$27.20 \pm 8.90$	$8.78 \pm 4.14$	8.7±2.56	9.06±4.30			
p>0.05	Male	26.04±10.09	$8.46 \pm 4.54$	8.61±2.69	9.71±4.33			
Marital status								
n=150	Single	27.65±9.10	9.09±4.14	8.43±2.44	10.13±4.45			
p>0.05	Married	26.17±9.73	8.09±4.06	8.19±4.16	9.16±4.52			
Income status								
n=150	Minimum wage and below	28.20±9.50	9.26±4.19	8.94±3.02	$10.20 \pm 4.38$			
p<0.05	Above the minimum wage	25.04±7.32	8.17±3.93	8.23±1.59	8.64±3.30			
The presence of headaches								
n=150	Headache-free group	22.00±7.80	7.10±3.59	$7.55 \pm 2.95$	$7.50 \pm 3.48$			
p<0.05	The group with headaches	26.94±9.22	8.57±4.33	9.03±2.39	9.43±4.00			
Interictal headache group								
n=45	Tension-type headache	26.31±10.06	8.68±4.38	8.01±2.45	9.46±4.03			
p>0.05	Migraine	25.01±7.37	7.72±3.46	$8.58 \pm 2.00$	8.44±3.75			

emphasise the diminished quality of life in epilepsy patients with headache. These disorders share numerous characteristics, and frequent recurrence in this population negatively affects quality of life. Therefore, it is crucial to consider shared etiopathogenesis when both disorders coexist and to plan treatments accordingly. Prophylactic treatment appropriate to headache was started for all patients in the headache group participating in the study. The absence of medication overuse headache in the study can be explained by the fact that epilepsy patients avoid excessive analgesic use because they think it may affect their current antiepileptic treatment.

Several limitations of this study should be considered when interpreting its results.

#### **Study Limitations**

- 1.A relatively small sample size may have reduced the generalizability of our findings to a broader population of patients with epilepsy. A larger sample size would enhance the statistical power and the external validity of the results.
- 2. The study was conducted at a single center, which may have introduced selection bias and limited the diversity of the patient population.
- 3. Study did not examine the effect of seizure frequency on the quality of life in detail.
- 4. Absence of comprehensive mental state evaluations may have limited our understanding

### CONCLUSION

In the context of epilepsy, clinicians often prioritise diagnosis and treatment of the primary condition, while the management of comorbidities, such as headaches, may receive less attention. The findings from this study emphasise the importance of accurately diagnosing and addressing headaches in individuals with epilepsy. By considering the complex relationships between epilepsy, headaches, and quality of life, a comprehensive treatment approach can be developed that addresses both the primary condition and its comorbidities. This integrated approach has the potential to significantly reduce the burden of disease in this patient population, ultimately improving their overall quality of life and well-being.

#### ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of Hitit University Faculty of Medicine Clinical Researches Ethics Committee (Date: 16.03.2023, Decision No: 2023-33).

**Informed consent:** Written consent was obtained from the patient participating in this study.

Referee Evaluation Process: Externally peer reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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

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