Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2024.304611.3477 Volume 30, Issue 7, Oct. 2024
Manuscript ID ZUMJ-2407-3477
DOI 10.21608/zumj.2024.304611.3477
Original article

Demographic and Characteristics of Primary Headache in Egyptian Epileptic Patients

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Submit Date 19-07-2024
Revise Date 23-07-2024
Accept Date 31-07-2024

Abstract

Background: Migraine is a chronic neurovascular illness marked by episodic headaches with autonomic symptoms, presented more in epileptic patients and the cause is unknown.

Objectives: The study aimed to investigate the different types of primary headache disorders among epileptic patients and demographic characteristics of those patients.

Subjects and methods: This comparative analytical prospective study was conducted at Neurology Department and Outpatients Epilepsy and Headache Clinics, Faculty of Medicine, Zagazig university on 69 cases with epilepsy who were allocated into two groups: group (1): 46 Epileptic patients suffering from primary headache disorder and group (2): 23 Epileptic patients without headache.

Results: There was substantial variance between the epileptic cases with migraine concerning post ictal timing of headache that was elevated in episodic migraine than chronic migraine. Dull aching headache, stress triggers, holocranial location of headache, monthly frequency of headache were substantially elevated in tension type headache than other groups. While throbbing headache was substantially elevated in migraine with aura and those without aura than tension type of headache , also aura, abnormal sleep as triggers for headache was substantially elevated in migraine with aura than other groups. There was substantial variation between epileptic cases with migraine regarding triggers ($p<0.05$). Stress was main trigger in episodic migraine, while work over load main trigger in chronic migraine.

Conclusion: Headache and epilepsy are common neurological illnesses, and their link is not well understood. Individuals with epilepsy may experience disabling headaches, which are a prevalent comorbidity that can add to their difficulties. Epileptic people are particularly prone to primary headaches. Despite headache may have a temporal link with one seizure attack, post-ictal headache is more frequent in individuals with active epilepsy and untreated.

Keywords: Primary Headache, Epilepsy, Migrane.

Introduction

Epilepsy and primary headache are the most frequent recurrent neurological conditions, both of them have similar features as episodic nature, certain triggering factors which may trigger both such as sleep deprivation, shared underlying pathogenic mechanisms or imbalance between inhibitory and facilitatory neurotransmitters and membrane channel function modification [1].

Migraine and epilepsy commonly co-exist in the same individuals , interestingly the prevalence of epilepsy in migraine cases ranges between 1-17% which is much higher than general population which ranges between 0.5-1% , and the migraine incidence increased in epileptic cases compared to those without epilepsy [2]. Furthermore one of these conditions may trigger or imitate the other as a result of their comorbidity [3].

At first appearance, it may appear unrelated. However, a rising investigation has revealed extensive links between these disorders. It may appear unusual that migraine occupies a place in the borderland of epilepsy, but this claim is backed by various pieces of data, including the fact that their differentiation is often difficult [4].

The variety of antiepileptic medications that work well for both conditions, some of which are used to prevent migraines, such as topiramate and valproic acid also provides evidence that the pathogenetic pathways underlying epilepsy and migraine are similar [5].

Visual signs of occipital seizures can be confused with visual auras in migraine, despite the fact that the majority of cases exhibit distinguishing characteristics. Visual auras in migraine are shown as colorless blinking lights, or more commonly as zig-zagging lines that begin in the center of the visual field and advances to the edge of the hemifield in 4 to 30 minutes. They are typically accompanied by scotoma [6].

A proper diagnosis is the first step to effectively treating any ailment. According to the findings of a recent research, neurologists underestimate the incidence of headaches in people with epilepsy. This finding implies that neurologists need to be more cognizant of the connection between epilepsy and headache. An EEG recording during the symptomatic phase is necessary if atypical or chronic headaches that do not improve with conventional treatment point to a potential epileptic cause [7].

The aim of this study was investigating the different types of primary headache disorders among epileptic patients.

Methods

This comparative analytical prospective study was conducted on 69 cases with epilepsy at Neurology Department and Outpatients Epilepsy and Headache Clinics, Faculty of Medicine, Zagazig university during the period from March 2023 to December 2023. Patients were given written informed consent, outlining the procedure and any potential risks, and IRB permission was obtained (Number: 10921). The research was conducted under the World Medical Association's Code of Ethics (Helsinki Declaration) for human research. Two groups of 69 participants, 21 males and 48 females, ranging in age from 22 to 53 years, were created: group (1) consisted of 26 epileptic patients with main headache disorder, and group (2) consisted of 23 epileptic patients without headache.

Individuals whose epilepsy has been verified by the diagnostic standards established by the International League Against Epilepsy (ILAE) [8], Participants in the study were to be at least 18 years old and have a verified diagnosis of primary headache condition as defined by the International headache society (IHS) third edition of the International Classification of Headache condition (ICHD-3) [9].

The study excluded cases with severe mental retardation, behavioural abnormalities, learning disabilities, unconfirmed diagnosis of single seizures, psychogenic seizures, or secondary epilepsy, cases with secondary headache disorders or medication overuse headache, patients who were medically unstable or in urgent need of medical attention, patients who had received any preventive migraine treatment within the previous week, patients who were under the age of 18, pregnant women, patients with obesity, diabetes mellitus, metabolic syndrome, autoimmune or inflammatory disorders, hypertension, or ischemic cerebrovascular disease were not included in the study.

The epilepsy sheet and the headache impact test 6 (HIT6) questionnaire were used to gather information about the patients' past. A general and neurological examination was also performed to confirm the type of headache and to determine its cause. Laboratory tests included the complete blood count , erythrocyte sedimentation rate, liver function tests , kidney function tests , and random blood sugar. Within a day of the migraine headache starting, two 10-milliliter blood samples were taken in the laboratory department of Zagazig University. These samples were placed in glass tubes with 1500 kallikrein inactivator units of trasylol and 35 micrograms of dipotassium EDTA. After being placed in an ice bath, the tubes were centrifuged for 15 minutes at 4°C at 2000×g. After the plasma was extracted from the cells, it was kept at -80°C and examined using an ELISA kit that was sold commercially.

The six-item HIT-6 questionnaire, which assesses the frequency of severe headaches, was completed by the subjects. The six items are scored on a frequency basis, with a total score ranging from 36 to 78. We made use of the HIT-6's verified Arabian translation. Based on the acquired HIT-6 score, the disability was assessed using the following four impact grades [10]: Little-to-no impact (grade 1: HIT-6 score: 36-49), moderate impact (grade 2: HIT-6 score: 50-55), substantial impact (grade 3: HIT-6 score: 56-59) and severe impact (grade 4: HIT-6 score: 60-78).

EEG data obtained using 21 surface electrodes positioned in accordance with the global 10-20 system. The EEG apparatus (XEROX, model number 900w, power 100-240 volts, serial number F1AC7B0046089, manufactured by Taipei country 234 Taiwan company) was used for recording, along with photic stimulation, hyperventilation for three minutes (if there are no contraindications).

Statistical Analysis:

All data were analyzed utilizing SPSS 23.0 for windows. Quantitative data were presented as the mean ± SD, median (range) and range and qualitative data were presented as absolute frequencies (number) & relative frequencies (percentage). Chi square test (X2).

Results

There was no substantial variation between epileptic patients with headache and those without regarding demographic data (Table 1).

There was no remarkable variation between epileptic cases with headache and those without headache regarding characters of epilepsy (Table 2).

There was substantial variance among the studied groups as regard post ictal timing of headache that was higher in migraine with aura and those without aura than tension type headache while there was no substantial variation concerning other characters and treatment of epilepsy (Table 3).

There was remarkable variance between the epileptic cases with migraine regarding post ictal timing of headache that was higher in episodic migraine than chronic migraine while there was no substantial variation regarding other characters and treatment of epilepsy (Table 4).

Dull aching headache, stress triggers, holocranial location of headache, monthly frequency of headache were substantially elevated in tension type headache than other groups. While throbbing headache was substantially elevated in migraine with aura and those without aura than tension type of headache. Also, aura, abnormal sleep as triggers for headache was substantially elevated in migraine with aura than other groups (Table 5).

There was substantial variance between epileptic patients with migraine regarding triggers ($p<0.05$). Stress was main trigger in episodic migraine, while work over load main trigger in chronic migraine. (Table 6).

Table 1: Demographic data of the studied groups

		Epileptic patients with headache (n=46)	Epileptic patients without headache (n=23)	P value
Age (years)	**Mean ± SD**	41.27± 8.41	39.56 ± 9.20	0.476
	Range	27-53	22-53	
Sex	**Male**	11 (23.9%)	10 (43.5%)	0.096
	Female	35 (76.1%)	13 (56.5%)	
Occupation	**Yes**	17 (37.0%)	9 (39.1%)	0.861
	No	29(63.0%)	14 (60.9%)	
Family history of epilepsy	**Yes**	18 (39.1%)	7 (30.4%)	0.479
	No	28 (60.9%)	16 (69.6%)	
Family history of headache	**Yes**	7 (15.2%)	2 (8.7 %)	0.728
	No	39 (84.8%)	21 (91.3%)	

Data expresses as mean, (standard deviation), (range), t, Student 't test, compared between groups, $p>0.05$ no significant, χ 2: Chi-square test, f:fisher exact test

Table 2: Characters of epilepsy of the studied groups

	Epileptic patients with headache (n=46)	Epileptic patients without headache (n=23)	P value
Age of onset Mean ± SD range	22.34 ± 5.85 11-32	21.69 ± 5.88 11-31	0.565
Type of epilepsy			
Focal	32 (69.6%)	12 (52.2%)	0.299
Generalized	10(21.7%)	9 (39.1%)	
Focal with secondary generalization	4 (8.7%)	2 (8.7%)	
Frequency of epileptic attacks			
Several attack /week(most frequent)	6 (13.0%)	1 (4.3%)	0.771
One attack / month	8 (17.4%)	5 (21.7%)	
One attack / year	16 (34.8%)	8 (34.8%)	
Less than one attack per year (least frequent)	16 (34.8%)	9 (39.1%)	
Duration of attack (min) Median (range)	2.26 ± 1.17 2(1-4)	2.82 ± 1.07 3(1-4)	0.053 u
Number of used antiepileptic drugs			
Monotherapy	22 (47.8%)	7 (30.4%)	0.374
Polytherapy	22 (47.8%)	15 (65.2%)	
No treatment	2 (4.4%)	1 (4.4%)	
Data expresses as mean, (standard deviation) ,(range), t, Student 't test ,or Mann-Whitnney u test compared between groups, p>0.05 no significant, χ 2 :Chi-square test, f:fisher exact test			

Table 3: Characters and treatment of Epileptic patients with headache

	Epileptic patients with headache (n=46)			P value
	Migraine with aura (n=8)	Migraine without Aura (n=20)	Tension type headache (n=18)	
Age of onset **Mean±SD** **Range**	25.25±0.89 24-26	22.7±6.48 13-32	20.67±5.86 11-29	0.167
Type of epilepsy				
Focal	6(75%)	14 (70%)	12 (66.7%)	0.137
Generalized	0 (0%)	4 (20%)	6(33.3%)	
Focal with secondary generalization	2 (25%)	2 (10%)	0 (0%)	
Frequency of epilepsy attacks				
several attacks /week (most frequent)	0 (0%)	4 (20%)	2 (11.1%)	0.557
one attack / month	0 (0%)	4 (20%)	4 (22.2%)	
one attack / year	4 (50%)	6 (30%)	6 (33.3%)	
less than one attack per year (least frequent)	4 (50%)	6 (30%)	6 (33.3%)	
Duration of attack (min) **Mean±SD** **Range**	2.0±1.3 1.5(1-4)	2.50±1.2 2.5(1-4)	2.12 ±1.02 2(1-4)	0.485u

	Epileptic patients with headache (n=46)			P value
	Migraine with aura (n=8)	Migraine without Aura (n=20)	Tension type headache (n=18)	
Timing of headache **Pre ictal** **Ictal** **Post ictal** **Inter ictal**	2 (25%) 0 (0%) 6 (75%) 0 (0%)	0 (0%) 0 (0%) 14 (70%) 6 (30%)	4(22.2) 2(11.1%) 10 (55.6%) 2 (11.1%)	**0.015***
Number of Treatment				
Monotherapy	2(25%)	10 (50%)	10(55.6%)	0.263
Polytherapy	6(75%)	8 (40%)	8 (44.4%)	
No treatment	0 (0%)	2 (10%)	0 (0%)	
Data expresses as mean, (standard deviation) ,(range), t, Student 't test, or u: Mann-Whitnney u test compared between groups, χ 2 :Chi-square test, f:fisher exact test, p>0.05 no significant, *p<0.05 significant				

Table 4: Characters and treatment of epileptic patients with migraine

	Epileptic patients with migraine (n=28)		P value
	Episodic migraine (n=16)	Chronic migraine (n=12)	
Age of onset **Mean±SD** **Range**	24±5.3 13-30	22.66±6.08 15-32	0.542
Type of epilepsy			
Focal	10 (62.5%)	10(83.3%)	0.174
Generalized	4 (25.0%)	0	
Focal with secondary generalization	2 (12.5%)	2 (16.7%)	
Frequency of attacks			
>1 week	2 (12.5%)	2 (16.7 %)	0.321
>1 month < 1 week	2 (12.5%)	2 (16.7%)	
>1 year < 1 month	4 (25.0%)	6 (50%)	
< 1 year	8 (50%)	2 (16.7%)	
Duration of attack (min) **Mean±SD** **Range**	2.8±1.2 1-4	1.8 ±1.1 1-4	0.066
Timing of headache **Pre ictal** **Ictal** **Post ictal** **Inter ictal**	2 (12.5%) 0 (0%) 14 (87.5%) 0 (0.0%)	0 (0.0%) 0 (0%) 6 (50.0%) 6 (50.0%)	**0.004***
Monotherapy	8 (50%)	4(33.3%)	0.211
Polytherapy	8 (50%)	6 (50.0%)	

	Epileptic patients with migraine (n=28)		P value
	Episodic migraine (n=16)	Chronic migraine (n=12)	
No treatment	0 (0%)	2 (16.7%)	
Data expresses as mean, (standard deviation) ,(range), t, Student 't test, or u: Mann-Whitnney u test compared between groups, χ 2 :Chi-square test, f:fisher exact test, p>0.05 no significant, *p<0.05 significant			

Table 5**:** Characters and treatment of Epileptic patients with headache

	Epileptic patients with headache (n=46)			P value
	Migraine with aura (n=8)	Migraine without Aura (n=20)	Tension type headache (n=18)	
Characters of headache				
No	0 (0%)	0 (0%)	0 (0%)	**<0.001***
Throbbing	8 (100%)	20 (100%)	4 (22.2%)	
Dull aching	0 (0%)	0 (0%)	14 (77.8%)	
Aura				
Yes	8(100%)	0 (0%)	0 (0%)	**<0.001***
No	(0.00%)	20 (100%)	18 (100%)	
Triggers				**0.001***
stress	0 (0%)	6 (30%)	12 (66.7%)	
Abnormal sleep	6 (75%)	4 (20%)	4 (22.2%)	
Work load	2 (25%)	10 (50%)	2 (11.1%)	
Location				
Unilateral	4 (50%)	14 (70%)	4 (22.2%)	
Bilateral	4 (50%)	6 (30%)	0 (0%)	**<0.001***
Holocranial	0 (0%)	0 (0%)	14 (77.8%)	
Duration of headache (hr)	10±8.6 4-24	14±9.1 6-36	18±15 2-48	0.152
Headache impact test-6 score	74.0±6.18 65-80	66.6±8. 4 54-78	50.75±9.96 43-74	**<0.001***
Frequency of headache				
Daily	2 (25%)	10 (50%)	0 (0.0%)	
Weekly	4 (50%)	6 (30%)	7 (33.3%)	**0.006***
Monthly	2 (25%)	4 (20%)	11 (55.6%)	
Data expresses as mean, (standard deviation) ,(range), t, Student 't test, or u: Mann-Whitnney u test compared between groups, χ 2 : Chi-square test , p>0.05 no significant, *p<0.05 significant				

Table 6: Characters and treatment of epileptic patients with migraine

	Epileptic patients with migraine (n=28)		P value
	Episodic migraine (n=16)	Chronic migraine (n=12)	
Characters of headache			
Throbbing	16 (100.0%)	12 (100.0%)	-
Aura			
Yes	6 (37.5%)	2 (16.7%)	0.401
no	10 (62.5%)	10 (83.3%)	
Triggers			
Stress	6 (37.5 %)	0 (0.0%)	**0.026***
Abnormal sleep	6 (37.5%)	4 (33.3%)	
Work load	4 (25.0%)	8(66.7%)	
Location			
Unilateral	12 (75.0%)	6 (50.0%)	0.241
Bilateral	4 (25.0%)	6 (50.0%)	
Duration headache (hr)	15.5±10.8 4-36	9.33±3.9 6-16	0.22
Headache impact test-6 score	70.1±6.8 62-78	66.83±10.3 54-80	0.316

Data expresses as mean, (standard deviation),(range), t, Student 't test, or u: Mann-Whitnney u test compared between groups, $\chi 2$:Chi-square test , $p>0.05$ no significant, *$p<0.05$ significant

Discussion

The epilepsy is a brain condition known to be marked by a persistent propensity to produce epileptic seizures as well as the disease's psychological, neurobiological, cognitive, and social repercussions , it is one of the most prevalent neurological disorders in the world, impacting about 50 million individuals. Compared to cases without epilepsy, those who have the condition are far more likely to report having a poor health-related quality of life (HRQOL). Determining the burden of epilepsy is a more complicated process that takes into account not just physiological dysfunction but also psychological and social dysfunction in addition to epileptic episodes [11].

The quality of life is negatively impacted by a number of comorbidities, which can range from uncommon physical conditions like asthma or digestive issues to mental or cognitive impairment. Headache, particularly migraine, is among the most prevalent co-occurring conditions in epilepsy. About 24% of people with epilepsy also suffer from migraines. In addition, individuals with epilepsy had a 2.4-fold higher likelihood of receiving a migraine diagnosis compared to the general population. Conversely, the incidence of epilepsy in migraineurs ranges from 1 to 17%, which is significantly increased than the incidence of epilepsy in the general population [4].

Primary headache and epilepsy have a reciprocal relationship in which one can occur before or later, or even simultaneously. Headache episodes are temporally associated to the incidence of epileptic seizures, occurring as ictal, pre-, post-, or inter-ictal occurrences. Epilepsy and headaches frequently coexist [12].

The aim of this study was to investigate the different types of primary headache conditions among epileptic patients.

In the current study we found that there was no substantial variance between epileptic cases with headache and those without regarding age and sex.

In agreement with our findings, Han [2] stated that there was no remarkable variation between the migraine and control groups in age and gender. Alemam and his colleagues. [13] showed that there was no substantial variance was found among migraine cases and controls regarding age and sex. Mameniškienė and his colleagues.[14] revealed that the frequency of headaches among individuals with epilepsy did not differ statistically significantly based on a person's sex.

Unlikely, Duko and his colleagues.[12] revealed that, in comparison to men, women had a significantly greater pooled prevalence of headaches among epilepsy patients. Steiner and his colleagues. [15] established that headaches are typically more common in women than in men in the general population. This could be clarified by the fact that sex hormones are linked to primary headaches like migraines. In females, sex hormones impact the cells surrounding the trigeminal nerve and the associated cerebral vasculature. Particularly crucial for sensitising these cells to migraine triggers are the estrogens.

In the current study, we found that the variances between epileptic cases with and without headaches in terms of age at onset, type of epilepsy, duration of epilepsy, frequency of attacks, length of attack, and quantity of antiepileptic medications taken were statistically insignificant.

In the same context, Osama and his colleagues.[16] observed that the type of headache and medication type had a statistically negligible connection. The monotherapy group experienced significant headache impact more frequently than the polytherapy group, although there was no remarkable variance. Mainieri and his colleagues.[1] also found that individuals treated with polytherapy experienced headaches more frequently, and they hypothesised that patients who are refractory to multiple treatments may experience headaches frequently as well.

On the other hand, Sayed and his colleagues.[17] revealed that the age at which epilepsy began, the length of the epilepsy, the kind of epilepsy, the frequency of seizures, and the EEG results were all statistically substantially varied between the two groups. However, there were no substantial variations between the two groups' family histories of headaches.

In the current study we found that there was insignificant difference among group with migraine with aura, group without aura, group with tension type headache, chronic and episodic migraine regarding age, sex and family history of epilepsy.

Mameniškienė and his colleagues. [14] reported that there were no variations in occurrence by sex; tension-type headaches were the most prevalent form found. Migraines were the second most prevalent type of headache among individuals with epilepsy. Sayed and his colleagues.[17] reported that regarding headache types, they discovered that migraines including, migraines without aura, migraines with aura, and probable migraines were the most common in cases with epilepsy. Tension-type headaches were the second most common kind.

We found in our study that there was a substantial variance in post-ictal headache timing between the analysed groups, with episodic migrainers experiencing a higher post-ictal timing of headache than chronic migrainers.

Similar findings were obtained by Osama and his colleagues.[16] who demonstrated that cases with focal to bilateral tonic-clonic seizures had significantly more inter-ictal headaches ($p=0.04$) based on the type of seizure than patients with focal and primary generalised seizures; there was no correlation between the types of seizure and pre- or post-ictal headaches. Sayed and his colleagues.[17] stated that in terms of the period of headache, post-ictal headache is the most prevalent form, followed by inter-ictal and, less frequently, pre-ictal headache. This could be attributed to the increased ease with which cortical spreading depression can be attained in the post-seizure phase and the triggering influence of epileptic seizures on headache occurrence. Mainieri and his colleagues. [1] claimed that patients with migraineurs had a substantial correlation with post-ictal headache (post-IH). Additionally, there was a strong correlation found between post-IH and tonic-clonic seizures, high seizure frequency, and antiepileptic polytherapy.

Our current findings clearly revealed that dull aching headache, stress triggers, holocranial location of headache, monthly frequency of headache were substantially elevated in tension type headache than other groups while throbbing headache was substantially elevated in migraine with aura and those without aura than tension type of headache. Also, aura, abnormal sleep as triggers for headache was substantially elevated in migraine with aura than other groups. There was no substantial variance between episodic migraine and chronic migraine regarding characters and treatment of headache

Conclusion

The link between headache and epilepsy, two prevalent neurological illnesses, is still not well understood. Disabling headaches are one of the most prevalent comorbidities that epileptic patients experience and can further stress them. Among those with epilepsy, primary headaches are common. Post-ictal headache is more common in people with active epilepsy and is often undertreated, despite the fact that headaches can have any temporal association with a single seizure episode. Additional studies on large sample size and multicenters are required.

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Citation

Elmotayam, A., Mohammed, H., Saleh, M., Fahmy, A. Demographic and Characteristics of Primary Headache in Egyptian Epileptic Patients. *Zagazig University Medical Journal*, 2024; 30(3198-3206): 3198-3210. doi: 10.21608/zumj.2024.304611.3477