Original Article

Pattern, Frequency, and Correlates of Seizure-Related Headache in Enugu, Southeast Nigeria

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Abstract

Introduction: The association of headache and epilepsy has long been recognized in clinical practice. Primary headache, especially migraine, is episodic and shares common genetic and pathologic pathways. Current definition of epilepsy underscores the impact of other neurologic comorbidities such as headache in the burden of epilepsy. There is a paucity of data on seizure-related headache in Nigeria. **Objectives:** The objectives of this study were to describe the pattern and correlates of seizure-related headache among people with epilepsy (PWE) attending medical outpatient clinics in Enugu, Southeast Nigeria. **Materials and Methods:** Data were collected from the epilepsy register of PWE attending medical outpatient clinics in two teaching hospitals in Enugu. Data were analyzed using the SPSS statistical software. **Results:** The overall prevalence of headache among PWE was 48% (73/152). A history of migraine was reported in 3 (2%) of the patients. The commonest form of headache was postictal headache 24 (15.8%). Preictal headache was reported by 16 (10.5%), out of which 4 (4.5%) were reported as possible auras. Headache pain was mainly aching 44 (60.3%) and generalized 41 (56.2%). Seizure-related headaches correlated with medical history of alcohol use (P = 0.04). Positive history of head injury and epilepsy-related head injury weakly correlated with having headache (P = 0.07), respectively. **Conclusion:** PWE often have seizure-related headaches. Such headaches occur mainly after seizures. Careful evaluation of PWE should include the burden and impact of headache in the lives of these patients.

Keywords: *Epilepsy, headache, migraine, Nigeria, seizures*

Introduction

Epilepsy is a neurologic disorder characterized by an enduring predisposition to generate epileptic seizures and is usually associated with neurobiological, cognitive, psychological, and social consequences.[1] This definition of epilepsy underscores the impact of other neurologic comorbidities in the burden of epilepsy. Because seizures are paroxysmal, most people with epilepsy (PWE) appear normal in-between seizures; hence, the impact of comorbidities may easily be overlooked. Headache is a common neurologic disorder associated with epilepsy.[2,3] Primary headaches, especially migraine, have long been associated with epilepsy.[3] Both migraine and epilepsy share a common genetic predisposition. Some genetic mutations, such as CACNA1A and ATP1A2, have been described in people with both epilepsy and migraine,[4] and both disorders have similar pathophysiologic mechanisms including an imbalance between excitatory and

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inhibitory factors that result in spells of altered brain function and autonomic symptoms.[2] Clinically, both epilepsy and migraine have similar features and follow usually reliable preictal, ictal, and postictal manifestations.[5] Furthermore, some anti-seizure drugs such as topiramate are effective in the treatment of primary headaches.[6]

In developing regions such as Sub-Saharan Africa, where epilepsy is underdiagnosed and undertreated, the burden of headache in PWE is likely to be huge.[7,8] The prevalence of headache in epilepsy varies depending on headache subtypes, time of headache, and types of seizures.[9-11] Migraine disorders were reported in up to 31.7% of PWE.[7,10-14] PWE are 2.4 times more likely to be diagnosed with migraine than are people in the general population.[13]

The association between epilepsy and headache has been described as bi-directional,[14,15] and cortical cellular hyperexcitability is assumed to be the common pathophysiological mechanisms between seizures and headache.[16] In migraine, for instance, hyperexcitability has been related to cortical spreading depression, whereas in seizures it has been related to hypersynchronous neuronal discharges.[17,18]

Seizure-related headaches may be classified as interictal, ictal, preictal, and postictal.[17,18] Interictal headaches in PWE are common and tend to occur independent of seizures[10,11,19,20]; nevertheless, it may also be the only ictal manifestation of an epileptic seizure.[21,22] Infections may cause headaches and trigger seizures which may appear as seizure-related. Headache is also a common side effect of some anti-epileptic drugs.[23] Preictal headache may represent an aura in some focal seizures.[11]

The co-occurrence of epilepsy and headache (primary or secondary) will increase the burden of epilepsy. This burden may be higher in women than men, and peak in the second and third decades of life corresponds to the peak ages of epilepsy and primary headache.

The general aim of this study was to describe the pattern and correlates of seizure-related headache among PWE attending medical outpatient clinics in Enugu, Southeast Nigeria.

Materials and Methods

This cross-sectional study was performed in the medical outpatient clinics of the University of Nigeria Teaching Hospital Enugu and Enugu State University Teaching Hospital. Data were collected from the epilepsy register of PWE attending the medical outpatient clinic of both hospitals. All patients gave their consent before recruitment into the epilepsy register database. Data were retrieved from the register using a structured questionnaire that included sociodemographic variable, history of seizure-related headaches, history of primary headaches as well as other variables. Patients with psychogenic seizures or suspected psychogenic seizures were not included in the database of the register and thus were also excluded from the index study. Questionnaires were filled by the key investigator or research assistants. Based on the available information in the database, PWE with cognitive impairment and those with single epileptic seizures were not included in the current study. Cases of incomplete data or illegible data were also excluded.

Headache was classified based on the time of occurrence relative to an epileptic seizure. Interictal seizures were defined as headaches that occur long (at least 24 h) before or after seizures. The subtype of headaches was classified based on when most headache occurred based on clients' subjective feelings. Preictal headache was defined as headache that occurs in close association with seizures or evolving into a seizure. Ictal headache was defined as headache that occurs when seizure has started in clients with focal seizures, and postictal headache was defined as headache that occurs after seizures or on awakening from postictal sleep. Ethical clearance was obtained from the Ethics Committee of the teaching Hospitals.

Sample size was calculated using the Cochrane formula[24]: $N= (z^2pq)/e^2$, where N is the required sample size, z the 95% confidence level, and e the desired level of precision of 0.05. p is 6.4% which is the estimated prevalence of migraine in Enugu[20] and q is the value $1-p$.

$N = (1.96)^2 (0.064 \times 0.936)/0.0025 = 81.4$. Assuming 90% response rate, in order to compensate for attrition, a minimum of 89 patients were selected from the pool of medical outpatients registered in the unit.

Statistical methods

The SPSS version 22 (IBM Corporation, New York, NY, USA) was used for database management and statistical analysis. Data were presented in tables. The statistical methods included Student's t-test for unpaired observations and χ^2 test for comparison of categorical data. Distribution of headache subtypes and types of seizures were calculated as the percentage of participants. Mean and median were calculated and values were presented as graphs where applicable. In all, $P < 0.05$ was regarded as statistically significant. Conclusions were drawn at this level of significance at 95% confidence level.

Results

One hundred and fifty-two PWE were reviewed during the period of the study. A little more than half were males (53.3%), whereas 71 (46.7%) were females. The male-to-female ratio of those screened was 0.9:1. Most participants were aged 20–34 years with a mean age of 33.6 (15.3) years. Males were older than females by almost 7 years ($P < 0.01$). Other characteristics of the population are shown in Table 1. Most of them stopped at (or completed) secondary school (7–12 years of formal education). Medical comorbidities and risk factor for epilepsy showed that head injury was the commonest risk factor reported. Hypertension was noted in 12.5% and stroke in 6.6%. Alcohol was used by 30.3% and 0.1% sniffed glue [Table 1].

Seizure characteristics

Table 2 shows some relevant seizure characteristics. Epilepsy on an average started more than 10 years earlier in females ($P < 0.01$). The age of onset of epilepsy is shown in Figure 1. The mean age of onset was lower in females ($P < 0.01$). About 11.2% of the patients started having seizures after 49 years (18.5%

Table 1: Age and gender distribution of the patients

Gender	Male (%)	Female (%)	Total (%)	*P*-value
N (%)	81 (53.3)	71 (46.7)	152 (100)	0.37
Age (years)				
Mean age (sd)	36.9 (17.4)	29.7 (14.2)	33.6 (15.3)	0.01
Median age	30	25	27	
Age group				
<20	5 (26.1)	10 (14.1)	15 (9.9)	
20–24	18 (33.3)	21 (29.6)	39 (25.7)	
25–29	14 (17.3)	15 (21.1)	29 (19.1)	
30–34	9 (11.1)	12 (16.9)	21 (13.8)	
35–39	9 (11.1)	12 (16.9)	12 (7.9)	
40–44	3 (3.7)	3 (16.9)	5 (3.3)	
45–49	5 (6.2)	2 (2.8)	7 (4.6)	
50–54	5 (6.2)	1 (1.4)	6 (3.9)	
55–59	4 (4.9)	1 (1.4)	5 (3.3)	
≥60	9 (11.1)	4 (5.6)	13 (9.9)	
Level of education				
No education	10 (12.3)	5 (7)	15 (9.9)	
Primary	27 (33.3)	5 (7)	32 (21.1)	
Secondary	31 (38.3)	49 (6)	80 (52.6)	
Tertiary	13 (16)	12 (16.9)	25 (16.4)	<0.01
Level of education				
Hypertension	11 (13.6)	8 (11.3)	19 (12.5)	
Stroke	9 (11.1)	1 (1.4)	10 (6.6)	
Diabetes	2 (2.5)	1 (1.4)	3 (2)	
HIV/AIDS	3 (3.7)	—	3 (2)	
Dementia	5 (6.2)	2 (2.8)	7 (4.6)	
Mental retardation	1 (1.2)	3 (4.2)	4 (2.6)	
Alcohol abuse	3 (3.7)	2 (2.8)	5 (3.3)	
Ataxia	1 (1.2)	—	1 (0.7)	
Blindness	—	1 (1.4)	1 (0.7)	
Down's syndrome	—	1 (1.4)	1 (0.7)	
History of head injury	16 (19.8)	16 (22.5)	32 (21.1)	
History of brain surgery	1 (1.2)	1 (1.4)	2 (1.3)	
Heart failure	1 (1.2)	—	1 (0.7)	
Rheumatoid arthritis	—	1 (1.4)	1 (0.7)	
Substance use				
Alcohol	34 (42)	12 (16.9)	46 (30.3)	
Cigarette	7 (8.6)	3 (4.2)	10 (6.6)	
Snuff	7 (7.4)	—	7 (4.6)	
Marijuana	6 (7.4)	—	7 (4.6)	
Glue	—	1 (1.4)	1 (0.7)	

Table 2: Gender distribution of seizure characteristics

Gender	Male (%)	Female (%)	Total (%)	*P*-value
Age of onset				
Mean age (sd)	26.3 (21.7)	14.4 (14.9)	20.9 (19.7)	<0.01
Median age	18	12	17	
Seizure type				
Focal	40 (49.4)	44 (62)	84 (55.3)	
Generalized	41 (50.8)	27 (38)	68 (44.7)	0.12
Last seizure episode				
< 24 h	17 (21)	20 (28.2)	37 (24.3)	
1–7 days	22 (27.2)	12 (16.9)	34 (22.4)	
1–4 weeks	15 (18.5)	12 (16.9)	27 (17.8)	
1–6 months	12 (14.8)	11 (15.5)	23 (15.1)	
>6 months	8 (9.9)	8 (11.3)	16 (10.5)	
Do not remember	7 (8.6)	8 (11.3)	15 (9.9)	0.7
Total	81 (53.3)	71 (46.7)	152 (100)	

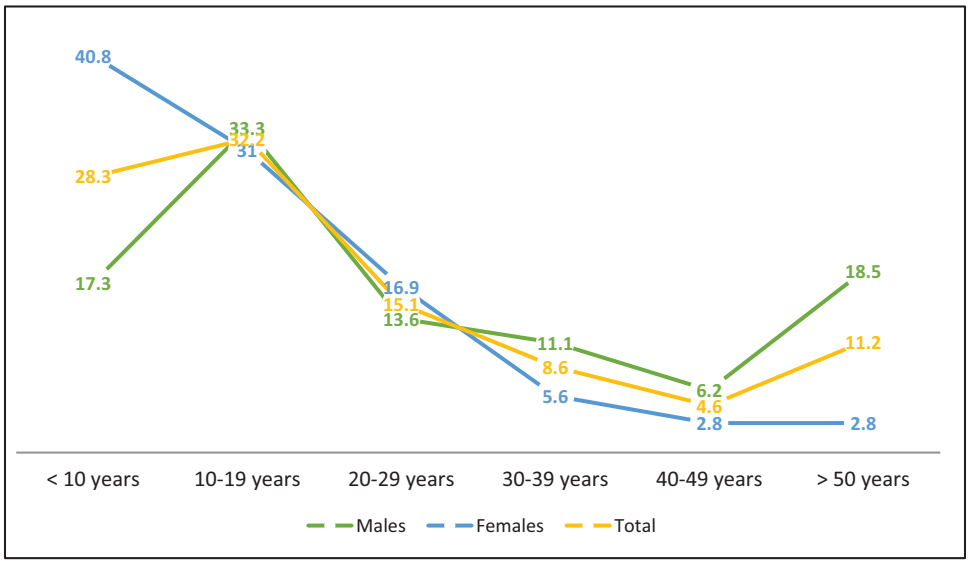

Figure 1: Age of onset of epilepsy (%)

males and 2.8% females). Most patients had clinical features suggestive of focal seizures but this was not statically significant. About 24.3% (37) visited the clinic less than 24 h after having seizures, whereas 6-month seizure freedom was 9.9%.

Seizure-related headaches

Pattern and gender distributions of headache are shown in Table 3. Three out of the 152 PWE reported a past medical history of migraine and 48% had headaches overall. There was no statistical difference on the gender distribution of headache occurrence ($P = 0.36$). Most headaches occurred after seizures 24 (15.8%), followed by preictal headache was reported by 16 (10.5%). Four (25%) of those with preictal headache reported a headache that frequently ended with seizures (possible ictal headache). Interictal headache was reported in 20 (13.2%) of the subjects, whereas 13 (8.6%) reported having experienced all forms of headache. Subjective assessment of headache revealed that they were mainly aching 44 (60.3%), generalized 41 (56.2%), and less likely to be occipital (9.6%). The proportion of headache type by timing is shown in Figure 2. Seizure-related headaches correlated with medical history of alcohol use ($P = 0.04$). Positive history of head injury and epilepsy-related head injury weakly correlated with having headache ($P = 0.07$, respectively) [Table 4].

Discussion

Headache and epilepsy are the two common neurologic disorders reported in adult Nigerians.[25,26] The severity of both disorders varies widely and may be complicated by one another in the same subject. The frequency and pattern of seizure-related headache, however, has not been studied in the country.

The general characteristics of the subjects as well as seizure characteristics are similar to those of previous

Table 3: Characteristics of seizure-related headaches

Gender	Male (%)	Female (%)	Total (%)	*P*-value
History of headaches	37 (49.2)	36 (52.1)	73 (48)	0.36
History of migraine	2 (2.5)	1 (1.4)	3 (2)	0.55
Timing of headaches				
Preictal	7 (8.6)	9 (12.7)	16 (10.5)	
Headache aura (ictal)	3 (4.3)	1 (2.8)	4 (4.5)	
Postictal	13 (16)	11 (15.5)	24 (15.8)	
Interictal	12 (4.8)	8 (11.3)	20 (13.2)	
All types	5 (6.2)	8 (11.3)	13 (8.6)	0.68
Quality of pain				
Aching	20 (54.1)	24 (66.7)	44 (60.3)	
Throbbing	15 (40.5)	11 (30.6)	26 (35.6)	
Pulling	2 (5.4)	1 (2.8)	3 (4.1)	0.52
Location of pain				
Frontal	6 (16.2)	7 (19.4)	13 (17.8)	
Temporal	2 (5.4)	6 (16.7)	8 (11)	
Occipital	5 (13.5)	2 (5.6)	7 (9.6)	
Generalized	22 (59.5)	19 (52.8)	41 (56.2)	
Unspecified	2 (5.4)	2 (5.6)	4 (5.5)	0.47
Total	81 (53.3)	71 (46.7)	152 (100)	

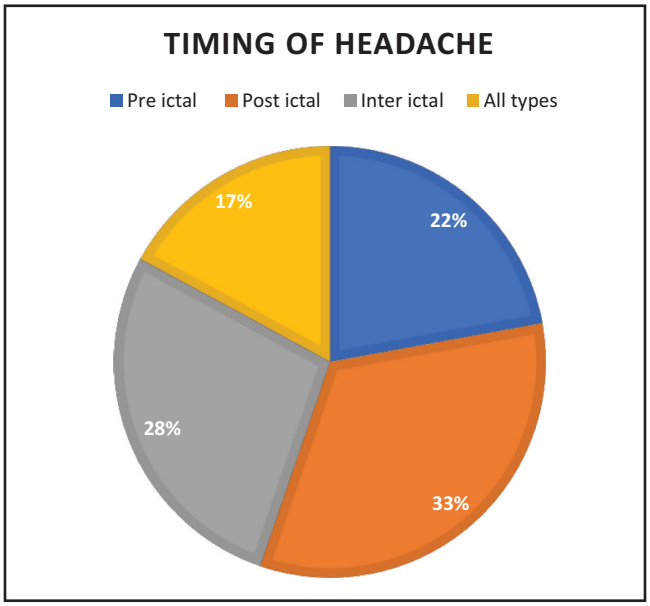

Figure 2: Timing of headaches

studies and reports from the African continent[25-28]; however, there was a small peak after 49 years (11.2%). This may be related to the wide range of comorbidities reported in this study; many of which are strong risk factors for epilepsy in older adults. This finding may suggest a changing pattern in the age of onset and etiology of epilepsy. We also recorded a high rate of head injury among these patients, a factor which is supported by high rates of road traffic accidents and violence in the community.[29,30] Substance use has long been recognized as a cause of epilepsy,[31] and this study supports that. Some of the substances used by the patients may be due to epilepsy-related mood problems. Finally, it is also important to note that these substances are possible causes of headaches.[32,33]

Seizure characteristics showed a younger mean age of onset in females. This may be attributed to a better health-seeking behavior among females. Another possible reason may be the high number of cardiovascular diseases and stroke which are traditionally commoner in males and are known to occur later in life. More PWE had seizures that could be clinically characterized as focal reflecting the high rates of epilepsy risk factors, especially head injury reported in the study. A previous study has reported a higher rate of focal seizures in the region.[26] Six-month seizure freedom in the index study was a mere 9.9%, whereas 24.3% reported within 24 h of seizures. Local experiences suggest that assessing seizure control among Nigerians living with epilepsy is difficult because of patients get lost to follow-up and many stop their medications arbitrarily.[28] Thus, reasons for poor seizure control many range from non-adherence to medications, use of non-orthodox means of treatment, and use of fake drugs.[34,35]

Review of headache characteristics did not show any no gender differences in the distribution of the various variables studied. The overall prevalence of headache in PWE was 48% similar in males and females. A study from Lithuania reported a higher prevalence of headache in PWE, but like the index study, there was no statistically significant sex-related difference in the prevalence of primary among PWE.[8] In community-based studies, the prevalence of primary headache is usually greater in females than in males.[25]

Table 4: Correlates of seizure-related headaches

Gender	*r* (*P*-value)
Age	−0.03 (0.7)*
Gender (1 male, 2 females)	0.05 (0.53)**
Age of onset of epilepsy	−0.12 (0.89)*
History of head injury (1 yes, 2 no)	−0.15 (0.07)**
Stroke (1 yes, 2 no)	0.14 (0.08)*
Hypertension (1 yes, 2 no)	0.05 (0.58)*
Use of tobacco (1 yes, 2 no)	−0.11 (0.17)*
Alcohol use (1 yes, 2 no)	**−0.17 (0.04)***
History of epilepsy-related head injury (1 yes, 2 no)	−0.15 (0.07)*

*Pearson's correlation statistic

**Pearson's correlation statistic

About 2% in the index study had a previous history of migraine. Epidemiologic connections between migraine and epilepsy have long been established.[7,9,19,20] The prevalence of epilepsy in people with migraine ranges from 1% to 32.9% with a median of 5.9%, while the prevalence of migraine in PWE from 8% to 15%.[7-9,12,19,20] Ottman and Lipton[13] reported a migraine prevalence of 24% among PWE and 26% in the relatives with epilepsy. They also found that migraine was 2.4 times higher in persons with epilepsy than in persons without epilepsy. The risk of migraine in epilepsy is elevated in both idiopathic and symptomatic epilepsy.[13] The small proportion with a history of migraine in the index study may suggest that headache-related problems might have been neglected in favor of epilepsy, as in most people with epilepsy and migraine, attacks tend to occur independently.[18,19]

The frequency of interictal headache in the index study was 13.2%. Studies with epilepsy patients confirmed that PWE may suffer from various types of headaches and that the presence of headache significantly added the burden of disease in epilepsy patients.[7,36] Nevertheless, some studies have reported that interictal headache, especially migraine, is not encountered more often in patients with epilepsy than expected in the general population,[37-41] and that only peri-ictal headache is more common and occurs in more than one-third of patients with epilepsy.[42]

Reasons for this include definition of terms, patient selection, and the possible effect of cofounders. Studies within the past 10 years have documented rates ranging from 20.8% to 77.9%.[5,10,20,26]

The commonest form of seizure-related headache reported among PWE is postictal headache,[7,36,43] and that the presence of headache significantly added the burden of disease in epilepsy patients.[7,37] Preictal headache was noted in 10.5% and postictal seizures in 18.8% of our patients. The reported incidence of prodromal, ictal, and postictal headache was 4.4%, 1.5%, and 24.5%, respectively, in Korean epilepsy patients at their first visit.[43,44] Mainieri *et al.*[20] reported 48.3% of interictal headache, 23.7% prevalence of peri-ictal headache, 6.7% prevalence of preictal headache, and 19.1% of postictal headache; a pattern similar to the index study, however, those rates are different. In another study, Syvertsen *et al.*[36] found that 44% and 6% had postictal and preictal headaches, respectively. About 4.5% of PWE in the index study had what looked like ictal headache. In these patients, headache attacks were time-locked with seizures. In one study, ictal headache was reported in 0.8% of PWE less than 4.5% in the index study.[20] Ictal headache has been reported[10,21,22] and is common in certain forms of myoclonic epilepsy and epilepsy syndromes.[18]

The causal relationship between epilepsy and headache is complex and multifactorial.[11,18] Primary headaches including migraine may cause epilepsy by inducing brain ischemia and injury, and epilepsy may cause migraine by activating the trigeminovascular system and neurogenic inflammation.[18] There is therefore a bidirectional relationship between epilepsy and migraine because of lack of correlation between time of onset of both disorders and the presence of the other.[18] Clinical interrelationship between headache and epilepsy also exists in certain epilepsy syndromes such as benign epilepsy of childhood with occipital paroxysms and benign Rolandic epilepsy.[18] Shared environmental risk factors and etiologies are also contributory to the comorbidity of epilepsy and headache. The risk of migraine is higher in subjects with head injury[3]; however, this is far from universal. Furthermore, postictal headaches are more likely to occur after falls following a seizure as part of the ictal and postictal states. In our index study, peri-ictal headache weakly correlated to history of previous head injury.

Reasons for high proportion of postictal headache also included head banging and generalized muscle jerking related with seizure activity, especially generalized tonic-clonic seizures.

The quality of headache pain and its location may affect its severity. Peri-ictal headache may resemble primary headaches[45] and thus may have severe impact on the overall quality of life. Our finding suggests that most PWE may have headaches resembling tension headache and migraine. These two types of headaches are known to negatively impact patient's quality of life. Tension headache and migraine have been reported to be the most common headache types in PWE.[20,36]

In conclusion, patients with epilepsy often have seizure-related headaches. Such headaches can occur before or after seizures and may even represent an aura. Headache in PWE may easily be overlooked by physicians during treatment and follow-up, thus negatively impacting on the quality of life. Careful evaluation of PWE should include the burden and impact of headache in the lives of these patients. Large population and multi-center data are needed to fully establish the burden of headache and its subtypes in PWE.

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Conflicts of interest

There are no conflicts of interest.

References

1. Fisher RS, van Emde Boas W, Blume W, Elger C, Genton P, Lee P, *et al*. Epileptic seizures and epilepsy: Definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). Epilepsia 2005;46:470-2.
2. Kim DW, Lee SK. Headache and epilepsy. J Epilepsy Res 2017;7:7-15.
3. Cianchetti C, Pruna D, Ledda M. Epileptic seizures and headache/migraine: A review of types of association and terminology. Seizure 2013;22:679-85.
4. Spillane J, Kullmann DM, Hanna MG. Genetic neurological channelopathies: Molecular genetics and clinical phenotypes. J Neurol Neurosurg Psychiatry 2016;87:37-48.
5. Rajapakse T, Buchhalter J. The borderland of migraine and epilepsy in children. Headache 2016;56:1071-80.
6. Bagnato F, Good J. The use of antiepileptics in migraine prophylaxis. Headache 2016;56:603-15.
7. Mameniškiene R, Karmonait I, Zagorskis R The burden of headache in people with epilepsy. Seizure 2016;41:120-6.
8. Steiner TJ, Stovner LJ, Katsarava Z, Lainez JM, Lampl C, Lantéri-Minet M, *et al*. The impact of headache in Europe: Principal results of the Eurolight project. J Headache Pain 2014;15:31.
9. Förderreuther S, Henkel A, Noachtar S, Straube A. Headache associated with epileptic seizures: Epidemiology and clinical characteristics. Headache 2002;42:649-55.
10. Wang XQ, Lang SY, He MW, Zhang X, Zhu F, Dai W, *et al*. High prevalence of headaches in patients with epilepsy. J Headache Pain 2014;15:70.
11. Wang XQ, Lang SY, Zhang X, Zhu F, Wan M, Shi XB, *et al*. Comorbidity between headache and epilepsy in a Chinese epileptic center. Epilepsy Res 2014;108:535-41.
12. Bellini B, Arruda M, Cescut A, Saulle C, Persico A, Carotenuto M, *et al*. Headache and comorbidity in children and adolescents. J Headache Pain 2013;14:79.
13. Ottman R, Lipton RB. Comorbidity of migraine and epilepsy. Neurology 1994;44:2105-10.
14. Haut SR, Bigal ME, Lipton RB. Chronic disorders with episodic manifestations: Focus on epilepsy and migraine. Lancet Neurol 2006;5:148-57.
15. Rogawski MA. Common pathophysiologic mechanisms in migraine and epilepsy. Arch Neurol 2008;65:709-14.
16. Striano P, Belcastro V, Verrotti A, Parisi P. "Comorbidity" between epilepsy and headache/migraine: The other side of the same coin! J Headache Pain 2011;12:577-8; author reply 579.
17. Verrotti A, Striano P, Belcastro V, Matricardi S, Villa MP, Parisi P. Migralepsy and related conditions: Advances in pathophysiology and classification. Seizure 2011;20:271-5.
18. Silberstein SD, Lipton RB, Haut S. Migraine. In: Engels J Jr, Pedley TA, editors. Epilepsy: A comprehensive textbook. 2nd ed. Philadelphia: Wolters Kluwer/Lippincott Williams and Wilkins. Health; 2008. Vol. 3. pp. 2733-43.
19. Marks DA, Ehrenberg BL. Migraine-related seizures in adults with epilepsy, with EEG correlation. Neurology 1993;43:2476-83.
20. Mainieri G, Cevoli S, Giannini G, Zummo L, Leta C, Broli M, *et al*. Headache in epilepsy: Prevalence and clinical features. J Headache Pain 2015;16:556.
21. Cianchetti C, Dainese F, Ledda MG, Avanzini G. Epileptic headache: A rare form of painful seizure. Seizure 2017;52:169-75.
22. Seyffert S, Kvatum W. An atypical presentation of epilepsy: What a headache! J Neurol Transl Neurosci 2017;5:1078.
23. Shovron S. Handbook of epilepsy treatment. 3rd ed. West Sussex, UK: Wiley-Blackwell; 2010. pp. 192-9.
24. Cochran WG. Sampling techniques. 2nd ed. New York: John Wiley and Sons, Inc.; 1963.
25. Ezeala-Adikaibe BA, Onyekonwu C, Okudo G, Onodugo O, Ekenze S, Orjioke C, *et al*. Prevalence of primary headaches in an urban slum in Enugu South East Nigeria: A door-to-door survey. Headache 2014;54:1601-10.
26. Ezeala-Adikaibe BA, Orjioke C, Ekenze O, Ijoma U, Onodugo O, Molokwu O, *et al*. Prevalence of active convulsive epilepsy in an urban slum in Enugu South East Nigeria. Seizure 2016;35:100-5.
27. Epilepsy: A Public Health Imperative. Geneva: World Health Organization; 2019. Available from: https://www.who.int/publications-detail-redirect/epilepsy-a-public-health-imperative. [Last accessed on 2021 Aug 14].
28. Onwuekwe IO, Onodugo OD, Ezeala-Adikaibe B, Aguwa EN, Ejim EC, Ndukuba K, *et al*. Pattern and presentation of epilepsy in Nigerian Africans: A study of trends in the southeast. Trans R Soc Trop Med Hyg 2009;103:785-9.
29. C Onyemaechi NO, Nwankwo OE, Ezeadawi RA. Epidemiology of injuries seen in a Nigerian tertiary hospital. Niger J Clin Pract 2018;21:752-7.
30. Onwuchekwa RC, Echem RC. An epidemiologic study of traumatic head injuries in the emergency department of a tertiary health institution. J Med Trop 2018;20:24-29.
31. Banerjee PN, Hauser WA. Incidence and prevalence. In: Engels J Jr, Pedley TA, editors. Epilepsy: A comprehensive textbook. 2nd ed. Philadelphia: Wolters Kluwer/Lippincott Williams and Wilkins. Health; 2008. Vol. 1. pp. 45-56.
32. Elkind AH. Drug abuse in headache patients.Clin J Pain 1989;5:111-20.

33. Beckmann YY, Seçkin M, Manavgat Aİ, Zorlu N. Headaches related to psychoactive substance use. Clin Neurol Neurosurg 2012;114:990-9.
34. Nwani PO, Nwosu MC, Enwereji KO, Asomugha AL, Arinzechi EO, Ogunniyi AO. Epilepsy treatment gap: Prevalence and associated factors in southeast Nigeria. Acta Neurol Scand 2013;128:83-90.
35. Epilepsy in the African Region: Bridging the Gap. The Global Campaign Against Epilepsy "Out of the Shadows" ILAE/IBE/WHO Global Campaign Against Epilepsy, 2002.
36. Caprara F, Leticia A, Rissado JP, Royes F. Fernando L. Michele RF. *et al.* Characteristics of post-ictal headaches in patients with epilepsy: a longitudinal study. Seizure 2020;81:244-9.
37. Parisi P, Striano P, Trenité DG, Verrotti A, Martelletti P, Villa MP, *et al*. "Ictal epileptic headache": Recent concepts for new classifications criteria. Cephalalgia 2012;32:723-4.
38. Belcastro V, Striano P, Parisi P. Interictal and periictal headache in patients with epilepsy: Migraine-triggered seizures or epilepsy-triggered headache? Eur J Neurol 2013;20:1333-4.
39. Belcastro V, Striano P, Parisi P. "Ictal epileptic headache": Beyond the epidemiological evidence. Epilepsy Behav 2012;25:9-10.
40. Chen YC, Tang CH, Ng K, Wang SJ. Comorbidity profiles of chronic migraine sufferers in a national database in Taiwan. J Headache Pain 2012;13:311-9.
41. Kwan P, Man CB, Leung H, Yu E, Wong KS. Headache in patients with epilepsy: A prospective incidence study. Epilepsia 2008;49:1099-102.
42. Duchaczek B, Ghaeni L, Matzen J, Holtkamp M. Interictal and periictal headache in patients with epilepsy. Eur J Neurol 2013;20:1360-6.
43. Ito M, Adachi N, Nakamura F, Koyama T, Okamura T, Kato M, *et al*. Characteristics of postictal headache in patients with partial epilepsy. Cephalalgia 2004;24:23-8.
44. HELP Study Group. Multi-center study on migraine and seizure-related headache in patients with epilepsy. Yonsei Med J 2010;51:219-24.
45. Nahid J, Hakimeh J. The prevalence of migraine and tension type headaches among epileptic patients. Caspian J Neurol Sci 2015;1:41-6.