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Original Article

Study of Primary Headache Disorders among Patients with Epilepsy

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ABSTRACT

Introduction: *Headache is one of the common comorbidities among the patients with epilepsy which worsens quality of life of an epileptic patient. The link between headache and epilepsy has long been known. Primary headaches, especially migraine, share some common features with epilepsy. This study was to explore the patterns of primary headache disorders among the patients with epilepsy attending a tertiary care hospital.* ***Methods & Materials:*** *This cross-sectional descriptive type of observational study was conducted in the Department of Neurology of Mymensingh Medical College Hospital during a period of one year and six months from May 2020 to October 2021. Total 80 patients with clinically diagnosed cases of epilepsy with age more than 12 years of both male and female gender were taken as study population according to inclusion and exclusion criteria. Informed written consent was ensured from participants or their legal guardians. A semi-structured case record form containing the necessary information including the frequency and patterns of headache disorders, types of epilepsy and socio-demographic characteristics were used for data collection.* ***Results:*** *The mean age of the respondents was 27.36 ± 10.18 (SD) years with a majority in the age group of 20 to 29 years 36.3%. Among the patients female was 57.5%. Most of the respondents belonged to middle and lowerincome group which was 92.5%. The frequency of primary headache disorders was 60.0%, among them most common headache pattern was tension-type headache 56.2% followed by migraine headache 39.6%. Among the peri-ictal headache postictal headache was the most common which was 43.75% of all the respondents.* ***Conclusion:*** *Frequency of primary headache disorders in epileptic patients was high in this study where tension type headache was most common 56.2%.*

Keywords: *Epilepsy, Primary Headache, Peri-Ictal Headache.*

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INTRODUCTION

Introduction The global prevalence of present headache problems (symptomatic at least once in the previous year) is estimated to be greater than 50% [1]. Headache problems are particularly unpleasant throughout productive years of life (late teens to 50s), and the societal cost – mostly in lost working hours and reduced productivity–is significant. In general population, the life-time prevalence of headache is about 46% and that of migraine is 10-22% [2]. The prevalence of headache in epilepsy patients ranges from 46 to 52.2% globally with migraine headache prevalence approximately doubled in epileptic individuals [3]. Epilepsy is a neurological condition that affects people of all ages and is one of the world's most common non-communicable diseases [4]. Despite the fact that epilepsy accounts for only 0.5% of the worldwide disease burden, 80 % of epileptic patients live in under developed nations [5]. Several genetic abnormalities have been discovered in migraine and epilepsy families, including CACNA1A and ATP1A2, FHM, and the concept of channelopathy can be applied to patients with these mutations [6]. The association between these two episodic neurological illnesses is significant, and more laboratory and clinical research would reveal the true link between headache and epilepsy [7]. Observed that 83.2 percent of epileptic patients had headache issues. Headache worsens quality of life in epileptic patient specially those who has long history of headache or more frequent headaches or in migraineurs [8]. Found that 48.5 percent of their epileptic patients experienced inter-ictal headache, migraine was more common than tension type headache [9]. The ratio of headaches was lower in male patients compared with females, and females experienced migraine-type headaches more frequently compared with

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males (p=0.006). In their prospective study included 86 adult patients (54 females, 32 males). Headache was present in 47.6% of patients, tension type headache (TTH) in 16.3%, migraine with aura in 13.9%, migraine without aura in 12.8%. Other primary headaches were 2.4%. They concluded that patients with epilepsy often have headaches, particularly a migraine headache. Recruited 62 subjects aged ≥18 years from the hospital's neurology out-patient and divided them into two equal groups, epileptics and non-epileptics [10]. Primary headache disorders were more common in epileptic group (61.3%) than the non-epileptic group (32.2%) (p=0.021). The tension-type headache was the most common (45.2%) followed by migraine-type headache (12.9%) in the epileptic group. Inter-ictal headaches were significantly related to "focal to bilateral tonic–clonic" seizures (p=0.046). The prevalence of headache among patients on polytherapy (69.2%) was higher than that of patients on monotherapy (52.9%). The pooled estimated prevalence of headache among patients with epilepsy was considerably high (48.4%). Prevalence of inter-ictal headache (IIH) (42.2%) and post-ictal headache (PIH) (43.1%) were higher when compared to tensiontype headache (TTH) (26.2%), migraine with aura (26.0%) and migraine without aura (10.4%) They also found that prevalence of headache was much greater in females [3]. This study might help to determine types of epilepsy, the patterns and frequency of primary headache disorders in epilepsy patients, relationship of primary headache disorders with types of seizures and temporal relationship of headache with seizure and thus helps to take measures regarding proper management of both headache and epilepsy, thus enhancing quality of life of patient with epilepsy, reducing headache associated lost time in epilepsy patients.

METHODS & MATERIALS

Study design: This was a cross-sectional descriptive type of observational study.

Place of Study: This study was conducted in the Department of Neurology at Mymensingh Medical College and Hospital, Mymensingh (MMCH).

Period of Study: The study was conducted during the period of one year and six months from May 2020 to October 2021.

Study population: The clinically diagnosed cases of epilepsy who were more than 12 years of both gender and who visited the out and in-patient Department of Neurology at Mymensingh Medical College and Hospital were selected as study population.

Sample method: Purposive type of non-probability sampling technique was followed.

Sample size: Sample size and the statistical basis of it:

The sample size of this study was determined by the following equation.

Sample size (n) = $\frac{z2pq}{d2}$

So, calculated sample size was 364 But due to limited period of data collection and lack of patients it was possible to enroll 80 patients in this study.

Selection Criteria:

Inclusion Criteria:

- Patients with a clinically diagnosed case of epilepsy with age more than 12 years
- Both male and female gender
- Willing to participate in the study

Exclusion Criteria:

- Patients with structural brain lesions
- Non epileptic seizures
- Patient with secondary headache

1. Headache attributed to cranial and/or cervical vascular disorder
2. Non-vascular intracranial disorder
3. Patients with infection of brain and meninges (encephalitis, meningitis)
4. Patients with metabolic abnormalities (hypoglycemia, substance abuse, alcohol withdrawal)
5. Trauma or injury to the head and/or neck.

Data collection technique: This cross-sectional descriptive type of observational study was conducted in the Department of Neurology, MMCH. Patients attending the respective department with clinically diagnosed cases of epilepsy (at least two or more unprovoked seizures 24 hours apart) with age more than 12 years, both male and female gender were selected for study. Data of 93 patients were collected initially and after matching the inclusion and exclusion criteria finally 80 patients were selected as study population. The study objectives were described to the participants or their legal guardians and informed written consent was taken from each patient or their legal guardians. A semi-structured case record form containing the necessary information including the frequency and patterns of headache disorders, types of epilepsy and socio-demographic characteristics were used for data collection. Each patient underwent detailed history taking and recalled their frequency and pattern of primary headache disorders and types of seizures, relation of primary headache disorders with peri ictal headache, clinical characteristics relevant to primary headache disorders and types of seizures. All information were recorded in separate case record form.

Data processing and analysis: Data were analyzed by using SPSS version 23.0. Qualitative variables were summarized by frequency and percentage. Quantitative variables were summarized by mean and standard deviation (SD). One-way anova test, Chi square test and Fisher's-exact test were done to analyze data.

RESULTS

Total of 80 patients with clinically diagnosed cases of epilepsy aged more than 12 years of both genders were selected fulfilling inclusion and exclusion criteria. This study was aimed to evaluate patterns and frequency of primary headache disorders among the patients with epilepsy. The results of the study were arranged in tables and figures.

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Table – I: Distribution of the demographic study (*n*=80)

Age	Frequency	Percent
13 to 19 years	19	23.7
20 to 29 years	30	37.5
30 to 39 years	21	26.2
40 to 49 years	7	8.8
50 to 59 years	3	3.8
Gender		
Male	34	42.5
Female	46	57.5
Residence		
Urban	31	38.7
Rural	49	61.3
Education		
No formal education	9	11.2
Primary School	26	32.5
Secondary School	21	26.3
Higher Secondary	16	20.0
Graduate of Above	8	10.0
Occupation		
Housewife	19	23.7
Student	21	26.3
Service	13	16.3
Business	12	15.0
Farmers	6	7.5
House workers	5	6.2
Unemployed	4	5.0
Socio-economic Status		
Lower class	27	33.7
Middle Class	47	58.8
Upper Class	06	7.5

Majority of the respondents were in the age group of 20 to 29 years 30 (37.5%) followed by in decreasing order 30 to 39 years 21 (26.2%), 13-19 years 19 (23.7%), 40 to 49 years 7 (8.8%) and 50 to 59 years 3 (3.8%). The mean age of the respondents was 27.36 ± 10.18 (SD) yrs. Majority of the respondents were female 46 (57.5%) where male respondents were 34 (42.5%). The majority of the respondents were from rural areas 49 (61.3%) while 31 (38.7%) of patients came from urban areas. Respondents were studied up to primary school 26 (32.5%) and followed by secondary school 21 (26.3%), higher secondary school 16 (20.0%), graduation 8 (10.0%), and only 9 (11.2%) had no formal education. Majority of the respondents were students 21 (26.3%) followed by in decreasing order housewives 19 (23.7%), service holders 13 (16.3%), business person 12 (15.0%), farmers 6 (7.5%), unemployed 5 (6.2%) and house workers 4 (5.0%). That majority of the respondents belonged to middle class 47 (58.8 %) where lower class was 27 (33.7 %) and upper class was 6 (7.5%) respectively (Table-I).

Table – II: Distribution of the respondents by the types of seizures (*n*=80)

Types	Frequency	Percent
Primary generalized tonic-clinic seizure	58	72.5
Absence seizure	4	5.0
Myoclonic seizure	2	2.5
Simple partial seizure	7	8.7
Complex partial seizures	5	6.3
Complex partial to secondary generalization	4	5.0
Total	80	100.0

The primary generalized tonic clonic seizure was the most common seizure type 58 (72.5%), Focal seizure was then the next common type 16 (20%). Simple partial, complex partial and complex partial to secondary generalization was found in 7 (8.7%), 5 (6.3%), 4 (5.0%) patients respectively. Absence seizure was found in 4 (5.0%) and myoclonic seizure in 2 (2.5%) patients. There wasn't any other type of seizure found in the study population (Table-II).

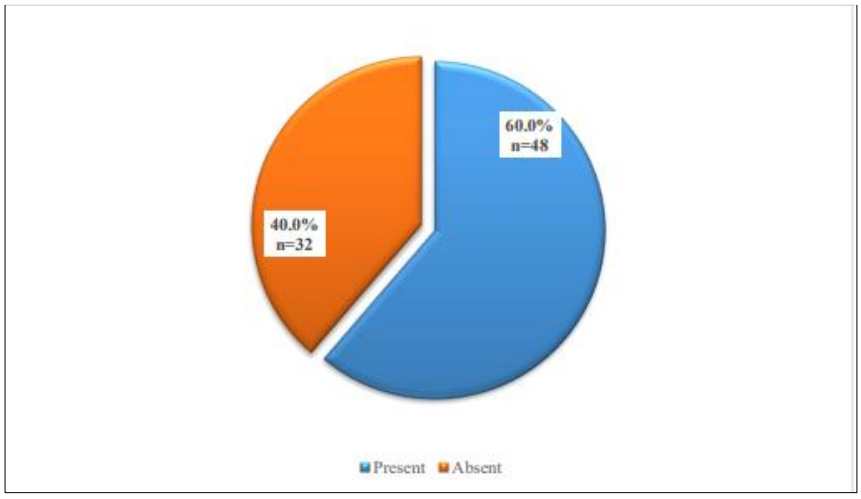

Figure – 1: Distribution of the respondents according to the proportion of primary headache disorders (*n*=80)

Among all the respondents, 48 (60.0%) of epilepsy patients reported primary headache disorders (Fig-1).

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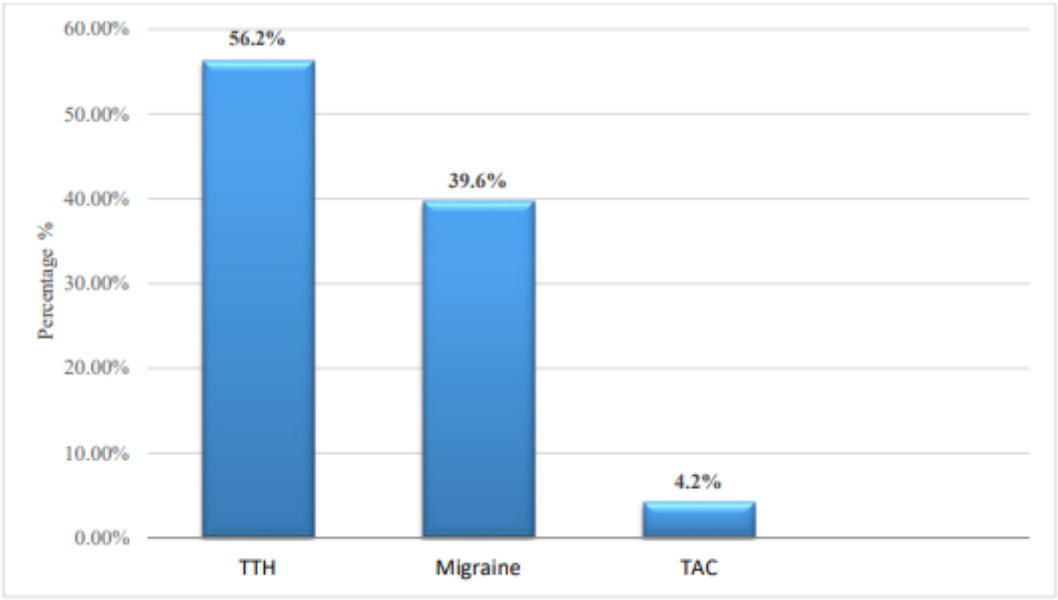

Figure – 2: Distribution of the respondents according to the pattern of primary headaches (*n*=48)

The majority of the respondents were diagnosed with tension-type headache (TTH) 27 (56.2%), migraine type headache was next common type 19 (39.6%). Trigeminal autonomic Cephalalgia was 2 (4.2%)(Fig-2).

Table – III: Distribution of patients of primary headache disorders (n=48) by genders

Gender	Patternofprimaryheadache			Total	p value
	TTH n(%)	Migraine n(%)	TAC n(%)	n(%)	
Female	15(51.7)	13 (44.8)	1 (3.5)	29 (100.0)	
Male	12(63.1)	6 (31.6)	1 (5.3)	19 (100.0)	0.648*
Total	**27 (55.2)**	**19 (39.6)**	**2 (4.2)**	**48 (100.0)**	

TTH=Tension type headache, Mig=Migraine, TAC= Trigeminal Autonomic Cephalalgia *p value was determined by Chi-square test

Among the patients with primary headache disorders 29 (60.4%) were female. Tension type headache (TTH) was the most common type for both female (51.7%) and male (63.1%). Migraine was the second most common type primary headache, female 13 (44.8%), male 6 (31.6%). Trigeminal Autonomic Cephalalgia was relatively rare in both genders. The p-value determined by the Chi-square test suggested that there was no significant difference between gender and patterns of primary headache disorders. (p>0.05) (Table-III).

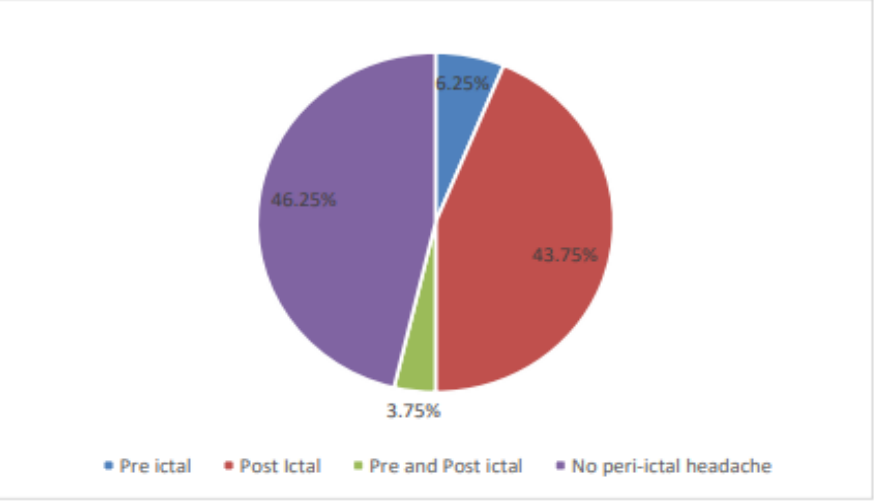

Figure – 3: Distribution of Respondents by peri-ictal headache

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Figure 3 showed that among the peri-ictal headache post-ictal headache was most common 35 (43.75%) followed by pre-ictal headache 5 (6.25%). Both pre-ictal and post-ictal headache was noticed in 3 (3.75 %) of patients and 37 (46.25%) patients did not show any peri-ictal headache. There was no ictal headache in this study.

DISCUSSION

This study was aimed to estimate patterns and types of epilepsy patients and characteristics and proportion of primary headache disorders among those patients with epilepsy, describing their sociodemographic profile and temporal relationship with seizure occurrence. The proportion of primary headache disorders was found 60.0% in this study which was slightly higher than the previous studies. Globally, the prevalence of headaches in epileptic patients ranges from 46% to 52.2%, with the prevalence of migraine nearly doubled in those with epilepsy [3]. Wang et al. [11] also found that 60.1 percent of epilepsy patients had headaches. In a recent study in Lithuania on 280 (61.4% of them were women) patients with epilepsy mean age was (37.8 ± 14.5). 83.2 percent of the respondents reported some type of headache which was higher comparative to other studies [8]. In this study, patients were within 13 to 59 years of age range. Amongst the patients, 29 (36.25%) were in 20-29 years age group, followed by 21 (26.25%) within 30-39 years, 19 (75 %) within 13-19 years, 8 (10%) within 40-49 years and 3 (3.75%) within 50-59 years age group. The mean (SD) age of the respondents was 27.36 ± 10.18 (SD) years. Many reports stated that the average age was 35.2 years and the mean (±SD) of the study population was 24 ± 11.9 years, Rashid and Alam., et al [12] which is consistent with this study. In this study, the most common age of presentation of epilepsy was 13-39 years which was 87.5%. Mannan et al [13] reported similar findings (16-31 years) in Bangladesh. Rahman et al. [14] in their study noticed that mean age of onset of migraine was 34.24±7.09 years, TTH was 36.20±7.58 years and cluster headache was 33.91±7.48 years. These epidemiological results were first reported and stressed by Verrotti et al. [15] which were conducted in the paediatric age group. Belcastro et al [16] have also reported that the epidemiological behaviour in this field is different comparing adult and paediatric patients. Among the study population, the predominant patient profile was found women 57.5%. Haque et al. [17] found female patients' predominance (67% female and 33% male) in a hospital-based study. Among the patients suffering from migraine 84.4% were female where male was 15.6% Rahman et al., [14]. This has probably been attributed to the effect of female sex hormones specifically influence of oestrogen. The well-known female preponderance in patients with primary headache disorders was also evident in this study. There was found a higher proportion of women 13 (41.9%) compared to men 6 (30.0%) suffering from migraine which was consistent with the previous study where migraine was more common in women than men [14]. Premenstrual migraines are known to occur during or after the time when the female hormones, oestrogen and progesterone, decrease to their lowest levels [18]. In this study majority of the respondents were studied up to primary school 32.5% (n=26) and followed by in decreasing order secondary school 21(26.25%), higher secondary school 16 (20.0%), graduation 8 (10%), and only 9 (11.25%) had no formal education.These findings were compatible with another study in Bangladesh [12]. Majority of the respondents were students by occupation 21 (26.25%) followed by in decreasing order housewives 19 (23.75%), service holders 13 (16.25%), business person 12 (15%), farmers 6 (7.5%), unemployed 5 (6.2%) and house workers 4 (6.2%).Rashid and alam et al12] also reported in their findings that most of the respondents were students (42.9%), followed by 14.7% housewives, 11.8% service holders and 7.1% did business works and a total of 23.5% of respondents were engaged in some other type of occupation, which is similar with the present study results. Among all the respondents, the majority belonged to middle class group 58.75%, followed by lower class 33.75% and upper class 7.5%. These findings correlated with other study findings [12]. In this study tonic-clonic seizure was most common type 72.5%, absence seizure 5%, focal seizure was 20%. Mohammad et al. [19] in their study found that generalized tonic-clonic (54.3%), absence (7.45%), tonic (3.9%), and myoclonic (1.6%) seizures were all common among the generalized epilepsies. Partial seizure was 14.9%. Primary headache disorders, particularly migraine and tension-type headache (TTH), are globally prevalent [20,21,22]. A hospital based study in Bangladesh on 1684 patients reported that about 22.98% of patients with Neurology outpatient department were presented with headaches [23]. In Bangladesh, another study with a large sample of 3440 headache patients found that 71.13% had a tension-type headache and 16.05% had a migraine [24]. The proportion of tension-type headache (TTH) in this study was 50.98% and migraine 36.73% was the second most frequent cause of headache. A Chinese study found a prevalence of TTH 66.9% in a tertiary care centre [25]. In other studies, the prevalent of TTH was 47.7% in Zimbabwe [26]. 25.5 percent by Quesada et al.,[26] in Cuba. There has been wide variations and differences in the epidemiology of tension-type headache across different cultures [27, 28]. Post-ictal headache (post-IHA) begins immediately after cessation of seizure is the most frequent headache type associated with seizures. Post-ictal headache can be of the migraine type, tension-type, or unclassified type of headache [12,29]. In the present study, among the peri-ictal headaches post-ictal headache was most common 35 (43.75 %) followed by pre-ictal headache 5 (6.25%). Both pre-ictal and post-ictal headache was noticed in 3 (3.75%) of patients. There was no ictal headache in this study group. Indeed, there was a significantly higher proportion of post-ictal headaches in relation to primary headache disorders. Post-ictal headache was present significantly more in TTH group where pre-ictal along with pre and post ictal headache was present significantly more in migraine group. Peri-ictal headache in epileptic patients was significantly associated with types of primary headache disorders in this study ($p< 0.05$).

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CONCLUSION

The frequency of primary headache disorders was 60% in epilepsy patients. Most common headache pattern was tension type headache (56.25%) followed by migraine headache (38.77%). Post ictal headache (81.39%) was the most common peri-ictal headache among the patient with epilepsy. Peri-ictal headache in epileptic patients was significantly associated with types of primary headache disorders in this study ($p < 0.05$)

Limitations

- All samples were collected from a single center
- Sampling method was purposive

Recommendations

Risk factors associated with headache among the epilepsy patients should be explored and identified.

Conflict of Interest: None.
Source of Fund: Nil.

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