

Migraine in epileptic Patients Epidemiology and Clinical Characteristics:

Louay hashim sheet*, Mohammad tawfik ridha**

ABSTRACT:

OBJECTIVE.:

To study the prevalence and clinical characteristics of migraine in epileptic patients and to compare these epidemiological and clinical data with those in general population

BACKGROUND:

Systematic investigation of the characteristics of seizure-associated headaches is rare. Although data on the prevalence and characteristics of migraine in general population are numerous, few studies have investigated the relation between migraine and epilepsy

METHODS:

One hundred seventy two epileptic patients (98 female and 74 male) participated in a semi-standardized interview and study about headaches particularly migraine type.

RESULTS:

Seventy four out of the 172 epileptic patients had headache of one type or another (57%), migraine occurred in 34 patients (19.7%), female migraineurs (24 cases) and male (10 cases) (female/male ratio 2.4:1). Migraine occurred in isolation in 18 cases and was mixed with other headache types in 16 cases. Migraine cases without aura constituted 67.7% (23 cases), and with aura 31.3% (11 cases). In non-aura cases female (18 cases) outnumbered male (5 cases), unlike in aura cases (6 female vs 5 male cases)

CONCLUSION :

Migraine is much more prevalent in epileptics (19.7%) than in general population (11-12%). Other wise migraine in epileptics has similar clinical characteristics to migraine in general population including clinical varieties and gender distribution

KEY WORDS: Epilepsy, headache , migraine

INTRODUCTION:

Headache and epilepsy are common disorders that lead to neurological consultation. Frequently both conditions occur in the same patient. Epileptics may get headaches in direct relation to their seizures (preictal and postictal headache) or they may share general population in their headaches like (migraine and tension headache). Comorbidity of migraine and epilepsy has long been suspected but has seldom been systematically investigated^(1,2). The degree of association between the two disorders is important from both clinical and theoretical points. Practically an association would imply that clinicians treating either disorder should have high index of suspicion of the other and should be well informed about diagnosis, classification and treatment of both disorders. When the two disorders occur together treatment strategies of one should include consideration of

the other. Theoretically an association could provide clues to the a etiology of both conditions^(3,4). Some suggest common genetic causes for migraine and epilepsy⁽⁵⁾. Neuronal hyperexcitability might explain the comorbidity of migraine and epilepsy⁽⁶⁾.

.In epileptic patients headache tends to be overlooked by both the patient and the treating physician either because epilepsy is viewed as the more serious disorder or because headache is considered as part of the seizure manifestation and hence given minor attention⁽⁷⁾. In one study in epileptic patients having migraine, the diagnosis of migraine had been overlooked in 56% of cases. A careful detailed assessment of headache is therefore required by any physician treating epileptic patients⁽⁸⁾.

Epilepsy is defined as two or more unprovoked seizures, in a given patient^(9,10). It occurs in 1% to 2% of the population⁽¹¹⁾. In 1981, the International League Against Epilepsy proposed a classification of epileptic seizures on the basis of clinical and

*Baghdad Teaching Hospital.

**Sheik Zaid Hospital.

EEG criteria. This classification is widely accepted and divides seizures into three major categories: partial (simple, complex and secondary generalized), generalized (convulsive or non convulsive), and unclassified⁽¹²⁾.

Many cases of seizures and epilepsy result from a dynamic interplay between endogenous factors (genetic predisposition), epileptogenic factor (e.g brain lesion) and precipitating factors (psychological or physical stress, sleep deprivation, hormonal changes, certain medications etc⁽¹³⁾). Among drugs that can cause seizures are analgesics (like tramadol and meperidine), psychotropics (antidepressant, antipsychotic, lithium) and sedation-hypnotic withdrawal. Headache is probably the most common human malady and the most prevalent neurological symptom associated with any disease.

In 1988 the International Headache Society (IHS) published a comprehensive classification of headache that replaced previous efforts and achieved common acceptance^(14,15).

Migraine is defined as a benign and recurring syndromes of headache, nausea, and vomiting and /or symptoms of neurological dysfunction in various admixtures. This dysfunction includes photophobia, visual disturbance, parasthesias, vertigo and conscious alterations⁽¹³⁾. Estimates of the prevalence of migraine have varied around 10-12%^(16,18,19). Prevalence among Caucasians is in range of 13-18% among women and 4-6% among men, ie it is three times higher in women than in men⁽¹⁷⁾. In women migraine with out aura is more prevalent than in men, while the prevalence of migraine with aura is about equal in both sexes. It is three times higher in women than men⁽¹⁷⁾. Studies generally found that in adults migraine without aura is more prevalent than migraine with aura⁽¹³⁾.

The overall prevalence of migraine with aura is probably around 4%, distinctly less than the prevalence of migraine with out aura in women and about equal to that in men⁽²⁰⁾.

In migraine without aura (common migraine) no focal neurological disturbance precedes the recurrent headaches, however, the moderate to severe pain, pulsating quality, unilateral location, aggravating factors, nausea and /or vomiting,

photophobia, phonophobia and multiple attacks lasting 4-72 hours; all point to the diagnosis⁽¹⁹⁾.

In migraine with aura (classic migraine) headache is associated with characteristic premonitory sensory, motor or visual symptoms⁽²¹⁾

Drugs effective in prophylaxis of migraine include B adrenergic agents (propranolol), anticonvulsants (sodium valproate), tricyclic antidepressants (amitriptyline and nortriptyline), MAO inhibitors (phenelzine), serotonergic drugs (methysergide, cyproheptadine) and others (verapamil).

PATIENTS AND METHODS :

In the period (October 2003 to November 2004) 172 cases of epilepsy that presented to neurological outpatient of Alsalam hospital (Mosul), and Baghdad teaching hospital were sequentially studied.

Method of collection of cases

Collection of cases was random i.e. all cases of epilepsy that presented in the outpatient or in the ward were submitted to full clinical and investigational assessment.

Diagnosis of cases:

Epilepsy was defined as: lifetime history of two or more unprovoked seizures with or without abnormal EEG. All cases were submitted to full clinical and investigational assessment. All information were plotted in format

Cases below 10 years of age, and cases with abnormal imaging were excluded, so also cases in whom imaging was indicated but not done.

Then in each case of epilepsy a detailed history of headache was taken. In those in whom history of headache was positive, full information about the following details of headache was taken; duration, site, character, intensity, aggravating factors, associated symptoms, onset, family history, number of attacks, aura history; clinical examination and investigation, all were plotted.

Headache type was categorized according to IHS criteria

Statistical analysis of data was done. All tables were analyzed by female/ male ratio with p value.

RESULTS:

A total number of 172 (74 male and 98 female) cases of epilepsy were studied and classified. male: female ratio was 1:1.3. Age range 11-60 y

Table 1: classification of epilepsy cases with gender distribution

| Type Of Epilepsy | Numbers | % | Male | Female | M/ F ratio |
|------------------------------------|---------|-------|------|--------|------------|
| Partial | 15 | 8.7% | 6 | 9 | 1:1.5 |
| Partial with secondary Generalized | 108 | 62.5% | 38 | 70 | 1:1.8 |
| Primary Generalized | 49 | 28.5% | 30 | 19 | 1.5:1 |
| Total | 172 | 100% | 74 | 98 | 1:1.3 |

Age distribution 67 % of cases fell in the first two age groups (11-30y)

Table2 Epilepsy numbers and gender distribution according to age groups

| Age/ years | epilepsy | | | | |
|------------|----------|------|----|----|------------|
| | No | % | M | F | M /F ratio |
| 11-20y | 62 | 36% | 29 | 33 | 1:1.1 |
| 21-30y | 54 | 31 % | 23 | 31 | 1:1.3 |
| 31-40y | 32 | 19% | 13 | 19 | 1:1.4 |
| 41-50y | 19 | 11 % | 9 | 10 | 1:1.1 |
| 51-60y | 5 | 3% | - | 5 | - |
| total | 172 | 100% | 74 | 98 | 1:1.3 |

Type of headache:

Out of the 172 cases, 74cases(43%)had headache of one type or another, either pure form i.e. one

type of headache (45cases) or mixed form i.e. more than one type of headache (29cases). 98cases(57%) had no headache. Table 3

Table 3 Numbers and percentages of different type of headache

| Type of headache | No. Of epileptic patients who had headache | %To all epilepsy | %To all headache | M | F |
|--------------------|--|------------------|------------------|----|----|
| Migraine | 34 | 19.7% | 46% | 10 | 24 |
| Postictal headache | 41 | 23.8% | 55% | 20 | 21 |
| Tension headache | 21 | 12.2% | 28.5% | 12 | 9 |
| Preictal headache | 6 | 3.4% | 8.2% | 3 | 3 |
| Cluster headache | 1 | 0.58% | 1.3% | 1 | - |
| Total | 103 | 43% | 139% | 46 | 57 |

Migraine group:

Out of the group of migraine cases (total 34 patient), 18 had pure migraine (10.5 % of epileptic

patients) and 16 had migraine mixed with other types of headache (9.3%). Female gender predominated in all groups. Table4

Table4-Occurrence of migraine in association with other types of headache in epileptic patients

| Migraine | M | F | Total | %To all epileptic | %To all headache |
|-------------------|----|----|-------|-------------------|------------------|
| Alone | 5 | 13 | 18 | 10.5% | 24.3% |
| Mixed | 0 | 16 | 16 | 9.3% | 21.6% |
| With postictal H. | 2 | 3 | 5 | 3% | 7% |
| With tension H. | 3 | 7 | 10 | 6% | 13% |
| With preictal H. | - | 1 | 1 | 0.6% | 1.3% |
| Total | 10 | 24 | 34 | 100% | 46% |

Prevalence of migraine in epileptics: migraine (13.5%). The overall occurrence of 24 cases out of the 98 female had migraine (24.5%) migraine in the epileptics was 19.7%. Table5 while 10 cases out of the 74 male epileptics had

Table5 Occurrence of migraine in epileptics according to Gender distribution

| Sex | Total no. Of epilepsy | Total no. Of migraine | % |
|--------|-----------------------|-----------------------|-------|
| Male | 74 | 10 | 13.5% |
| Female | 98 | 24 | 24.5% |
| Total | 172 | 34 | 19.7% |

Type of migraine and gender differences:

Amongst the 34 migraineurs 23(67.7%)had migraine without aura and 11(32.3%) had migraine with aura.

Among the 24 female migraineurs 18 had migraine without aura and 6 with aura. While among the 10 male

migraineurs 5 had no aura and 5 had aura. The distribution of cases in male and female according to presence of aura is shown in table 6

DISCUSSION:

Both the epileptic patient and the treating physician so often dismiss headache. Headache may sometimes be even more distressing to the patient than the seizure it self. If enough attention is given to this symptom additional suffering from pain may be avoided and some therapeutic modulations may be made. Although there is plenty of literature on epilepsy and headache separately, there is little material on comorbidity of both conditions .The subject of this study is new, at least in our country. The study was held with the following question in mind aiming at finding answers to it, is migraine different in epileptics from general population in the following points: prevalence, gender distribution, distribution of non aura & aura cases and gender distribution of these clinical subtypes?

Prevalence of headache

43% of epileptic patients had headache, whereas 57% denied any headache. Forderreuther etal in a German study reported 34% occurrence of headache in their epileptics, and Yamane etal in a Brazilian syudy reported 46% occurence of headache in epileptics^(22,23).

Types of headache :

Postictal headache predominated occurring in 23.8% followed by migraine (19.7%), tension

headache (12.2%), preictal (3.4%) and cluster headache (0.5%) in descending order. Most of headache patients, however, had more than one type of headache at different times of their illness. Seizure associated headaches have been variably reported in other works. In the above mentioned German study postictal headache constituted the highest proportion (23.4%), followed by migraine (18.7%), tension headache (12.3%) , preictal headache (1.1%) in that order. While in the Brazilian study the highest proportion was migraine (20%), followed by postictal headache (12%), tension headache (8%) and preictal headache (6%). The competition in the prevalence of the type of headache in epileptics in all the studies was between migraine and postictal headache. While in the Brazilian study migraine predominated, in the German and the present work migraine came next to postictal headache .It is noticeable that the percentages of postictal headache and migraine in our work are very close to those in the German work. There are other works in literature on comorbidity of headache and epilep6sy but without going into details of types of headache^(22,23).

Table6- Type of migraine and gender difference:

| Sex | Total no. of migraine | Non aura migraine | % | Aura migraine | % |
|--------|-----------------------|-------------------|-----|---------------|-----|
| Male | 10 | 5 | 50% | 5 | 50% |
| Female | 24 | 18 | 75% | 6 | 25% |
| Total | 34 | 23 | 67% | 11 | 33% |

Table7: Comparison between the three studies

| Studies | Total % of headache in epileptic | % of migraine | %of tension | % of post ictal | .% of pre ictal | % of others |
|-----------------|----------------------------------|---------------|-------------|-----------------|-----------------|---------------------------|
| Present study | 43% | 19.7% | 12.2% | 23.8% | 3.4% | 0.58% cluster headache |
| Brazilian study | 46% | 20% | 8% | 12% | 6% | 18% unclassified headache |
| German study | 34% | 18.7% | 12.3% | 23.4% | 1.1% | . |

It is noticeable that in all the works migraine occurred in about one fifth of epileptics being 19.7%,20% and 18.7% .And the similarity of the percentages is evident.

More over in all the three studies migraine cases approached to around half of the headache cases,

being (34migraine out of 74cases of headache) in our study, (64 migraine out of 115) in the German study and (10 migraine out of 23 cases) in the Brazilian study. In table 8 the similarity of these proportions is clearly shown.

Table 8: Numbers and percentages of migraine to headache in the three studies

| Study | No. Of migraine | No. Of headache | % |
|-----------|-----------------|-----------------|------|
| Present | ٣٤ | ٧٤ | 45.9 |
| German | ٦٤ | ١١٥ | 55.6 |
| Brazilian | ١٠ | ٢٣ | 43.4 |

Prevalence of migraine in epileptics:

Compared to literatures account on the prevalence of migraine in general population that ranges from 10-12%, it becomes evident that prevalence of migraine in the epileptic is higher than in the general population. Reports of lower prevalence of migraine in Asian than Caucasian populations make this difference even more outstanding in our Asian country⁽¹⁷⁾. Controlled group was not taken in our work. However, if we take the higher account of the prevalence of migraine in general population, which is 12%, and compare it to that in epileptics, which is 19.7%, the difference will be statistically highly significant (p 0.00004). It is difficult to explain the persistently high prevalence of migraine in epileptics except on genetic basis. This suggestion appears frequently in the literature. Begal et al state that the paroxysmal nature of both conditions (migraine and epilepsy), the comorbidity of them and the utility of anti epileptic drugs in the treatment of migraine all underline links between epilepsy and migraine. They also state that the presence of either migraine or epilepsy rises the risk of the other disorder . Moreover some types of epilepsy are well reported to be associated with migraine like benign rolandic epilepsy⁽²⁴⁾. Andermann and Andermann summarized 13 studies reporting the prevalence of epilepsy in patients with migraine that was much

higher than in general population. Also they summarized 4 studies reporting the prevalence of migraine in epileptics, which was also higher than in general population^(1,2). In an attempt to confirm a genetic basis to this comorbidity, Ottman et al investigated comorbidity of migraine and epilepsy in a large population of patients and their families, they reported a cumulative incidence of migraine in 24% of epileptics and 23% of the relatives of the epileptics compared to 12% in relatives without epilepsy and concluded that migraine and epilepsy were strongly associated. They indicated that the risk of migraine in persons with epilepsy and their relatives was more than twice the risk in persons without epilepsy⁽³⁾. Authors have suggested that treatment strategies for epilepsy and migraine should include consideration of presence of comorbid disease. Agents potentially useful for both should be considered and epileptogenic medications should be avoided in migraineurs having epilepsy⁽²⁴⁻²⁸⁾.

Gender distribution of migraine in epileptics

:Female male ratio was 2.4:1. Several population studies have confirmed similar ratios (gender ratio of 2-3 female to 1 male)⁽²⁵⁾. The range being 13-18% in female & 4-6% in male .This gender difference is remarkably uniform across races and geographical locations and there has been many attempts at its explanation on hormonal and

psychological bases⁽²⁶⁾. While the female male cases in our epileptic population retained this universal proportion of (2 - 3:1) their percentages (prevalence) stood much higher than in general population being 24% in female epileptics

Type of migraine :

In our epileptic population the type of migraine whether non aura type (common migraine) or aura type (classical migraine) was not different from that in general population. Migraine without aura predominated over migraine with aura in epileptics and this was also demonstrated in two other works on migraine in general population by Stewart etal and Olsen etal^(20,21).

In our female migraineurs the number of non-aura cases was three times the aura cases (18 versus 6), while in male migraineurs both types were equally shared (5 each). Hence the preponderance of non-aura cases among epileptics is not absolute and is merely due to preponderance of female gender

(compared to 12-18% in general population) and 13% in male epileptics (compared to 4-6% in general population)⁽¹⁷⁾ .

amongst them. Stewart etal and Olsen etal have likewise demonstrated that adult migraine without aura was more prevalent than with aura in female and that both types were of equal prevalence in male population^(20,21). These conclusions have been summarized in table(9).

Table 9 Aspects of migraine in epileptics compared to general population

Hence, apart from its prevalence, which is considerably higher in epileptic population, migraine is similar in its clinical characteristics, distribution of clinical subtypes and gender distribution in both epileptic and non epileptic (general)populations.

| Character | Migraine in epileptics | Migraine in general population |
|--|------------------------|--------------------------------|
| Prevalence | 19.7% | 11 - 12% |
| Prevalence in female gender | 24.5% | 13 – 18% |
| Prevalence in male gender | 13.5% | 4 – 6% |
| Female to male ratio | 2.4 : 1 | 2 – 3:1 |
| Ratio of non aura to aura cases in female gender | 3 : 1 | 2 – 3:1 |
| Ratio of non aura to aura cases in male gender | 1 : 1 | 1 : 1 |

REFERENCES:

1. Andermann E, Andermann F. migraine epilepsy relationships epidem. and genetic aspects. In : Andermann FA, Lugarest E, eds .Migraine and epilepsy .boston: Butterworths ,1987:281-291
2. Marks DA, Ehrenberg BL. Migraine-related seizures in adults with epilepsy, with EEG correlation . Neurology 1993;43:2476-2483.
3. Ottman R, Susser M. Data collection strategies in genetic epidemiology: the epilepsy family study of columbia university. J Clin Epidemiol 1992: 45:721-72.
4. Matias-Guiu J ,Galiano L ,Vioque J ,Falip R ,Martin R .A case- control study to evaluate the associated of epilepsy and migraine .Neuro epidemiology 1992;11:313-314.
5. Oak Ridge, Tennessee , — Migraine and epilepsy have more in common than researchers thought, says Lisa Stubbs, a genetics researcher at the Department of Energy's (DOE) Oak Ridge National Laboratory (ORNL). January 20, 1997.
6. Tobias L, Sandra D; Katrin Isbruch; Hans D, Andreas H, .Clinical Characteristics of Patients With Comorbidity of Migraine and Epilepsy - Headache, Vol 43, Issue 6, pp_ 672-677 (Abstract)_files \\2014.gif"
7. Richard Lipton , Columbia's School of Public Health and the Albert Einstein College of Medicine -- February 10 Columbia University 995 -- Vol. 20, .New York, N.Y. 10027, (212) 854-3283.

8. Ruth Ottman, Hauser WA, Susser M, Columbia's School of Public Health and the Albert Einstein College of Medicine. Columbia University Record -- February 10, 1995
9. Chang B, Lowenstein D: Mechanism of disease: Epilepsy. N Engl J Med 349:1257, 2003.
10. Hauser WA, Annegers JF, Epidemiology of epilepsy in Laidlaw JP, Richens A, Chadwick D: Text book of epilepsy; 4th ed. New York. Churchill livingstone, 1992, 23-45.
11. Adams RD. Commission on classification and terminology of the international league against epilepsy: proposal for revised clinical and electroencephalographic classification of epileptic seizure, Epilepsia 22: 489. 1981 (ADAM, principles of neurology 2001).
12. Classification and diagnostic criteria for headache disorders cranial neuralgias, and facial pain. International Headache Society. Cephalalgia, 1988;8;(SUPPL7)1-96.
13. Breslau N, Rasmussen BK. The impact of migraine: Epidemiology, risk factors, and comorbidities. Neurology 2001; 65:4-12.
14. Rasmussen BK, Olesen J: Migraine with aura and migraine without aura: an epidemiological study. Cephalalgia 12:221, 1992.
15. Sanin LC, Mathew NT, Bellmeyer L et al. The international headache society (IHS) headache classification as applied to a headache clinic population. Cephalalgia 1994;14:443-446
16. Adams RD. Headache and other craniofacial pain (chapter 10), principles of neurology, seventh edition. MC Graw-Hill 2001.
17. Lipton RB. Epidemiologic studies of migraine. JAMA 1992;67:64-69.
18. Beckett BE. Headache disorder. In: Dipiro JT, Talbert RL, Yee GC, et al. Pharmacotherapy, a pathophysiologic approach. 3rd edition. Stamford, Appleton and Lange, 1997; 1279-91.
19. Lipton RB, Stewart WF, VonKorff M. Burden of migraine societal cost and therapeutic opportunities. Neurology 1997;48:4-9.
20. Stewart WF, Lipton RB, Celentano DD, et al: Prevalence of migraine headache in the United States: relation to age, income, race, and other sociodemographic factors. JAMA 1992; 267:64.
21. Olesen J, Larsen B, Lauritzen M: Focal hyperemia followed by spreading oligemia and impaired activation of rCBF in classical migraine, ANN neurology 1081;9:344.
22. Forderreuther S, Henkel A, Noachtar S, Straube A. Neurologische Klinik und Poliklinik Klinikum Grosshadern, Ludwig-Maximilians University Munich, Germany.
23. L.E. Yamane, M.A. Montenegro, M.M. Guerreiro. University of Campinas, SP, Brazil, comorbidity headache and epilepsy in childhood.
24. Bigal ME, Lipton RB, Cohen J, Silberstein SD. Epilepsy and migraine. Epilepsy Behav 2003;4:13-24.
25. Breslau N, Rasmussen BK. The impact of migraine; epidemiology, risk factors, and co-morbidities. Neurology 2001;56(suppl 1):54-512.
26. Lipton RB, Scher AL, Kolodner K, et al. Migraine in the United States: epidemiology and patterns of health care use. Neurology 2002;58:885-894.
27. Lipton RB, Stewart WF, Celentano DD, Reed ML, undiagnosed migraine headache: a comparison of symptom-based and physician diagnosis, Arch Intern Med 1992;152:1273.
28. Solomon GD. Management of the headache patient with medical illness Clin J pain 1989;5:95-99.

