

Clinical features of epilepsy at 2 referral hospitals in Northern Iran

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ABSTRACT

الأهداف: للتحقق في الخصائص الديموغرافية والسريية للصرع في 2 من مستشفيات الإحالة في شمال إيران .

الطريقة: في هذه الدراسة المستعرضة نقيم 300 من المرضى تأكد التشخيص إصابتهم بالصرع حسب عيادات طب الأعصاب في مستشفى 22 بهممن و 17 شهريور، مشهد، إيران، تم تقييمها خلال الفترة ما بين ابريل 2011م وديسمبر 2012م. جمعت وحللت المعلومات الديموغرافية ومعلومات المرض .

النتائج: كان متوسط عمر المرضى 31.5 ± 15.3 سنة. أحرز تشخيص المرض بعد حوالي 10 شهراً من ظهور الأعراض، وكانت فجوة المعالجة 28%. كانت المضادات الأكثر استخداماً على التوالي هي فالبروات الصوديوم، كاربامازيبين والفينوباربيتال. واعتبر النوبة العامة في 78%، النوبة الجزئية في 22% ومزيج منهم في 11% من المرضى. كانت النوبة التوتورية الرمعية (72%) من النوع الأكثر شيوعاً من الصرع المتعمم وكان نوبة الصرع العامة الثانوية هي النوع الأكثر شيوعاً من الصرع الجزئي .

الخاتمة: الميزة الوبائية لمرض الصرع فيما يتعلق العمر والجنس في منطقتنا هو نفسه من أجزاء أخرى من العالم . النوع المتعمم هو الأكثر شيوعاً من الصرع والنوبة التوتورية الرمعية هي النوع الأكثر شيوعاً في منطقتنا .

Objective: To investigate the demographic and clinical characteristics of epilepsy in 2 referral hospitals in northern Iran.

Methods: In this cross-sectional study, we evaluated 300 patients with the confirmed diagnosis of epilepsy referred to the Neurology clinics of 22-Bahman, and 17-Shahrivar Hospitals, Mashad, Iran, from April 2011 to December 2012. We collected and analyzed demographic and disease information.

Results: The mean age of patients was 31.5 ± 15.3 years. The diagnosis of disease had been made approximately 10 months after the onset of symptoms, and the treatment gap was 28%. The most widely used anticonvulsants were sodium valproate,

carbamazepine, and phenobarbital. Generalized seizure was seen in 78%, partial seizure in 22%, and a combination of them in 11% of patients. Tonic-clonic seizure (72%) was the most common type of generalized epilepsy, and secondarily generalized seizure was the most frequent type of partial epilepsy.

Conclusion: The epidemiological features of epilepsy in our region with regard to age and gender are the same as other parts of the world. The generalized type is the most common form of epilepsy, with tonic-clonic seizures being the most frequent type in our area.

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Epilepsy is a common and chronic neurological disorder that affects individuals of all ages and is characterized by recurrent (2 or more) unprovoked epileptic seizures.¹ Seizure is an episode of involuntary movement, which may involve a part of the body or the entire body (generalized) and may be accompanied by loss of consciousness and control of bowel or bladder function. Seizure episodes are caused by abnormal electrical discharge in a group of brain cells. The

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age-adjusted prevalence and incidence of epilepsy in the general population are approximately 5 per 1000 person-years, and 50 per 100,000 person-years.² The lifetime prevalence rate of epilepsy in developed countries is 3.5 to 10.7 per 1,000 person-years.^{3,4} Epilepsy affects 50 million people worldwide.⁵ The prevalence and incidence of epilepsy and consequently its burden is higher in developing countries than in developed countries.⁶ Approximately 80% of patients with epilepsy live in developing countries and so 80% of the disease burden is attributed to developing countries.⁶ Detailed classification of seizures and epilepsy is essential to understanding its nature, with a rational plan of investigation and decision making regarding the timing and duration of treatment and choice of antiepileptic drug. As our country is a developing country, better understanding of epilepsy features could provide better management and control of disease, and so decrease the burden of it. As the epidemiological and clinical characteristics of epilepsy are not yet completely understood in Iran, this study aimed to investigate the demographic and clinical features of epilepsy in 2 referral hospitals in our region.

Methods. This cross-sectional descriptive study was conducted on 300 patients with the confirmed diagnosis of epilepsy referred to Neurology clinics of 22-Bahman and 17-Shahrivar Hospitals, Mashad, Iran, from April 2011 to December 2012. Mashad is the central of Khorasan Razavi province located in the Northeast of Iran. This province with a population of 5,994,402 and an area of 118,854 Km² is the fourth largest province in Iran. The large and main medical centers have been located in Mashad city, and patients from the surrounding cities and villages refer to these centers generally. A confirmed diagnosis of epilepsy based on the International League Against Epilepsy (ILAE) criteria⁷ with at least one EEG with paroxysms and brain imaging documents, cooperation during the study period, and age higher than 5 years, were the criteria for inclusion in the study. All eligible patients during the study period were included in the study consecutively. Patients with a single episode of seizure, patients not cooperating, and those with drug-induced epilepsy such as tramadol-induced epilepsy were excluded.

Epilepsy was defined and diagnosed based on the criteria of ILAE for Epilepsy (2 episodes of seizure due to pathologic and unpredictable discharge of the brain cells with more than 24 hours interval). Criteria of the International League Against Epilepsy were used for classification of seizures.⁷ The treatment gap was defined as percentage of persons with epilepsy

who are not appropriately treated. A census method was used for sampling, and eligible patients were selected consecutively. To collect data regarding history, neurological examination, EEG and neuroimaging findings, a questionnaire was designed and completed for each patient.

The study protocol was approved in ethics committee at Mashhad University of Medical Sciences and informed consent was obtained from the patients before enrollment. The study was conducted according to the principles of Helsinki Declaration revision 2013.⁸

Statistical analysis. Data analysis was performed using the Statistical Package for Social Sciences version 18.00 for Windows (SPSS Inc., Chicago, IL, USA) using independent sample t-test, Chi square, and McNemar test. Data are presented as mean±SD for quantitative data and number and percent for categorical data. *P*-values ≤0.05 were considered significant.

Results. In this study, 300 persons with epilepsy including 162 men (54%) and 138 women (46%) were included. The mean age of patients was 31.5±15.3 years, and most of the patients were in the age group of 21-30 years. The literacy level of most of the patients was higher than diploma (approximately 61%) and others (39%) were below diploma. One hundred and seventy-one patients (57%) were married and others were single. The mean time after the onset of symptoms was 107.1±93.5 months, and the mean time passed from diagnosis was 92.9±82.7 months at the time of study. In other words, the diagnosis of disease had been made around 15 months after the onset of symptoms. The frequency of drugs taken by the patients is shown in Table 1. The most widely used drug was sodium valproate. Most of the patients (146 patients, 48.66%) received monotherapy (Table 1). Physical examination was normal in 91.3% of patients (274). The EEG was unremarkable in 29% of patients, and the neuroimaging findings were unremarkable in 85.3% of patients. The average number of seizure episodes was 15.3±11.3. The frequency of different seizure types is shown in Table 2. Generalized seizure was seen in 78%, partial seizure in 22%, and combination of them in 11% of patients. Tonic-colonic seizure with a prevalence of 72.3% was the most common type of generalized epilepsy, and secondarily generalized seizure was the most frequent type of partial epilepsy. The results indicate that patients with a disease onset of age less than 40 years (*p*=0.013), and those with higher education (*p*=0.001) began treatment significantly earlier during the disease course.

Discussion. The results indicate that most of the persons with epilepsy were in the age group of

Table 1 - Distribution of medication type used by epileptic patients from Northern Iran. (N=300).

Drug	n	(%)
None	85	(28.3)
Sodium valproate	83	(27.7)
Carbamazepine	56	(18.7)
Phenobarbital	7	(2.3)
Sodium valproate and carbamazepine	11	(3.7)
Carbamazepine and phenobarbital	18	(6.0)
Sodium valproate and phenobarbital	7	(2.3)
Sodium valproate and carbamazepine and Phenobarbital	21	(7.0)
Alprazolam	12	(4.0)

Table 2 - Frequency of seizure types amongst the epileptic patients from Northern Iran (N=300).

Seizure type	n	(%)
<i>Generalized</i>		
Tonic-clonic	217	(72.3)
Absence	4	(1.3)
Tonic	4	(1.3)
Atonic	4	(1.3)
Myoclonic	4	(1.3)
<i>Partial</i>		
Simple	8	(2.7)
Complex	18	(6.0)
Partial seizures evolving to secondarily generalized seizures	30	(10.0)
Complex partial secondarily generalized	7	(2.3)
Simple partial secondarily generalized	4	(1.3)

21-30 years, and there was a 10-month gap between symptom onset and disease diagnosis. A few studies have been conducted in different parts of our country on populations of different ethnicity,⁹⁻¹¹ however, they are not complete and are lacking in some aspects, necessitating further studies in other regions. Among these studies, Ebrahimi et al's⁹ study in Kerman, Iran was population based. Most of the patients in our study had higher education with at least a diploma. This finding is similar to other studies.¹² Burton et al in Tanzania,¹³ showed that there is an association between epilepsy and perinatal events as well as family history of non-febrile seizures and lack of academic education. We did not assess this relationship in our study as we did not include a control group.

The most widely used antiepileptic drugs in our study were sodium valproate, carbamazepine, and phenobarbital. The drugs used in the previous studies from this region were not sufficiently reported. In the present study, 28% of patients were not taking any medication (treatment gap). The treatment gap in Wang et al's study in China was 41%.¹⁴ Kobau et al,¹⁵ showed that there is no drug history in a fourth of patients with active epilepsy and recent seizures in California. Noronha et al,¹⁶ in a study from Brazil found that 38% of patients with active epilepsy had inadequate medical treatment, and 19% were not receiving any medication. Wang et al¹⁷ estimated that approximately 90% of patients with epilepsy in developing countries are not receiving appropriate treatment. As our study was hospital-based, we could not compare our findings of treatment gap with those of mentioned studies as our study is limited to only 2 hospitals and the results do not indicate the status of treatment in all patients in the region. Treatment gap indicates the results of many medical, political, social, economic, and cultural factors and there is a larger treatment gaps in countries with lower incomes.¹⁸

The EEG was normal in approximately half of our patients. It has been shown that around half of the patients with epilepsy may have normal interictal EEG, and around 10% of patients never show interictal spikes. Therefore, a normal or negative EEG cannot rule out the clinical diagnosis as the specificity of EEG in diagnosis of epileptic disorders is higher than its sensitivity.¹⁹ Neuroimaging was unremarkable in more than 85% of patients. Imaging is performed to rule out secondary etiologies of epilepsy like structural abnormalities, underlying gross pathologies, and acute neurological lesion or illness in specific cases, and it is not indicated for all cases of epilepsy. Therefore, the rate of abnormality in the imaging may be different.¹⁹

The present study showed that the younger patients and those with higher education level begin treatment earlier in the course of disease. Such analysis has not been performed in previous studies in this field. Only 8 patients in our study were admitted following the first seizure attack. It seems that the first attack of seizure often is assumed trivial. However, such analysis has not been performed in any previous studies in our region or other studies.

In this study, tonic - clonic seizure was the most common type of epilepsy in generalized types, and secondarily generalized seizure was the most frequent type of focal epilepsy. These results are similar to other previous studies in Iran.^{9,11} This high rate of generalized seizures in our study may be explained by the method

of the study because our study was hospital-based and probably more patients with generalized seizures refer to a hospital clinic instead of outpatient clinics. Also, this high rate of generalized seizures in our study may be due to an overestimation, as generalised seizures are more dramatic and more likely to be noticed.

In the study by Burton et al in Tanzania,¹³ the most common seizure was focal secondarily generalized type in 73 patients (65.2%) and generalized seizures in 19 patients (16.9%). Picot et al's study from France²⁰ reported 61.1% partial, and 30.9% generalized seizures, which are different to our results. In Forsgren et al's study in northern Sweden,²¹ the most common form of epilepsy was partial epilepsy (333 per 100,000), and most (250 per 100,000) were secondarily generalized.

Of course, these differences in various studies could be due to the significant differences in the population structure of each region, and differences in the age structure of our country with other countries.²² The differences in the percentage of different types of seizures between this study and others studies, may be related to the diagnosis tests used (MRI, EEG, and so forth), or may be related to the method of our study that was hospital-based. Among the previous studies, only Faught et al,²³ in their study provided statistics on the prevalence and incidence of epilepsy in different races in the US. This analysis was not applicable in our study.

Lack of investigation of socio-economical conditions, lack of assessment of rates of active epilepsy, etiology, and disease control, and relapse rate after drug cessation is among important limitations of the present study. Also, as our study was hospital-based it may over estimated rate of tonic-clonic seizure, which is another limitation of this study.

Incidence, prevalence, and mortality of epilepsy are variable in different countries with different economies. In low-income and developing countries like ours, incidence, prevalence, and even mortality of epilepsy is higher than developed countries although the figure is the same in low-income individuals in developed countries.^{24,25} Although these 2 referral hospitals in our region are the only hospitals with a neurology ward in this region that treat epileptic patients, our study was hospital-based study and therefore does reflect the exact disease prevalence in the community as many patients with epilepsy may refer to private office or clinics.

As the epidemiology of the disease is different due to various factors such as education level, age pyramid structure, geographical and socio-economic, and demographic differences, it is necessary to examine the epidemiology of epilepsy separately in each region

to facilitate the diagnosis, treatment, and control of disease. Future large population-based studies, and systematic reviews and meta-analysis of previous studies from Iran are necessary to better describe and clarify the features of epilepsy in Iran.

In conclusion, according to the results, there is no significant difference in the age and gender distribution of our patients with other world countries. Generalized epilepsy is the most common form of epilepsy in our region and tonic-clonic seizure is the most common type in our area. Although our study was not an epidemiological study, the findings are important because of the large number of patients included in the study depicting the clinical features of epileptic disorders in our region.

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