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ORIGINAL ARTICLE / KLİNİK ÇALIŞMA

Prevalence of Epilepsy in the University Students Representing a Young Adult Population With Normal Intelligence

Normal Zekaya Sahip Genç Erişkinlerin Temsilcileri Olarak Üniversite Öğrencilerinde Epilepsi Prevalansı

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Summary

Objectives: Epilepsy is one of the most common neurological diseases and involves about 69 million patients worldwide. Especially in young adults, the social and private burden of epilepsy is high. The young adult population of Eastern Turkey has not been investigated with respect to the prevalence and risk factors of epilepsy. For these reasons we aimed to investigate the prevalence and some risk factors of active epilepsy in Kafkas University students as representatives the young adults of Eastern Turkey with normal intelligence.

Methods: The sample size for our study of consisted of a minimum of 1135 students. A total of 2000 questionnaires were distributed among the students and 1829 were accepted for statistical analysis. 43 students were identified as possibly having epilepsy and invited for further investigation. As a result, 7 participants were determined to have active epilepsy.

Results: The point prevalence of active defined epilepsy on December 30, 2010 was estimated to be 3.8/1000 for both sexes. The statistical analysis identified a history of febrile seizures and head trauma to be significant as risk factors for the development of epilepsy, while gender, family history of epilepsy, financial status, history of prematurity, cesarean or vaginal birth and parental consanguinity were not significant risk factors for epilepsy.

Conclusion: We can conclude that the prevalence of epilepsy in young adults in the eastern region of Turkey is comparable to those in developed countries.

Key words: Epilepsy; prevalence; risk factors; young adult.

Özet

Amaç: Epilepsi, dünya üzerinde yaklaşık 69 milyon kişiyi etkileyen en yaygın nörolojik hastalıklardan birisidir. Özellikle genç erişkinlerde epilepsinin sosyal ve özel hayat açısından getirdiği yük oldukça fazladır. Türkiye'nin doğusunda genç erişkin nüfus arasındaki epilepsi prevalansı ve risk faktörlerine dair yapılmış bir araştırma bulunmamaktadır. Bu nedenle, çalışmamızda Türkiye'nin doğusundaki normal zekaya sahip genç popülasyonun temsilcileri olarak Kafkas Üniversitesi öğrencilerinde epilepsi prevalansı ve risk faktörlerini araştırmayı amaçladık.

Gereç ve Yöntem: Çalışmamızın örneklem grubunun sayısı en az 1135 öğrenci olarak hesaplandı. Dağıtılmış olan 2000 anketten 1829'u istatiksel analiz için kullanıldı. 43 muhtemel epilepsi olgusu ileri incelemeler için hastanemize davet edildiler. Sonuç olarak, yedi katılımcıya aktif epilepsi tanısı konuldu.

Bulgular: 30 Aralık 2010 tarihi itibarıyla aktif epilepsinin nokta prevalansı 3.8/1000 olarak hesaplanmıştır. Epilepsi gelişiminde, febril nöbet öyküsü ve kafa travması istatistiksel olarak anlamlı risk faktörleri olarak saptanırken; cinsiyet, aile öyküsü, maddi gelir düzeyi, prematürite, doğum şekli ve akrabalık evliliği, epilepsi için istatistiksel olarak anlamlı risk faktörleri değildi.

Sonuç: Türkiye'nin doğusundaki genç erişkin nüfusta epilepsi prevalans değerlerinin gelişmiş ülkelerdeki ile karşılaştırılabilir düzeyde olduğunu söyleyebiliriz.

Anahtar sözcükler: Epilepsi; prevalans; risk faktörleri; genç erişkin.

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Introduction

Epilepsy continues to be one of the most common neurological diseases and involves about 69 million patients worldwide.[1] While the prevalence of epilepsy in low and middle income countries is 10 to 40 per thousand, this rate is reported to be 2.7-7 per thousand in developed countries.[2-6] The estimated proportion of the general population with active epilepsy (i.e. continuing seizures or the need for treatment) at a given time is 4 to 10 per 1000 people.[7] However, some studies in developing countries suggest that the proportion of active epilepsy is approximately 6 -10 per 1000.[7]

The prevalence rate of epilepsy tends to be high in early childhood and over 50 years of age.[6] In young adults, epilepsy is less frequent compared to the two peak periods described above. However, young adulthood is the most productive and socially active period in a person's life. Therefore in this age group, the social and private burden of epilepsy is high. It has an important influence on the educational, marital, legal and psychosocial well-being of young adults.

The occurrence of epilepsy is affected by many risk factors, such as genetic factors, peri- and prenatal events (i.e., asphyxia, low Apgar score, central nervous system infections, insults or hemorrhages), febrile seizures in early childhood; and cerebrovascular disorders, brain tumors or neurodegenerative causes in patients over the age of 50.[3] Especially in developing countries, low socio-economic status, central nervous system infections, head injury and consanguinity have been identified as possible causes of epilepsy in young people.[2,3]

To our knowledge, the young adult population of Eastern Turkey has not been investigated with respect to the prevalence and risk factors of epilepsy. For these reasons we aimed to investigate the prevalence and some risk factors of active epilepsy in young adults of Eastern Turkey. We chose Kafkas University students, who mainly represent the young adult population of eastern region of Turkey, according to statistical data from the Registrar's Office. We hypothesized that relatively low socio-economic status of this region and widespread consanguineous marriages may lead to an increased prevalence of epilepsy.

Materials and Methods

Study area, population and date

Kafkas State University is located in the city of Kars (Eastern Turkey) and provides higher education in vocational (associate), undergraduate, master's, and doctorate levels in the framework of global and local demand. There are 9 faculties, 4 schools, 7 vocational schools, 3 graduate schools and 16 research and application centers. According to data provided by the Registrar's Office of the university, about 15,226 resident students studied in the university in the 2012-2013 academic year. Distribution of students by region from which they came was as follows: Eastern Anatolia (48.85%), Southeastern Anatolia (8.66%), Mediterranean region (4.59%), Black Sea region (3.97%), Marmara region (3.87%), Central Anatolia (3.15%) and Aegean region (2.07%). The previous residence of some students was not defined (24.84%). Thus, our population represented young adults mainly from Eastern Turkey.

This study was conducted between December 2010 and February 2011 and was approved by the Ethics Committee of Kafkas University Medical Faculty.

Definitions

We used definitions from the Guidelines for Epidemiological Studies on Epilepsy by the Commission on Epidemiology and Prognosis, International League Against Epilepsy.[1,8]

Epilepsy is defined as a condition characterized by two or more epileptic seizures, unprovoked by any identified cause. The term "active epilepsy" is defined as the occurrence of at least one seizure in the past 5 years, regardless of treatment. Prevalence of active epilepsy was expressed as the number of people in a study population with active epilepsy (regardless of treatment) at a specified time.

Febrile convulsions are defined as convulsions and fever occurring after 1 month of age, without evidence of central nervous system infection or other recognized acute neurological causes.

We defined the term "parental consanguinity" as the matrimonial union between first cousins, including double first cousins.[9] Also, the term "prematurity" was used for neonates born before 37 weeks of gestation. For the definition of "head trauma", we used only trauma with loss of consciousness and/or amnesia.

Participants with a single seizure, provoked seizures due to acute metabolic, toxic, infectious and traumatic events, or

with nonepileptic events (syncope, pseudoseizures) were excluded from the study.

Determination of the sample magnitude

During 2010-2011 academic period in Kafkas University studied 13.500 students. Sample size was calculated using the formula $n= NZ^2_{\alpha}pq/d^2(N-1)$, where n is the sample size, N is the population size (13.500 students), Z is the critical value for our α level (we used 3.5), p is the presumed prevalence of the disease (0.01), q=1 - p, and d is the desired level of precision (we accepted d=0.01). According to the above formula, the sample size for our study should consist of a minimum of 1135 students.

Students from 9 faculties and 14 vocational and graduate schools were selected by a simple random sampling method. The point prevalence of active epilepsy in university students was calculated on December 30, 2010.

Questionnaire

The questionnaire included a pre-notice letter, with information about the study and the commitment of the authors to maintain confidentiality of the data provided.

The questionnaire was pretested to be as accurate as possible before the study. All questions were examined with regard to clarity and perspicuity. Next, 50 age-matched hospital staff completed the questionnaire in the presence of one of the authors, who did not comment on any of the questions. This process led to the elimination or modification of some questions and resulted in the formation of the final version of the questionnaire, which consisted of 30 items distributed over three sections.

The first section of the questionnaire included demographic information: name, surname, age, sex, faculty, previous residence of the student, smoking and alcohol use, number of siblings, socioeconomic level of the family, parents' education and kinship between parents.

The second section included six questions prepared by the World Health Organization for screening of epilepsy, and also questions prepared by Karaagaç et al. for epilepsy research in Turkey.[10,11]

The third section of the questionnaire consisted of items about the history of epilepsy of the participant and his/her first and second degree relatives, prematurity, vaginal or cesarean birth, head trauma, febrile convulsions, central nervous system infections, lumbar puncture and any antiepileptic or psychotropic medications.

Bearing in mind that some students may refuse to answer the questions, a total of 2000 questionnaires were distributed among the students and collected after 5 days. A total of 1878 questionnaires were answered, for a response rate of 93.9%. Forty-nine questionnaires were incomplete and were therefore excluded from the analysis. A total of 1829 questionnaires were accepted for statistical analysis.

The screening questionnaire identified 48 students (2.62%) as possibly having epilepsy or another convulsive disorder. After a telephone call, 43 students were invited for further investigation. A total of 41 subjects applied to the outpatient hospital. A detailed history of disease and, if necessary, electroencephalography (EEG) and magnetic resonance imaging (MRI) were performed for all invited patients. As a result, 7 participants (3 female and 4 male) were determined to have active epilepsy using diagnostic criteria, complete neurological and electrophysiological examination and MRI. Some participants provided variable information about possible previous epilepsy in remission and not able to document previous medical records about it; therefore we have not included the prediction of lifetime epilepsy in our study. Schematic illustration of stages of the study is shown in Figure 1.

These data were entered into the statistical software package SPSS for Windows, version 11.0 (SPSS, Inc., Chicago, IL). Descriptive statistics were performed on demographic and socioeconomic data, birth history and risk factors. To determine the risk factors of epilepsy, a χ^2 test was used. $P\leq0.05$

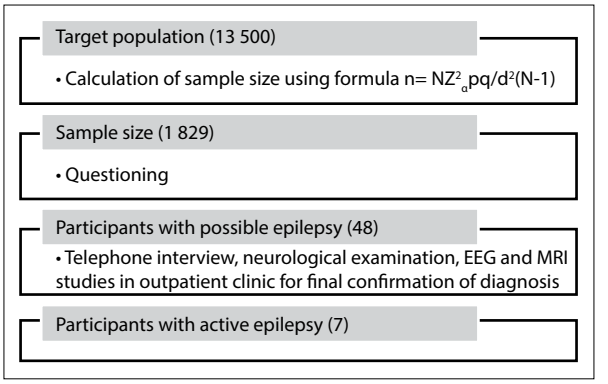

Fig. 1. Sampling method.

was considered as significant. Also, we used logistic regression analysis after adjusting the age variable to investigate possible individual risk factors for active epilepsy that were determined by the χ^2 tests.

Results

The sample population consisted of 1829 students with a mean age of 22.87±3.50. The age range was from 17 to 45. The interviewees were 805 females (44%) and 1024 males (56%); 35.4% of students previously resided in rural and 64.6% in urban regions. 43.2% of participants smoked and 6.6% used alcohol. Parents of 22.8% of students had a consanguineous marriage. Demographic and medical characteristics of 1829 participants are summarized in Table 1.

Among the 7 participants with epilepsy 3 (42.8%) were women and 4 (57.2%) were men. The mean age of patients with epilepsy was 25.6±6.1years.

The point prevalence of active defined epilepsy on December 30, 2010 was estimated to be 3.8/1000 for both sexes. The prevalence of active epilepsy was 3.7 per 1000 (95% confidence interval, 2.81-4.52) in females and 3.9 per 1000 (95% confidence interval, 3.55-4.78) in males. The relationship between prevalence for males and females was 1.05.

Table 1. Demographic and socio-economic characteristics of participants

	Number	Percent (%)
Gender		
Female	805	44
Male	1024	56
Residence		
Rural	646	35.4
Urban	1183	64.6
Consanguinity		
Yes	371	22.8
No	1254	77.2
Smoking		
Yes	791	43.2
No	1038	56.8
Alcohol utilization		
Yes	120	6.6
No	1038	93.4
Socioeconomic status		
Low	347	19.0
Middle	1454	79.5
High	28	1.5

All patients with defined epilepsy were previously under the supervision of a neurologist or a neurosurgeon. None of these patients had newly diagnosed epilepsy during the study. None of the patients had epileptic status during the disease. All patients were under medication: 4 patients were on monotherapy, and the other 3 patients had two medications, each. Four patients used valproate sodium, 3 used levetiracetam, and 3 used carbamazepine. All of the patients had motor seizures (one had primary, the other 6 had secondary generalized tonic-clonic seizures). None of the patients had any neurological deficits on neurological examination. One of the patients had an arachnoid cyst in the left temporal lobe and one had left mesial temporal sclerosis, as determined by MRI. In the other cases the MRI scan did not reveal any abnormalities.

EEG was performed on 41 students with suspected epilepsy and 4 of patients with active epilepsy had abnormal tracings such as focal slowing and/or interictal epileptiform activity. Our patients with epilepsy had different frequencies of seizures. One of the patients had 10 or more seizures per year, while others had been seizure-free for >1 year.

There was no statistically significant difference between the students in sample population and students with active epilepsy for a gender, family history of epilepsy, financial status, history of prematurity, cesarean or vaginal birth and parental consanguinity.

The χ^2 analysis identified a history of febrile seizures and head trauma to be significant as risk factors for the development of epilepsy (Table 2). Logistic regression analysis revealed that history of febrile convulsion and head trauma were found to be highly correlated with epilepsy development (Table 3).

Discussion

We studied the prevalence of active epilepsy in a representative population of young adults in the eastern region of Turkey and determined some possible risk factors for the disorder. The limited number of epilepsy prevalence studies in Turkey usually combines all age groups.[11-16] Studies investigating the prevalence of active or lifetime epilepsy for all age groups have been conducted in both rural and urban areas of Turkey. These studies reported various prevalence

Table 2. Some risk factors for epilepsy determined by χ^2 test. p≤0.05 were accepted as significant

	Epilepsy + %	Epilepsy - %	p
Febril convulsions			
Yes	1.7	98.3	χ^2=19.31
No	0.1	99.9	<0.001
Gender			
Male	0.4	99.66	χ^2=0.004
Female	0.4	99.66	0.629
Family history of epilepsy			
Yes	1.7	98.3	χ^2=5.92
No	0.3	99.7	0.067
Previous head trauma			
Yes	1.3	98.7	χ^2=7.77
No	0.2	99.8	0.020
Mode of delivery			
Vaginal	0.4	99.6	χ^2=0.406
Caesarean	0.0	100.0	0.674
History of prematurity			
Yes	0.9	99.1	χ^2=0.081
No	0.3	99.7	0.358
Consanguinity			
Yes	0.2	99.6	χ^2=0.056
No	0.4	99.8	0.401
Socioeconomic status			
Low	0.0	100.0	χ^2=0.437
Middle	0.7	99.3	0.685
High	0.0	100	

Table 3. Logistic regression odds ratios for the risk factors of epilepsy. p≤0.05 were accepted as significant

Risk factors	Odds ratios	95% CI	p
History of febrile convulsions			
No	1.00	4.65-13.82	<0.001
Yes	7.22		
History of previous head trauma			
No	1.00	2.95-8.89	<0.001
Yes	4.89		

rates, from 4.5 per 1000 to 17.3 per 1000 in the total population of Turkey.[11-16] The study conducted in the northeast region of Turkey reported the prevalence rate of epilepsy to be 5.3/1000 in all age groups.[15] The crude prevalence rate of epilepsy in comparative epidemiological study in Turkey and Pakistan was 7.0 per 1000 in all age groups.[14] Another two cross-sectional and case control studies conducted in a rural area of Turkey determined the prevalence of active epilepsy to 5.9 per 1000 and 10.2 per 1000 in all age groups.[11-13] Also, other researchers found the prevalence of active epilepsy for all ages to be 8.5 per 1000 in the urban areas of Turkey.[12]

Only a few combined studies conducted in Turkey included data on prevalence rate in the age range of our population.[15] Velioglu et al. reported that the prevalence of epilepsy in young adults (age 20-29) was 6.2/1000 in women and 4.3/1000 in men.[15] Similar results as a prevalence rate of

7.7/1000 in a comparable age population were reported in another study.[16] Calişir et al. reported high rates of active epilepsy (14.6 per 1000) in the 20-29 age range, in a combined study in urban areas of Turkey.[12] Thus, our study shows a similar prevalence of active epilepsy compared to studies that have been conducted in other regions of Turkey, except for the study of Calişir et al. On the other hand, our population did not include subjects with mental impairment, who may have more higher incidence (22-25 times greater) of epilepsy than subjects with normal intelligence.[17]

When compared to the prevalence rates worldwide, the prevalence of epilepsy varies between countries. The reported rates range from 3.14/1000 in China to 9.8/1000 in Benin for epilepsy in young adult populations.[18,19] Forsgen et al., in a European review, reported that the median prevalence was 5.4/1000 in the age groups 20-59.[20] For example, a study of the prevalence of epilepsy in Georgia, near the northeast border with Turkey, reported a rate of 8.1/1000 for the age range 21-40, higher than our rate among young adults.[21] Guekht A et al. reported the prevalence of epilepsy in the Russian Federation, another neighboring country, was 3.9 per 1000 in the age range 14-29 and 3.5 per 1000 in the age range 30-39.[22] Also, studies conducted in Africa found that epilepsy prevalence in ages 20-24 and 25-29 varied from 9.86/1000 to 7.18/1000 in Benin and in Kenya it was 4.0/1000 and 3.4/1000 (in males and females, respectively) in those aged 18- 28.[19-23] This variability in prevalence rates may be due to socio-cultural, socioeconomic and geographical specifications and differences in study design, case detection techniques and inclusion criteria.

As result of this study, we found that individuals with a history of febrile seizures and head trauma were more likely to have epilepsy, while a family history of epilepsy, prematurity, consanguinity, mode of delivery and gender were not statistically significant risk factors for epilepsy.

A history of febrile seizures was an important risk factor for the development of epilepsy identified in the present study, which has also been found in previous studies, especially in young populations.[24,25] Children with febrile seizures, but without neurological abnormalities and family history of epilepsy, have a 2.4% chance of developing epilepsy by age 25 compared with 1.4% for the general population.[26] Also, children with a neurological abnormality, family history of epilepsy and complex febrile seizures have a high risk (49%) of developing epilepsy.[27] We have also identified febrile seizures as a risk factor for developing epilepsy, although our patients were neurologically intact. On the other hand, we were not able to determine such details as whether participants with epilepsy had a history of prolonged or multiple seizures that were associated with complex (atypical) febrile seizures, which in turn are linked with an increased risk for epilepsy.[27]

Head trauma as risk factor for epilepsy has been found in numerous previous studies in the adult population.[22,28-30] In particular, in Asia, post-traumatic epilepsy is one of the major risk factors for epilepsy.[31] Li et al. reported that posttraumatic epilepsy accounted for 5% of total epilepsy and 20% of symptomatic epilepsy.[31] Although the leading cause of epilepsy in the present study was head trauma, none of the students with epilepsy had had several or moderate head injuries with skull fracture, documented focal neurologic deficit and/or 24 h or more posttraumatic amnesia and unconsciousness.

Our population is regarded as more homogeneous, with relatively high socio-cultural, socioeconomic and educational status than the rest of the country. In fact, previous studies have shown that low socioeconomic status, which is associated with low education, lack of home ownership and established risk factors for epilepsy (stroke and head injury), was a risk factor for epilepsy.[32,33] However, we did not find any correlation between socioeconomic status and epilepsy in our population, possibly because the proportion of our participants with low socioeconomic status was small (19%). From this it is also possible to say that the low prevalence rates in our population may be explained by the relatively high socioeconomic levels and absence of hazardous occupations.

Most studies on epilepsy in the adult population show a dominance of males.[2,3,20,34] In our study, epilepsy prevalence was slightly increased in males, though this difference is not statistically significant.

It is known that consanguinity is sometimes a major risk factor for genetic diseases, particularly idiopathic and cryptogenic types of epilepsy.[2,3] When we designed the present study, we hypothesized that consanguineous marriage, which is widely (34.4%) practiced in this region, may be a possible cause of epilepsy.[35] Our study population also had

a high rate of first-degree parental consanguinity (22.8%). However, we did not determine any direct association between epilepsy and parental consanguinity, similar to another study in this region in the pediatric population and some previous studies conducted in Turkey.[14,36] Additionally, the lack of a statistically significant difference between epilepsy and the existence of epilepsy in first and second-degree relatives indirectly indicates that genetically determined risk factors do not play a major role in our population.

Our study has some limitations: for example, participants may have given misleading information or misinterpretations of previous history of prematurity, severity of head trauma or febrile seizures. For these reasons, when discussing risk factors, we mean possible risk factors, not documentary established factors. In addition, as other limitation, some students did not want to participate in the study because of the possible stigma associated with epilepsy and the loss of confidentiality.

In summary, we can conclude that the prevalence of epilepsy in young adults in the eastern region of Turkey is comparable to those in developed countries. On the other hand, our study population did not include participants with characteristics that may be obstacles to participation in higher education, such as mental retardation and other morbidities, which probably increase the risk of epilepsy. Future studies in this region, which cover subjects from all ages, conditions and socioeconomic levels, will provide more reliable information about the prevalence of epilepsy and the role of such possible risk factors as age, gender, comorbidities, kinship, socioeconomic and socio-cultural status in the development of epilepsy.

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Declaration of Interest

Authors have no potential conflicts of interest.

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