Demographic and Clinical Findings of Patients Monitored in a Newly Established Epilepsy Outpatient Clinic in the Çukurova Region: Experiences of a Tertiary Hospital in Turkey

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Abstract

Objective: The aim of this study was to investigate the demographic and clinical findings of patients monitored at the newly established Epilepsy Outpatient Clinic at the University of Health Sciences Turkey, Adana Medical Faculty, Adana City Training and Research Hospital.

Methods: A total of 315 patients who were monitored between July 2021 and October 2022 at the Neurology Clinic's Epilepsy Outpatient Clinic of the University of Health Sciences Turkey, Adana Medical Faculty, Adana City Training and Research Hospital were included in the study.

Results: Of the patients, 161 were male (51.1%) and 154 were female (48.9%). The average age of the patients was 33.9±13.98, and the average seizure frequency was 33.51±98.49 per year. The most frequently observed risk factors included a family history of epilepsy (31.3%), febrile convulsions (19.7%), and head trauma (18.4%). Neuroimaging findings were pathological in 47.6% of the patients, and electroencephalography findings were pathological in 65.8%. Focal onset seizures were observed in 45.1% of the patients, while generalized onset seizures were seen in 46.7%. Monotherapy was administered to 52.7% of the patients, and polytherapy was given to 41.6%. In epilepsy patients aged eighteen and above, pathological findings in neuroimaging were significantly higher ($p<0.001$).

Conclusion: Epidemiological studies provide invaluable information about the characteristics of an epilepsy clinic. However, there is still a notable scarcity of studies related to the regional epilepsy profile in our country. In this study, the clinical and demographic data of the patients were largely consistent with the literature. We believe that the regular monitoring of patients in comprehensive epilepsy clinics will enhance patient compliance and the success of treatment.

Keywords: Epilepsy, epidemiology, neuroimaging

INTRODUCTION

Epilepsy is characterized by seizures that result from abnormal and excessive electrical discharges in cortical neurons and are not triggered by a definable event.[1] Epilepsy is one of the most common neurological disorders and affects individuals of all ages, races, social classes, and geographic regions. Community-based studies have reported that the prevalence of epilepsy is higher in developing countries than in developed countries.[2]

It is estimated that approximately 9% of the population may experience at least one seizure at some point in their lives. The decision to treat after the first seizure is determined by clinicians based on the risk of recurrent seizures, the potential impact of recurrent seizures, possible side effects of the treatment, and the patient's preference.[3,4] The goal in epilepsy treatment is to achieve seizure freedom with minimal side effects and maintain optimal quality of life. Unfortunately, under the busy general outpatient clinic conditions, sufficient time cannot be allocated to epileptic patients, and they cannot receive adequate treatment. It has been shown that establishing epilepsy outpatient clinics in hospitals enhances the regular monitoring of epilepsy patients, treatment success, seizure-free rates, patient compliance with treatment, and quality of life.[5,6]

In this study, the aim was to evaluate the demographic, etiological, clinical, and treatment characteristics of our epilepsy patients in the Çukurova region and to provide a basis for planning the general approach for use in applications.

METHODS

The study included 315 patients who were monitored between July 2021 and October 2022 at the Epilepsy Outpatient Clinic of the University of Health Sciences Turkey, Adana Medical Faculty, Adana City Training and Research Hospital. Patients' age, gender, history characteristics, risk factors, age of first seizure, type of seizure, history of status epilepticus (SE), antiepileptic drug (AED), treatment received, drug resistance, whether treatment was changed, reason for change, the rate of benefit from drug change, electroencephalography (EEG), and cranial imaging examinations were recorded retrospectively by scanning file data.

Statistical Analysis

Categorical measurements were summarized as number and percentage, while numerical measurements were expressed as mean and standard deviation (median and minimum-maximum where necessary). The chi-square test statistic was used for comparing categorical measurements between groups. For statistical analysis of the data, IBM Statistical Package for the Social Sciences statistics version 20.0 software was used. The statistical significance level was set at 0.05 for all tests.

RESULTS

Of the 315 patients presenting to the epilepsy outpatient clinic, 161 were male (51.1%) and 154 were female (48.9%). The average age of the patients was 33.9±13.98; the age range varied between 17 and 82. One hundred and ninety patients (66.7%) reported being unemployed.

The age of first seizure ranged from 0 to 78 years; the average age of first seizure was 20.12±16.23. Seizure frequency varied from 0 seizures per year to 5 seizures per day. The average seizure frequency was 33.51±98.49 per year. Thirty-three patients (10.7%) had a history of SE. The most common risk factors were a family history of epilepsy (n=95), febrile convulsion (n=60), and head trauma (n=56) (Table 1).

In 45.1% (n=142) of patients, seizures began focally, and in 46.7% (n=147) they began generally. Twenty-eight patients were diagnosed as having psychogenic non-epileptic seizures (PNES) based on detailed history, EEG, and video EEG examinations (Table 2). Eleven patients had isolated PNES, whereas seventeen had PNES.

Thirty-seven patients did not have an EEG recorded at our hospital. Out of the 278 patients who had an electroencephalogram, 95 (34.2%) had a normal EEG. Ninety-four patients (33.8%) had focal and 69 (24.8%) had generalized epileptiform abnormalities. Fourteen patients (5%) showed slowing in the baseline activity, and six patients (2.2%) had non-specific EEG changes (Table 3).

MAIN POINTS

- There is still a notable scarcity of studies related to the regional epilepsy profile in our country.
- The rate of abnormal neuroimaging findings was significantly higher in patients with a seizure onset age of >18.
- The incidence of status epilepticus in cases of drug-resistant epilepsy was found to be statistically significantly high.
- One-hundred ninety of our patients (66.7%) reported being unemployed.

Two hundred sixty-five patients had neuroimaging findings. Out of these, 152 (52.4%) were normal. Eight (3%) had mesial temporal sclerosis, 32 (12.1%) had encephalomalacia, five (1.9%) had cranial tumors, four (1.5%) had arachnoid cysts, seven (2.6%) had cerebral atrophy, eighteen (6.8%) had congenital malformations, and 39 (14.7%) had ischemic gliotic changes.

Eighteen patients (5.7%) were not receiving treatment, 166 patients (52.7%) were on monotherapy, and 131 patients (41.6%) were on polytherapy. Excluding the 18 patients not receiving treatment, 48 of the remaining 297 patients (16.1%) were diagnosed with drug-resistant epilepsy. Fifty-two patients (18.3%) were on antidepressants (Table 4).

Treatment was altered in 217 patients (71.6%). Of these 217 patients, 177 (81.6%) had seizures; five (2.3%) due to inappropriate medication, ten (4.6%) due to side effects, twenty-two (10.1%) due to being seizure-free, and three (1.4%) because they were in their reproductive years and were using sodium valproate. After the change in treatment, patients were re-evaluated. One hundred and fifty-nine patients (65.7%) were seizure-free, thirty-one (12.8%) had a reduction of more than 50%, forty-three (17.8%) had a reduction of less than 50%, three (1.2%) had a seizure when medication was reduced, and six (2.5%) saw no change in seizure frequency.

Table 1. Risk factors of patients

Risk factor	Number
Family history of epilepsy	95
Febrile convulsion	60
Head trauma	56
Hypoxia	35
Intracranial operation	18
Brain tumor	17
Cerebrovascular accident	10
Central nervous system infection	10
Perinatal risk factor	4
Congenital disease	1
No risk factor detected	9

Table 2. Clinical and electroencephalographic classification of epileptic seizures, (ILAE 2017)

Seizure type	Number	%
Generalized onset	147	46.7
Focal onset	142	45.1
Unknown origin	15	4.8
Psychogenic seizure	11	3.5

ILAE: International League Against Epilepsy

Table 3. EEG findings

EEG findings	Number	%
Normal	95	34.2
Focal epileptiform abnormality	94	33.8
Generalized epileptiform abnormality	69	24.8
Slowing in the baseline activity	14	5
Non-specific EEG changes	6	2.2

EEG: Electroencephalography

Table 4. Rates of antiepileptic drug usage

Antiepileptic drug	Number	%
Levetiracetam	206	70.5
Sodium valproate	83	28.4
Carbamazepine	83	28.4
Lacosamide	27	9.2
Lamotrigine	27	9.2
Topiramate	15	5.1
Phenytoin	9	3.1
Oxcarbazepine	5	1.7
Clonazepam	4	1.4
Zonisamide	4	1.4
Pregabalin	2	0.7
Clobazam	2	0.7
Gabapentin	1	0.3
Ethosuximide	1	0.3

DISCUSSION

Epilepsy is the second most common neurological disease worldwide after cerebrovascular diseases, significantly impairing functionality, thus negatively affecting work productivity and the economy of nations.[7] Regular monitoring of such chronic and severe dependence-inducing diseases and documenting their epidemiological data will facilitate treatment strategies and prevention methods. In this study, we aimed to evaluate the demographic and clinical characteristics of patients in our newly established epilepsy outpatient clinic.

Various factors play a role in controlling epileptic seizures and resistance to treatment. At the forefront of these is the etiology of the seizure. In our study, based on the anamnesis information obtained from the patient and their relatives, records were taken of family history, head trauma, febrile convulsion, congenital diseases, perinatal risk factors, brain tumor, intracranial operation, and history of cerebrovascular disease. As in many chronic diseases, the most frequently detected risk factor in our epilepsy cases was determined to be a family history (31.3%). Compared with the literature, this high rate might be due to the higher incidence of consanguineous marriages in our region. Population-based epidemiological studies have found that the risk of seizures or epilepsy among first-degree relatives of epileptic patients is two to three times that of the general population.[8,9] The familial risk varies depending on the underlying etiology. This risk is seen more than twice as often in those with epilepsy of unknown cause, and in those with prenatal risk factors, it can increase almost fivefold. In a population-based study by Christensen et al.[10] involving more than 1.6 million people, it was reported that positive family history increased the risk of developing epilepsy more than tenfold following severe head trauma.

The risk of epilepsy varies between 2.4% in children with simple febrile seizures and 6% to 8% in children with complex febrile seizures. In one cohort study, it was found that children with febrile convulsions were five times more likely to develop subsequent unprovoked seizures compared to those without.[11] Several hypotheses gain significance regarding the increased risk of epilepsy development due to febrile seizures. The first is that acute hippocampal edema, which develops during febrile convulsion, increases the risk of epilepsy by leading to mesial temporal sclerosis. However, in two major longitudinal studies evaluating the outcomes of febrile seizures, the authors reported that a small number of children (approximately 7%) developed acute hippocampal edema, and none of them developed epilepsy.[12,13] Another potential mechanism is inflammation. Another potential mechanism is inflammation. Evidence suggests an increase in cytokines, particularly interleukin (IL)-1b, in the seizure onset zone during febrile seizures.[14] Cytokines interact with neurotoxic neurotransmitters, modulating brain damage and subsequently promoting leukocyte diapedesis across the blood-brain barrier, which is presumed critical for epileptogenesis. However, studies have yielded contradictory results regarding the role of these cytokines in the development of febrile seizures.[15-17] Recent research increasingly highlights the role of genetic factors.[11,18] In our patient group, 19.7% (n=60) had a history of febrile convulsions.

Seizures following traumatic brain injury are classified as acute (emerging within 24 hours), early (occurring within the first 7 days), and late (occurring after 7 days). Post-traumatic epilepsy is defined as the emergence of two or more unprovoked seizures more than seven days after the injury. In the minutes to hours following the injury, disruption of white matter tracts leads to neurotransmitter release, free radical formation, calcium-mediated damage, angiogenesis, mitochondrial dysfunction, and inflammatory responses. It's believed that these events, due to alterations in GABA and aspartic acid release, result in an imbalance between excitatory and inhibitory neurotransmitters, playing a role in the pathogenesis of epileptogenesis.[19,20] In our epilepsy outpatient clinic, 18.4% (n=56) of patients had a history of head trauma.

EEG is a vital neurophysiological method for supporting the diagnosis of epilepsy, classifying seizure types, selecting AED, and predicting prognosis.[21] An EEG taken on the first day after a seizure is crucial for detecting epileptiform findings. The probability of detecting a typical epileptiform anomaly in the first routine EEG is on average 50%. With repeated EEGs, well-applied activation methods, and, if possible, sleep recordings, this rate increases to 82-92%. Not every patient with epilepsy will display interictal epileptiform discharges, and epileptic activity can also be observed in healthy adults.[22] In our clinic, out of 278 patients with EEGs, 95 (34.2%) had normal EEGs. PNES was observed in 28 (8.9%) of our cases. Of those evaluated in the video EEG unit, 11 were diagnosed with PNES, and their medications were gradually discontinued.

Neuroimaging is employed primarily to determine the etiology of focal-onset epilepsy and demonstrate anatomical changes associated with seizure activity. Particularly in cases of drug-resistant epilepsy, magnetic resonance imaging (MRI) is imperative. Only 29% of patients with hippocampal sclerosis can be treated with AEDs, while the post-surgical seizure-free rate rises to around 70%.[23] Literature review indicates that MRI negativity rates reported in studies range between 17% and 55%.[24-26] In studies, it has been reported that the likelihood of detecting lesions significantly increases in patients subjected to 3T MRI.[27-29] Observed epileptogenic lesions vary depending on socio-economic level, age, and type of epilepsy.

In a prospective study conducted at a tertiary epilepsy center involving 738 patients, 3T MRI was performed on patients with drug-resistant epilepsy, and 262 (35.5%) were found to be normal. The most common imaging finding was mesial temporal sclerosis in 132 patients (17.9%), followed by encephalomalacia in 79 patients (10.7%).[30] In another prospective study, the most common lesion type identified in patients was encephalomalacia (49%), with other prevalent lesion types being tumors (15%), cavernomas (9%), and mesial temporal sclerosis (9%). Additionally, authors reported that in 55% of patients with epileptogenic lesions, the EEG was normal, and the frequency of epileptic lesions was highest (81%) in focal-onset epilepsies.[25] In our study, 152 (57.4%) of the patients had normal MRI findings, 39 (14.7%) had ischemic/gliotic lesions, 32 (12.1%) had encephalomalacia, and 8 (3%) had mesial temporal sclerosis. The higher MRI negativity rate in our clinic compared to the literature could be due to the absence of 3T MRI and the radiologist's experience. In accordance with literature, the rate of abnormal neuroimaging findings was significantly higher in patients with a seizure onset age >18 ($p<0.001$) (Figure 1), and the presence of an epileptogenic MRI lesion did not influence the chance of having an abnormal EEG. These findings are consistent with the higher prevalence of symptomatic epilepsies in adults. However, in contrast to the literature, our study did not find a high rate of epileptogenic lesions in focal-onset epilepsies ($p=0.065$). The reason for this discrepancy may be that, due to the retrospective nature of our study, seizure onset patterns could not be determined accurately and that not all patients were followed by the epilepsy protocol and 3 T MRI was performed.

The objective in epilepsy treatment is to achieve maximum seizure control with minimum side effects in patients. Monotherapy is considered the gold standard for this aim. Studies have found it superior to polytherapy, especially in terms of side effects, drug-drug interactions, patient compliance, and quality of life.[31,32] In approximately half of the patients, seizure control is achieved with the first prescribed AED, while it's reported that in 11% to 37% of the remaining patients, seizures are controlled with the second monotherapy agent.[33,35] In a multicenter study documenting AED prescription data between 2013-2018, 68.19% of the patients were on monotherapy, 31.81% were on polytherapy, and the most frequently prescribed AED was levetiracetam (LEV).[36] In an epidemiological study between 2009-2017, AED prescription rates for patients were documented by age and gender. Despite valproic acid (VPA) being the most frequently prescribed, the prescription rate for LEV has been reported to consistently increase throughout the study period regardless of age and gender. Furthermore, the authors highlighted a significant decline in VPA prescriptions in recent years, especially in women of reproductive age and in the elderly.[37] Of our patients, 166 (52.7%) were on monotherapy, while 131 (41.6%) were on polytherapy. In line with the literature, the most commonly prescribed AED was LEV (71.5%).

Drug-resistant epilepsy is defined as a situation where sustainable seizure control cannot be achieved despite the use of two AEDs, either as monotherapy or in combination, that are appropriate for the seizure type and tolerated by the patient.[38] The resistance rate in adult epilepsy patients ranges between 30% and 40%. In one review, strong risk factors for drug-resistant epilepsy were reported as abnormal EEG (both slow waves and epileptiform discharges), SE, symptomatic etiology, multiple seizure types, and febrile convulsions.[39] Of the patients we treated for epilepsy, 48 (16.6%) had drug-resistant epilepsy. This rate was significantly lower compared to the literature.[40-42] We think that this low rate may be related to the fact that we have few lesional epilepsy patients and that we can follow up patients regularly and frequently. Consistent with the literature, the incidence of SE in these cases was statistically significantly higher ($p<0.001$) (Figure 2). However, the rates of detected pathology on MRI ($p=0.233$) and observed abnormal EEG findings ($p=0.83$) in drug-resistant epilepsy cases were not significantly higher.

In our clinic, treatment was modified for 217 patients. After the treatment change, 159 (65.7%) of the re-evaluated patients were seizure-free, 31 had more than a 50% reduction, and 43 (17.8%) had less than a 50% reduction in seizure frequency. Seizure recurrence was observed in three patients during medication reduction.

Depressive disorders are the most common psychiatric comorbidity in people with epilepsy, affecting about one-third and having a

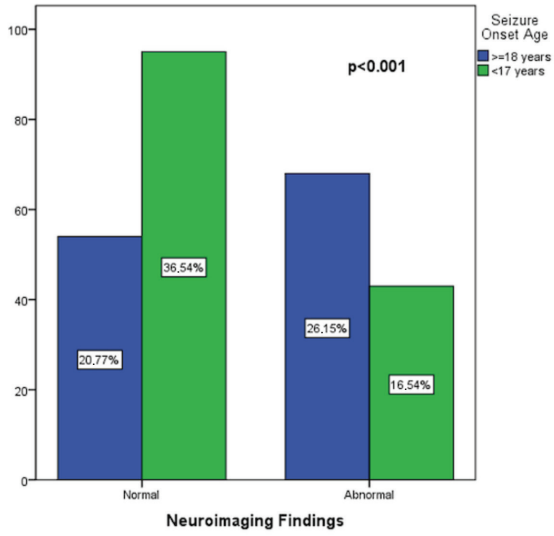

Figure 1. Relationship between seizure onset age and neuroimaging findings

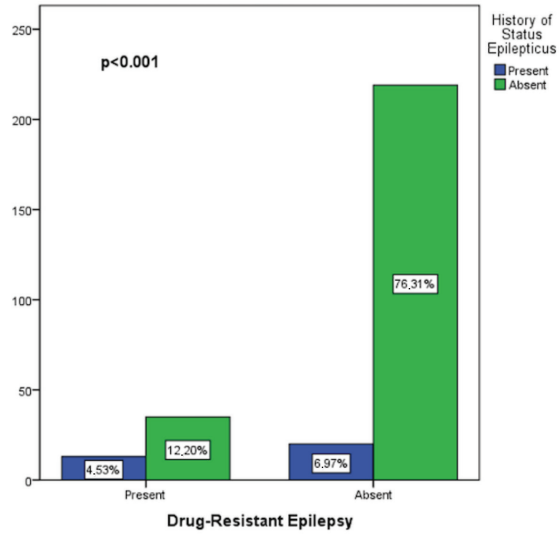

Figure 2. Association between refractory epilepsy and history of status epilepticus

significant adverse effect on quality of life. However, due to the fear that antidepressants might induce seizures, depression often remains untreated in people with epilepsy. In contrast, studies have shown that with antidepressant treatment, up to 97% of patients show improvement and it doesn't increase the frequency of seizures.[43] Of the patients followed up in our clinic, 52 (18.3%) were on antidepressant treatment.

Employment opportunities for individuals with epilepsy are unfortunately restricted in all countries around the world. In a case-control study conducted in Tanzania, researchers found a significantly lower rate of employment in people with epilepsy compared to the control group (33.3% vs 91.1%).[44] In a single-center cross-sectional study; even in an industrialized country like Hong Kong where unemployment is very low, the unemployment rate among epilepsy patients was found to be 33%, and this rate was reported to be quite high compared to the general population.[45] In a review published in Australia, authors reported that individuals with epilepsy are generally excluded from all employments requiring a uniform.[46] In our study, 190 patients (66.7%) reported being unemployed.

Study Limitations

The limitations of this study are; due to data being sourced from patient files, there could be inaccuracies in determining the type of seizure onset; the absence of 3T MRI examinations and the rate of MRI negativity possibly being high due to radiologist experience compared to the literature.

CONCLUSION

Our study provides valuable insights about epileptic patients in a tertiary hospital in Turkey and reflects a regional profile. In general, our findings were found to be consistent with the literature. We believe that evaluating sociodemographic and clinical features through community-based, multi-center comprehensive studies will potentially benefit the development of treatment strategies and achieve better outcomes.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from University of Health Sciences Turkey, Adana City Training and Research Hospital Clinical Research Ethics Committee (approval number: 128/2626, date: 08.06.2023).

Informed Consent: Retrospective study.

Author Contributions

Surgical and Medical Practices: Z.S.Ş., Concept: Z.S.Ş., H.B., Design: Z.S.Ş., H.B., Data Collection or Processing: Z.S.Ş., H.B., Analysis or Interpretation: Z.S.Ş., H.B., Literature Search: Z.S.Ş., H.B., Writing: Z.S.Ş.

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