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Demographic and clinical characteristics of children who were hospitalized and followed due to seizures

Nöbet nedeni ile yatırılan ve takip edilen çocuk hastaların demografik ve klinik özellikleri

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Abstract

Aim: Seizure is the most common neurological disorder of childhood. The causes of seizures in childhood, especially febrile convulsions (FC), is still not fully elucidated. In addition, diagnosis, follow-up and treatment are still controversial. In this study, we aimed to investigate the clinical/demographic features, laboratory results, electroencephalography and neuroimaging findings of children who were hospitalized and followed due to seizures.

Methods: This retrospective cohort study included 737 patients who were hospitalized and followed up due to seizures in the pediatric neurology department. Clinical features and laboratory results of the patients were evaluated.

Results: Among all, 53.1% of the patients who had febrile convulsions were males, 46.9% were females, and the mean age was 20.68 (5) months. The most important risk factors in febrile convulsion were positive family history (38.4%) and iron deficiency (42.9%). The most common source of infection was viral upper respiratory tract infections. While cerebrospinal fluid evaluations were normal in patients with ordinary febrile convulsions, that of 30 patients with complex febrile convulsions were coherent with meningitis. 437 patients were hospitalized with the diagnosis of epilepsy, among which 54.3% were males, and 45.7% were females. The mean age was 65.8 (54.8) months. Generalized tonic-clonic seizures were most common, while idiopathic epilepsy was the most frequently observed type. The most common risk factors in epilepsy patients were positive family history (26.2%), febrile convulsion (26.8%), and cerebral palsy (8.2%).

Conclusion: In this study, febrile convulsion and idiopathic epilepsy were the most determined causes of pediatric convulsion. Kinship marriage and positive family history are both the most important risk factors in febrile convulsions and epilepsy. Children with focal FC should be followed closely due to increased risk of epilepsy.

Keywords: Febrile convulsion, Seizure, Epilepsy

Öz

Amaç: Nöbet, çocukluk çağının en sık görülen nörolojik bozukluğudur. Çocukluk çağında nöbetlerin, özellikle febril konvülsiyonların nedenleri hala tam olarak aydınlatılamamıştır. Ayrıca tanı, takip ve tedavi halen tartışmalıdır. Bu çalışmada, nöbet nedeniyle hastaneye yatırılan ve takip edilen çocukların klinik özellikleri, laboratuvar sonuçları, elektroensefalografi ve beyin görüntüleme bulguları, tedavi yöntemleri ve demografik özelliklerinin araştırılması amaçlandı.

Yöntemler: Bu retrospektif kohort çalışmaya pediatrik nöroloji servisinde nöbet nedeniyle yatırılarak takip edilen 737 hasta dahil edilmiştir. Hastaların klinik özellikleri ve laboratuvar sonuçları retrospektif olarak değerlendirildi.

Bulgular: Hastaların 245'i febril konvülziyon, 437'si epilepsiydi. Febril konvülziyon geçiren hastaların %53,1'i erkek, %46,9'u kız, ortalama yaşları 20,6(5)aydı. Febril konvülziyon hastalarında en önemli risk faktörleri pozitif aile öyküsü(%38,4) ve demir eksikliği(%42,9) olarak belirlendi. En sık saptanan enfeksiyon kaynağı viral üst solunum yolu enfeksiyonlarıydı. Basit febril konvülziyon geçiren hastalarda beyin omurilik sıvısı değerlendirmeleri normalken, komplike febril konvülziyon geçiren 30 hastada menenjit ile uyumluydu. Epilepsi tanısı ile 437 hasta yatırılmıştı. Epilepsi hastalarının %54,3'ü erkek %45,7'si kadındı ve yaş ortalaması 65,8 (54,8) aydı. En sık jeneralize tonik klonik nöbetler görülmüştü ve en sık epilepsi tipi idiyopatik epilepsiydi. Epilepsi hastalarında en sık risk faktörleri pozitif aile öyküsü (%26,2), febril konvülziyon geçirme (%26,8) ve serebral palsiydi (%8,2).

Sonuç: Bu çalışmada çocukluk çağı nöbetlerinde en sık saptanan etiyolojik nedenler febril konvülziyon ve idiyopatik epilepsidir. Akraba evlilikleri ve pozitif aile öyküsü hem febril konvülziyonlarda, hem de epilepsi de en önemli risk faktörleridir. Fokal febril konvülziyon geçiren hastaların epilepsi gelişimi açısından yakın takibe alınmalıdır.

Anahtar kelimeler: Febril konvülsiyon, Nöbet, Epilepsi

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Introduction

A seizure is characterized by sudden, abnormal, and hypersynchronous discharge of cortical gray matter or brain stem neurons, sudden and temporary loss of consciousness, involuntary abnormal motor activity, sensory behavior, and autonomic dysfunction. The most common seizure type in childhood is febrile convulsion (FC), with an incidence of 2-5% [1,2]. Febrile convulsions are seizures that occur with fever, with no defined cause such as a central nervous system (CNS) infection, electrolyte imbalance, or poisoning in children older than 1 month of age who have not had a prior afebrile seizure. It is divided into two types as simple FC and complex FC, and occurs mostly around 18 months [3].

Epilepsy is sudden, iterative, and characteristically not triggered by an identifiable event. It is the most common neurological disease in childhood-adolescence. Epilepsy is most commonly seen in infancy. Its incidence decreases dramatically after the first year of life, and this decline continues throughout childhood [4]. In new clinical practice, epilepsy is defined by the presence of one of the following three conditions [5]:

1) At least two non-triggered (spontaneous) or reflex seizures with an interval of twenty-four hours

2) At least one non-triggered or reflex seizure and the risk of seizure recurrence within 10 years being similar to the risk in patients who had at least two untriggered seizures (at least 60%)

3) Presence of one of the epileptic syndromes

In our study, we aimed to investigate the seizure types, risk factors, and socio demographic characteristics of patients who were hospitalized and followed up due to seizures between January 2006-December 2010 at the Pediatric Health and Diseases Ward of our hospital.

Materials and methods

This retrospective cohort study includes 737 patients who were admitted to the pediatric neurology service of the Pediatric Health and Diseases Ward at Cumhuriyet University Medical Faculty Hospital between January 2006 and December 2010. Approval was obtained from the Ethics Committee of Cumhuriyet University Medical Faculty for the study (Approval date/number: 2010-06/09). Patients who were hospitalized and followed up due to seizures have been identified with scanned files from the hospital archive.

The patient's gender, age, parental consanguinity, family history of FC and epilepsy, gestational age, birth history, birth weight, additional diseases, seizure types, first seizure age, seizure frequency, treatment, neurological examination, EEG, imaging (computed tomography scan of the brain-CT or magnetic resonance imaging-MRI) and laboratory (complete blood count and routine biochemical tests, complete urinalysis, new-born screening results, cerebrospinal fluid results) results were compiled retrospectively from patient files.

Statistical analysis

TThe data in our study was uploaded to SPSS (version: 14.0) program. Chi-Square and Fisher's Exact Tests were used for determination of significance. Data were presented as numbers, mean and standard deviation, as necessary. $P<0.05$ was considered statistically significant.

Results

Among 737 patents included in the study, 245 patients had FC, 437 patients, epilepsy, and 55 (30 meningitis, 17 hypocalcemia, 5 hyponatremia, 3 hypoglycemia) patients had symptomatic seizures.

Among FC patients, 130 (53.1%) were males and 115 (46.9%) were females, with an overall mean age of 20.68 (5) months. The number of patients with complex and simple FC were 130 (53.1%) and 115 (46.9%), respectively. Consanguinity was detected between the parents of 54 patients (22%), 42 (17.1%) of which were 1st degree and 12 (4.9%) of which were 2nd degree kinship marriages. Ninety-four (38.4%) patients had a history of FC in their family. Family history (69/94) was significantly higher in the complex FC group than in the simple FC group (25/94) ($P=0.01$). Ninety-six (39.2%) patients had their first seizures before the age of one year, 111 (45.3%), between the ages of one and three years, and 38 (15.5%), between the ages of three and five years. The most frequent seizure type, generalized tonic-clonic seizures, were observed in 201 patients, followed by atonic seizures in 29 (11.8%), generalized tonic seizures in 9 (3.7%), clonic seizures in 4 (1.4%) and focal seizures in 2 (0.8%). Seventeen (6.9%) children were hospitalized with febrile status epilepticus (SE), among which ten (58.8%) were male, and 7 (41.2%) were female. Twelve had no seizure history while 5 had recurring FC.

Upper respiratory tract infections (URTIs) were the most common source of infection in 60% (147) of the patients (Table 1). The majority were considered viral upper respiratory tract infections based on examination and laboratory findings. One hundred and five (42.9%) patients had iron deficiency anemia.

Table 1: Fever causes of febrile convulsion patients

Fever causes	n	%
URTIs (viral/bacterial)	98/49	40/20
Pneumonia	28	11.4
EBV	3	1.2
UTI	23	9.4
AGE	25	10.2
Vaccine	6	2.4
STIs	4	1.6
Varicella	5	2.0
Sepsis	4	1.6
Total	245	100.0

URTIs: Upper respiratory tract infections, UTI: Urinary tract infection, EBV: Epstein Barr virus, AGE: Acute Gastroenteritis, STIs: Soft tissue infections

EEG was performed to 160 (65.3%) patients. EEG results were abnormal in 17% of those with complex FC and 4.3% of those with simple FC, the difference between which was significant ($P=0.02$). Prophylactic anti-epileptic medication was started in 138 (53.7%) cases. An afebrile seizure occurred during the follow-up of 14 FC patients (5.7%), all of which were diagnosed with epilepsy. All these patients had complex FC, the EEGs of all but one patient showed epileptic activity and 9 had focal seizures.

Computerized Brain Tomography (CBT), transfontanelle ultrasound and Magnetic Resonance Imaging (MRI) were performed to 49 (20%), 10 (4%) and 4 (1.6%) patients, respectively. All those who underwent imaging had febrile SE and complex FC. Benign external hydrocephalus, asymmetry in the lateral ventricles, arachnoid cyst, and

nonspecific nodular signal change were detected in 3 (1.2%), 2 (0.8%), 1 (0.4%) and 1 (0.4%) patients, respectively.

Among epilepsy patients, 251(54.3%) were male, and 211 (45.7%) were female, with an overall mean age of 65.8 (54.8) months. Forty (8.7%) patients were preterm, 416 (90%) were term and 6 (1.3%) were post-term. Seventy-four (16%) patients had a history of hypoxia during birth. Consanguinity was detected between the parents of 120 patients (25%), 106 (22.9%) of which were 1st degree and 14 (3%) of which were 2nd degree kinship marriages. One hundred and twenty-one (26.2%) patients had a history of seizures of their family, 100 (82.7%) of which had a history of FC, and 21 (17.3%), a history of epilepsy. In addition, 124 (26.8%) of epilepsy patients had a history of FC.

The seizure types of the patients are presented in Table 2. One hundred and forty-five (31.4%) patients were hospitalized with Status Epilepticus, among which no seizure histories were determined in 18 (12.4%). While 354 (76.6%) were using single anti-epileptic agents, 74 (16%) patients were taking 2 agents, and 34 (7.4%) were taking three or more.

Table 2: Seizure types of epilepsy patients

Seizure types	n	%
Partial		
Simple	15	3.4
Secondary Generalize	15	3.4
Complex	15	3.4
Generalized	12	2.7
Absence		
Tonic-clonic	269	61.6
Myoclonic	19	4.3
Tonic	13	3.0
Atonic	62	14.2
Lennox Gastaut Sydrome	3	0.7
Ohtahara Syndrome	1	0.2
Infantile Spasm	13	3.0
Total	437	100.0

One hundred and forty-nine (34%) epilepsy patients were considered to have idiopathic epilepsy. Neurological examinations of these patients were normal, and there were no concomitant diseases. The most common neurological disease was cerebral palsy (8.2%). Other commonly detected conditions included growth retardation in 36 (7.8%) patients, mental motor retardation in 29 (6.3%) patients, head trauma in 26 (5.6%), previous CNS (Central Nervous System) infection in 17 (3.9%), hydrocephalus in 7 (1.5%), undefined metabolic diseases in 7 (1.5%), Dyke Davidoff Masson Syndrome in 4 (0.4%), neurodegenerative diseases in 4, Rett Syndrome in 3 (0.6%), Glutaric Aciduria Type 1 in 3 (0.6%), Tuberous sclerosis in 2 (0.4%), kernicterus sequela in 2 (0.4%), and an intracranial mass in 1 (0.2%) patient. Cranial MRI was performed in 360 (77.9%) patients (Table 3).

Table 3: Cranial MRI findings of epilepsy patients

MRI findings	n	%
Normal	173	48
Ischemic gliotic lesion	40	11.1
Periventricular leukomalacia	38	10.5
Encephalomalasia	32	8.8
Atrophy	32	8.8
Nonspecific signal changes	14	3.8
Corpus callosum hypoplasia / agenesis	10/3	3.6
Hydrocephalus	7	1.9
Hypomyelination	4	1.1
Cerebrovascular disorders	4	1.1
Nodules/hamartoma compatible with tuberous sclerosis	2	0.55
Brain tumor	1	0.27

Discussion

Febrile convulsions are the most common pediatric seizures. Studies have reported that FC is more common in males compared to females. The male/female ratio has been reported as 1.46-1.8:1 in numerous studies [6-8]. In our study, the male/female ratio was 1.13:1, which was compatible with the literature. The first seizure is usually seen between 16 and 22 months [8-10]. In our study, the mean age of the first seizure was 20 months.

Although its etiology is still unknown, family history of FC, a disease of multifactorial-polygenic inheritance, was reported as 14.3-34% in first-degree relatives in numerous studies [6,8,11,12]. In our study, 38.4% of the patients had positive family history of FC, which supports familial predisposition.

The history of epilepsy in the families of patients ranges between 6.6-14% in previous studies [6,8,11,13]. In our study, the rate was 8.4%, coherent with the literature.

Especially in patients younger than one year of age, FC may be the only symptom of a central nervous system infection. The American Academy of Pediatrics suggests lumbar puncture for infants under 12 months of age presenting with simple FC, if not vaccinated against Haemophilus influenzae type B or Streptococcus pneumoniae or in case of antibiotic usage before the seizure [14]. However, in children with simple convulsions and normal neurological examinations, it is more preferred to use a follow-up approach without LP [8,15]. In our study, LP was performed to 79 patients with complex and simple FCs, and to 41 patients under 1 year of age. Central nervous system diseases were detected in 30 patients with complicated FC, and in none of the patients in the simple FC group. Based on our study, it may be suggested that stable patients with simple FC who had normal neurological examination findings can be followed without LP.

In febrile convulsions, the most common reason for fever is virus-induced URTIs [10]. Viral factors differ according to countries. Human herpesvirus (HHV-6) in the United States and Influenza A in Asian countries are the most frequently reported viral factors in FC [16,17]. In our country, according to a multicenter study by Carman et al. [18], at least one respiratory virus was detected in 82.8% of patients who had FC. In our study, active isolation studies have not been performed, but the most common reason for fever was viral URTIs based on physical examination and laboratory findings of the patients.

It is thought that low serum iron may lower the seizure threshold and lead to increased seizure occurrence in children with fever. In many studies, serum iron levels were low in patients with FC [8,19-21]. Iron deficiency anemia was detected in 105 (42.9%) of our patients in this study.

Anti-epileptic treatment is effective in preventing FC recurrence; however, the side effects may outweigh the benefits [3]. In particular, in simple FC, prophylactic long-term anti-epileptic usage is not recommended [22,23]. In our patient group, 132 patients (complex FC / simple FC 119/13) were treated with prophylactic phenobarbital treatment, and 12 patients (complex FC / simple FC 11/1) received intermittent rectal diazepam. The vast majority of patients undergoing treatment were complex FC patients. Although prophylactic long-term treatment is not recommended, the socio-economic level of the families, compliance with the treatment, and the geographical conditions of the region were effective in starting the treatment. In our study, the number of patients who started treatment was high, as

the socioeconomic level was low in the study area, and especially during winter, geographical access was frequently restricted.

Pediatric epilepsy is most commonly seen in nursing infants. Epilepsy decreases dramatically after the first year of life, and this decline continues throughout childhood [5]. As in FC, it is more common in males [24,25]. In our study, the male/female ratio was 1.18:1. The mean age of patients was 65.8 (54.8) months and 38.8% of the patients were under 2 years of age.

Many studies have shown that genetic factors make up about 40% of epilepsy etiopathogenesis [26]. Considering this information, idiopathic epilepsy has been reclassified as genetic epilepsy [27]. In the inheritance of epilepsy, consanguinity of parents and family history are of importance. In a case study in our country, the rate of kinship among parents of epilepsy patients was 16.2% [28]. In our study, the rate of consanguineous marriage was 25.9%.

In diverse studies, the rates of a family history of epilepsy were reported as 9.7% [29], 45.7% [30], and 63.3% [25], and 26.2% of patients were determined to have positive family history of seizures. About 17.3% of these patients had a history of epilepsy in their families and 82.7%, a history of FC. These differences can be explained with ethnic origin, inter-regional socioeconomic, and cultural factors.

Apart from genetic factors in children, prenatal and perinatal risk factors may be important in epilepsy and other neurological diseases. Perinatal asphyxia, preterm birth and brain damage are important risk factors for epilepsy, and under these conditions, the risk of occurrence epilepsy was reported as 18% [31]. In this study, 40 (8.7%) of epilepsy patients were born prematurely, and 74 (16%) of them had a history of perinatal asphyxia. Similarly, in a study conducted in our country, the rate of perinatal asphyxia was 13.3% [32]. We think that high rates of preterm delivery and perinatal asphyxia in our study is related to socioeconomic and geographical features of our region. Cerebral palsy (8.2%) was the most common risk factor for epilepsy in our study.

Head trauma is a known risk factor for epilepsy [33]. Especially in cases where post-traumatic consciousness changes occur, the occurrence risk of epilepsy increases. In a study conducted in our country, the rate of a history of head trauma in children with epilepsy was 12% [32]. In our study, a history of head injury was detected in 26 (5.6%) patients.

FC is considered a risk factor for epilepsy [32-35]. The risk of epilepsy after febrile convulsions is particularly high in complicated FC, developing in the form of focal seizures. Other risk factors include neuromotor growth retardation and a family history of epilepsy [35,36] The ratio of FC in patients who were followed-up with the diagnosis of epilepsy was between 12.4-36.3% [32,37,38]. In our study, epilepsy occurred during follow-up of 14 (5.7%) patients who had complex FC. Similarly, 124 (26.8%) epilepsy patients had a history of FC. As is seen, the history of FC in epilepsy patients is quite high compared to the rates of epilepsy detected in patients followed with FC diagnosis. This may be due to the short follow-up periods of FC patients, just as in our study.

Limitations

The main limitations of our study are its retrospective design and data being obtained from patient files. However, the first evaluation and all controls were made by pediatric neurologists. In addition, patient data were recorded on standard forms by pediatric neurologists. These factors reduced the limitation of the study due to its retrospective nature.

Conclusion

In our study, febrile convulsion and idiopathic epilepsy were the most determined causes of seizure etiology. Preterm birth, perinatal asphyxia, kinship marriage and positive family history are both the most important risk factors in febrile convulsions and epilepsy. These risk factors are preventable to a certain extent with more specific educational programs. Patients with complex FC who had focal seizures need to be monitored for a long-time for epilepsy occurrence. Furthermore, we suggest that patients with simple FC who are in good general condition can be monitored without LP. Iron deficiency should be investigated in patients with FC and treated, as necessary. Further, prospective, multicenter and long-term studies are needed to confirm our results.

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