Clinical Characteristics and Possible Risk Factors of Epilepsy in Children with Cerebral Palsy: A Tertiary-Center Experience

Serebral Palsili Çocuklarda Epilepsinin Klinik Özellikleri ve Olası Risk Faktörleri: Üçüncü Basamak Merkez Deneyimi

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ABSTRACT

Objective: The aim of this study was to evaluate the clinical characteristics of children with cerebral palsy (CP) and to investigate possible risk factors and prognosis of epilepsy in children with cerebral palsy (CP) with a special emphasis on drug-resistant epilepsy (DRE).

Material and Methods: A total of 145 pediatric patients who were followed up with a diagnosis of CP between 2019 and 2022 were evaluated. Demographic features, prenatal/perinatal history, etiology and type of CP, degree of impairment in motor and cognitive functions, seizure type, neuroimaging, and electroencephalography (EEG) findings were obtained retrospectively from hospital records. The patients were divided into two groups: CP patients with epilepsy and patients without epilepsy. Study variables were compared between these two groups and also between DRE and controlled epilepsy groups.

Results: There were 91 (63%) boys and 54 (37%) girls with a mean age of 11.1±4.2 years (3-18 years). Epilepsy was present in 107 (73.7%) cases and 40.1% of them had refractory epilepsy. Epilepsy was most common in the tetraplegic form of CP (p=0.028). Term gestation, birth weight of ≥2500 g, and history of neonatal seizures were significantly higher in patients with epilepsy (p=0.030, 0.010, and 0.030, respectively). Children with DRE were more likely to have tetraplegic CP (50%) and severe intellectual disability (56%).

Conclusion: Determination of potential risk factors is important in predicting the development of epilepsy in patients with CP, as it may provide closer follow-up of patients at high risk. Particular attention should be paid to the early identification and treatment of comorbid epilepsy in children with CP.

Key Words: Cerebral palsy, Epilepsy, Risk factors, Refractory epilepsy, Pediatric

ÖZ

Amaç: Bu çalışmada serebral palsili (SP) çocuklarda klinik özellikler ile epilepsi gelişiminde olası risk faktörlerinin ve epilepsi prognozunun değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: 2019-2022 yılları arasında SP tanısı ile takip edilen toplam 145 çocuk hasta değerlendirilmiştir. Olguların demografik bilgileri, prenatal/perinatal öyküsü, SP etiyolojisi ve tipi, motor ve bilişsel fonksiyonlardaki bozukluğun derecesi, nöbet tipi, nörogörüntüleme ve elektroensefalografi (EEG) bulguları hastane kayıtlarından retrospektif olarak toplanmıştır. Olgular epilepsisi olan ve epilepsisi olmayan SP hastaları olmak üzere iki gruba ayrılmıştır. Çalışma değişkenleri bu iki grup arasında ve ayrıca dirençli epilepsi ile kontrollü epilepsi grupları arasında karşılaştırılmıştır.

Bulgular: Olguların 91'i (%63) erkek, 54'ü (%37) kız ve ortalama yaşı 11.1±4.2 yıl (3-18 yaş)'tı. Toplam 107 (%73.7) olguda epilepsi mevcuttu ve bunların %40.1'i dirençli epilepsiydi. Epilepsi grubunda en sık SP tipi tetraplejik SP'di (p=0.028). Term gebelik, ≥2500 g doğum ağırlığı ve neonatal nöbet öyküsü epilepsili SP grubunda anlamlı olarak daha fazlaydı (sırasıyla p=0.030, 0.010 ve 0.030). Dirençli epilepsi grubunda tetraplejik SP tipi (%50) ve ağır zihinsel yetersizlik (%56) görülme oranı kontrollü epilepsi grubuna göre daha yüksekti.

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Contribution of the Authors / Yazarların katkısı*: *ARDICLI D: Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***DEDEOGLU O:*** Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in necessary literature review for the study.

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Sonuç: Serebral palsili hastalarda epilepsi gelişiminin öngörülmesinde olası risk faktörlerinin belirlenmesi, yüksek riskli hastaların yakın izlemi açısından önemlidir. Serebral palsili çocuklarda komorbid epilepsinin erken tanımlanması ve tedavisine özellikle dikkat edilmelidir.

Anahtar Sözcükler: Serebral palsi, Epilepsi, Risk faktörleri, Dirençli epilepsi, Pediatrik

INTRODUCTION

Cerebral palsy (CP) is the most common chronic neurodevelopmental disorder in childhood and occurs at a frequency of 1.5-3 per 1000 live births. Cerebral palsy is caused by damage to the developing brain before or during birth or in the first months of life, affecting muscle tone, movement, and posture, that is not progressive, but symptoms and signs may change with age (1). In addition to motor functional disabilities, children with CP are at increased risk for impairments in visual, auditory, sensory, cognitive, and behavioral functions and development of epilepsy.

It is well known that the general incidence of epilepsy in children with CP is high, ranging between 15-60% (1). Depending on the type of CP and accompanying comorbidities, the incidence of epilepsy may reach up to 90% (3, 4). The frequency of epilepsy has been reported as particularly more common in children with severe motor (tetraplegic CP) and cognitive impairments (4, 5). There are numerous reports on the predictive risk factors for the development of epilepsy in children with CP, including prenatal risk factors, perinatal complications, and history of neonatal seizures (3). Later in childhood, epileptic seizures may become resistant to anti-seizure medications and uncontrolled seizures put an extra burden with unfavorable impacts on neurodevelopment and quality of life.

Herein, we aimed to evaluate the clinical characteristics of patients with CP and to investigate possible correlations between pre/perinatal risk factors and epilepsy, with a special emphasis on drug-resistant epilepsy (DRE) in a group of children with cerebral palsy recruited from a single tertiary center in Turkey.

MATERIALS and METHODS

This is a single-center, cross-sectional, retrospective study including 145 children with CP followed at Ankara Bilkent City Hospital, Department of Pediatric Neurology between 2019-2022. Patients with CP diagnoses were extracted from the electronic-based hospital data system according to the ICD-10 classification, as code of G80 and subtypes were included. Patients aged 3-18 years with a follow-up of at least 12 months were included. Children initially diagnosed with CP and later had another diagnosis mimicking CP, such as neurometabolic or neurodegenerative disorders were excluded. The following data variables were collected: age, gender, type of CP, prenatal risk factors, natal history, postnatal complications, presence of neonatal seizures, the level of motor and cognitive impairment, neuroimaging results, data regarding epilepsy such as age at seizure onset, seizure type, frequency of seizures, number of anti-seizure medications (ASMs), and electroencephalography (EEG) findings.

Clinical diagnosis of CP was defined as non-progressive, static encephalopathy presenting with motor and postural disabilities, caused by damage to the developing brain. Types of CP were grouped as diplegic, hemiplegic, tetraplegic, dyskinetic, ataxic, and mixed form. The level of motor functional severity was based on the Gross Motor Function Classification Scale (GMFCS) (6). The cognitive status of patients was evaluated based on age-appropriate standardized psychometric tests in available patients. Gestational age of ≤37 weeks was considered prematurity and the age of gestation was categorized into the following groups: ≤30 weeks, 30–37 weeks, and >37 weeks. Birth weight was grouped as <1000 g, 1000–1499 g, 1500–2499 g, and ≥2500 g. Brain neuroimaging findings were classified according to the Magnetic Resonance Imaging Classification System (MRICS) proposed by Surveillance of Cerebral Palsy in Europe (SCPE): maldevelopments (disorders of cortical formation and other maldevelopments), predominant white matter injury (periventricular leukomalacia (PVL), intraventricular hemorrhage (IVH) or periventricular hemorrhagic infarct), predominant gray matter injury (basal ganglia/thalamus lesions, arterial infarctions or watershed lesions in parasagittal distribution), miscellaneous (nonspecific cerebral or cerebellar atrophy, ventriculomegaly) and normal (7). We classified types of seizures and epilepsies based on the 2017 International League against Epilepsy (ILAE) classification (8). Epilepsy types were classified into four groups: focal, generalized, combined focal and generalized, and unknown. Drug-resistant epilepsy was defined as persistent seizures despite the proper use of at least two ASMs. Controlled epilepsy was defined as having no seizures for more than 6 months. Patients whose antiseizure treatment was discontinued were also included in the controlled epilepsy group. EEG abnormalities were classified in the form of focal, generalized or multifocal epileptogenic activities and other abnormalities, including abnormal background activity and a history of specific patterns such as hypsarrhythmia or electrical status epilepticus during sleep -ESES.

Patients were divided into the following groups; Group 1: CP with epilepsy (n=107) and Group 2: CP without epilepsy (n=38). Demographic characteristics, prenatal/natal history, postnatal complications, type of CP, level of motor disabilities, and cognitive functional status of the two groups were compared. Those variables were also compared between the subgroups of DRE and controlled epilepsy.

Statistics

SPSS software, version 23.0 (SPSS, Chicago, IL), was used for the statistical analysis of the data. The variables were

investigated using visual (histograms, probability plots) and analytical methods (Kolomogorov-Smirnov/Shapiro-Wilk test) to determine whether or not they are normally distributed. Descriptive analyses were presented using means and standard deviations for normally distributed and medians and interquartile range (IQR) for the non-normally distributed and ordinal variables. Numbers and percentages are used for categorical variables. Median scores of all groups were compared with the nonparametric Mann-Whitney U test. The proportions of patients were compared by using the Chi-square test or Fischer's exact test in different groups. A p-value of <0.050 is considered to be statistically significant.

The study is approved by the institutional ethical committee of Ankara City Hospital (E2-22-2147).

RESULTS

A total of 145 patients (91 boys and 54 girls) were included. Mean age of the patients at last clinical visit was 11.1±4.2 years (3-18 years). The median duration of follow-up was 3.2 years. Parental consanguinity was present in 19 (13.1%) patients. The demographic and clinical features of our patients are demonstrated in Table I.

Eighty-three (57.2%) patients were born at term and 62 (42.8%) were born at preterm. The mode of delivery was vaginal in 73 (50.3%) and cesarean section in 72 (49.7%). Multiple gestation pregnancy was present in 11 (7.5%) patients. Data on birth weight was available in 109 patients, including ≥2500 g in 61 (55.9%), 1500-2499 g in 24 (22.0%), 1000-1499 g in 13 (11.9%,) and <1000 g in 11 (10.1%). A total of 107 (73.7%) patients had a history of hospitalization in the neonatal intensive care unit (NICU), with a median period of 21 days (IQR 11-45). Thirty-three patients (22.7%) had history of neonatal seizures and seven (4.8%) had history of neonatal hypoglycemia.

The most common etiologies of CP were hypoxic-ischemic encephalopathy (HIE) in 55 (37.9%) patients, followed by prematurity in 49 (33.8%). Other etiologies were stroke (n=14; 9.7%), brain malformations (n=11; 7.6%), neonatal sepsis/meningitis (n=6; 4.1%), and kernicterus (n=5; 3.4%). The etiology of CP was undetermined in 5 (3.4%) cases.

The most common CP types were spastic tetraplegia (n=39; 26.9%) and spastic hemiplegia (n=37; 25.5%) in our study. Children with tetraplegic and hemiplegic CP were mostly full-term babies (58.8% and 72.7%, respectively), while diplegic and dyskinetic CP forms were more frequent in the group of preterm births (73.3% and 66.7%, respectively). A statistical difference was observed between gestational age and type of CP (p=0.008). Birth weight was ≥2500 g in most of the patients with tetraplegic and hemiplegic CP (63% and 70%, respectively) compared to the other forms (p=0.013). Results of psychometric assessments were available in 112 (77.2%) cases. Patients with tetraplegic CP had more severe cognitive impairment compared to other types, as 67% of tetraplegic CP

Table I: Baseline clinical characteristics of patients with cerebral palsy (n=145)

Sex*	Male Female	91 (62.8) 54 (37.2)
Age at last clinical visit	Mean ± SD (min-max), years	11.1 ± 4.2 (3-18)
Etiology*	Hypoxic-ischemic encephalopathy (HIE) Prematurity Stroke Structural malformations Neonatal sepsis/meningitis Kernicterus Undetermined	55 (37.9) 49 (33.8) 14 (9.7) 11 (7.6) 6 (4.1) 5 (3.4) 5 (3.4)
Type of CP*	Diplegia Hemiplegia Tetraplegia Mixed Dyskinetic Ataxic	31 (21.4) 37 (25.5) 39 (26.9) 31 (21.4) 6 (4.1) 1 (0.7)
GMFCS scores*	GMFCS I GMFCS II GMFCS III GMFCS IV GMFCS V	14 (9.7) 40 (27.8) 24 (16.7) 44 (30.6) 22 (15.3)
Cognitive impairments*	Normal Mild impairment Moderate impairment Severe impairment	10 (8.9) 41 (36.6) 29 (25.9) 32 (28.6)

***:** *n (%),* ***SD:** standart deviation,* ***GMFCS:** gross motor function classification scale*

Table II: Comparison of study parameters in Group 1 (CP patients with epilepsy) and Group 2 (CP patients without epilepsy)

	Group 1 (n=107)	Group 2 (n=38)	p
Sex, n (%)			
Male	66 (61.7)	25 (65.8)	0.653
Female	41 (38.3)	13 (34.2)	
Age at last clinical visit (years)			
Median (IQR)	11.7 (8-15)	10.9 (5.9-13)	0.060
Etiology of CP, n (%)			
HIE	45 (42.1)	10 (26.3)	
Prematurity	31 (29.0)	18 (47.4)	
Stroke	11 (10.3)	3 (7.9)	
Structural malformations	10 (9.3)	1 (2.6)	0.031
Neonatal sepsis/meningitis	5 (4.7)	1 (2.6)	
Kernicterus	1 (0.9)	4 (10.5)	
Undetermined	4 (3.7)	1 (2.6)	
Gestational age			
Term (>37 w)	69 (64.5)	14 (36.8)	0.003
Preterm (≤37 w)	38 (35.5)	24 (63.2)	
Birth weight			
≥2500 g	51 (63.8)	10 (34.5)	
1500-2499 g	14 (17.5)	10 (34.5)	0.014
1000-1499 g	10 (12.5)	3 (10.3)	
<1000 g	5 (6.3)	6 (20.7)	
Mode of delivery			
Normal vaginal	43 (46.2)	13 (37.1)	0.355
Cesarean section	50 (53.8)	22 (62.9)	
History of NICU hospitalization			
Yes	78 (80.4)	29 (80.6)	0.985
No	19 (19.6)	7 (19.4)	
History of neonatal seizures			
Yes	29 (27.4)	4 (10.5)	0.034
No	77 (72.6)	34 (89.5)	
Type of CP			
Diplegia	22 (20.6)	9 (23.7)	
Hemiplegia	26 (24.3)	11 (28.9)	
Tetraplegia	33 (30.8)	6 (15.8)	0.028
Mixed	24 (22.4)	7 (18.4)	
Dyskinetic	1 (0.9)	5 (13.2)	
Ataxic	1 (0.9)	0	
GMFCS classification scores			
I	9 (8.5)	5 (13.2)	
II	29 (27.4)	11 (28.9)	0.536
III	16 (15.1)	8 (21.1)	
IV	33 (31.1)	11 (28.9)	
V	19 (17.9)	3 (7.9)	
Cognitive impairment			
Normal	6 (7.3)	4 (13.3)	
Mild	27 (32.9)	14 (46.7)	0.245
Moderate	22 (26.8)	7 (23.3)	
Severe	27 (32.9)	5 (16.7)	
MRI findings (MRICS classification)			
Normal	3 (2.9)	1 (2.6)	
Maldevelopments	11 (10.8)	0	0.036
Predominant white matter injury	43 (42.2)	26 (68.4)	
Predominant gray matter injury	36 (35.3)	9 (23.7)	
Miscallaneous	9 (8.8)	2 (5.3)	

***CP:** cerebral palsy, **IQR:** interquantile range, **HIE:** hypoxic ischemic encephalopathy, **NICU:** neonatal intensive care unit, **GMFCS:** gross motor function classification scale, **MRI:** magnetic resonance imaging, **MRICS:** magnetic resonance imaging classification system*

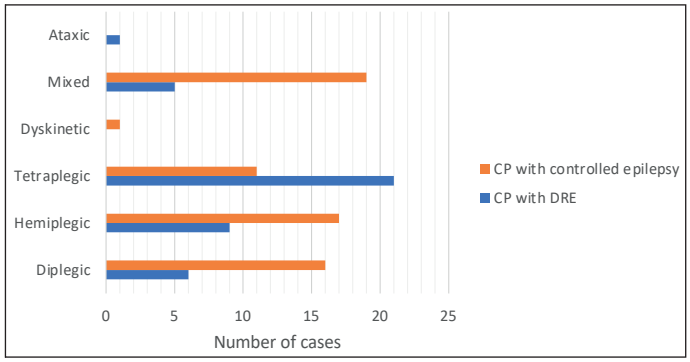

Figure 1: The distribution of cerebral palsy (CP) types in children with drug-resistant epilepsy (DRE) and controlled epilepsy.

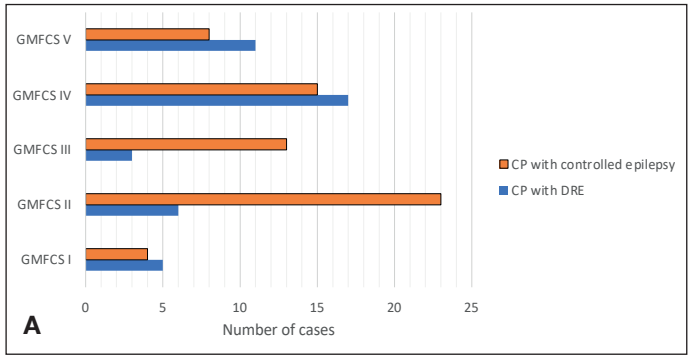

Figure 2A: The distribution of GMFCS levels in children with DRE and controlled epilepsy (GMFCS: Gross Motor Function Classification Scale, DRE: Drug-resistant epilepsy)

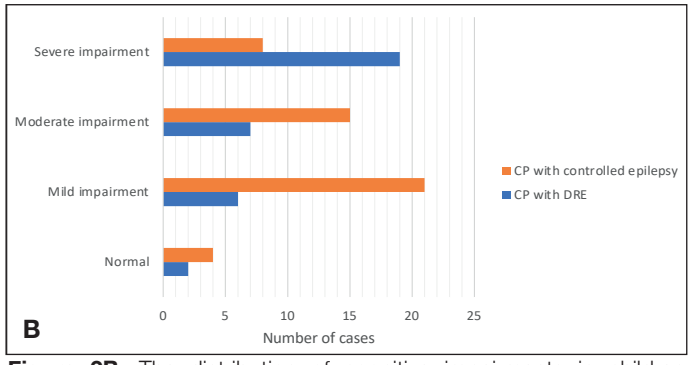

Figure 2B: The distribution of cognitive impairments in children with DRE and controlled epilepsy (GMFCS: Gross Motor Function Classification Scale, DRE: Drug-resistant epilepsy.

had a severe intellectual disability. In terms of motor functional status, 91 (63%) patients had a score of ≥ III, which indicated severe gross motor dysfunction.

Brain magnetic resonance imaging (MRI) data was available for 140 (97%) cases, which showed white matter predominance injury as the most common pathology (n=69; 49.3%), followed by gray matter predominant lesions (n=45; 32.1%), maldevelopments (n=11; 7.9%), other miscellaneous findings (n=11; 7.9%), and was normal in 4 patients (2.9%). The most common MRI abnormality among patients with diplegic CP was predominant white matter lesions (82.1%), mostly periventricular leukomalacia. Gray matter involvement was more common in cases with hemiplegic and tetraplegic CP, whereas white matter injury was predominant among patients with diplegic CP (p=0.003).

Among the included patients, epilepsy was diagnosed in 107 children (73.7%). Median age at study onset and male/female ratio was similar between the groups of CP patients with and without epilepsy (Table II). The median age at epilepsy-onset was 13 months (IQR 4-48) and the onset of seizures was before 24 months of life in 66 (61.6%) patients. Only four patients developed epileptic seizures beyond 10 years of age. Types of CP were diplegia in two, hemiplegia, and mixed form each in one patient. History of status epilepticus (SE) was noted in 12 patients (8.3%). A total of 73 patients (68.2%) were on polytherapy at the time of study enrollment.

Patients with epilepsy were mostly full-term (64.5% vs 36.8%, p=0.030) and had a birth weight of ≥2500 g (p=0.014). The history of neonatal seizures was statistically more frequent among patients with epilepsy (27.4%) compared to those without epilepsy (10.5%) (p=0.034). The most common etiologies of CP in Group 1 and Group 2 were HIE (42.1%) and prematurity (47.4%), respectively. Among the seven patients with a history of neonatal hypoglycemia, six had epileptic seizures during follow-up. In terms of mode of delivery and history of hospitalization in the NICU, there was no statistical difference between the groups (p=0.330 and 0.980, respectively). The most common CP forms were tetraplegic (30.8%) and hemiplegic (24.3%) in Group 1, whereas hemiplegic (28.9%) and diplegic (23.7%) in Group 2 (p=0.080). The distribution of GMFCS scores was similar between the groups (p=0.536). In terms of the degree of cognitive impairments, no statistical difference was detected between patients with and without epilepsy. MRI findings showed that predominant gray matter injury was more frequent in the epilepsy group than in CP without epilepsy (p=0.036). Majority of our cases (62%) had generalized tonic/tonic-clonic seizures as the predominant seizure type. According to epilepsy classification, 51 (47.7%) had generalized epilepsy, 34 (31.8%) had focal epilepsy, 9 (8.4%) had combined focal and generalized epilepsy, and the type of epilepsy was undetermined in 13 (12.1%) patients. Data regarding EEG results were available in 122 cases, of those, 91 (74.5%) showed abnormal findings. EEG abnormalities were as follows: focal (n=46; 50.5%), generalized (n=12; 13.2%), multifocal (n=19; 20.9%) epileptogenic activities, and other abnormalities (n=14; 15.3%).

Of the 107 children with epilepsy and CP, 43 (40.2%) had DRE. The median age of seizure-onset was earlier in patients with DRE than in controlled epilepsy (7 mo vs 24 mo, p=0.002). Neonatal seizure history was more common in patients with DRE than in controlled epilepsy (41.5% vs 18.8%, p=0.011). Eight of the 12 patients with a history of status epilepticus developed DRE during follow-up. Most common etiology of CP was HIE in the DRE group (52.4%). When the etiology of CP was compared with epilepsy outcome, seizure control was achieved in most

of those with prematurity and kernicterus etiology (p<0.001). The most common CP types were tetraplegic CP in the DRE group and mixed CP in the controlled epilepsy group (p=0.002) (Figure 1). Children with DRE were more likely to have GMFCS level >III (66.7%), and severe intellectual disability (56%) (Figures 2A-B). Predominant gray matter injury was the most frequent MRI abnormality among patients with DRE (42.5%). In terms of epilepsy type, there was no statistical difference between DRE and controlled epilepsy groups (p=0.158). Multifocal epileptic activities and a history of specific EEG patterns (hypsarrhythmia and ESES) on EEG were more frequent in patients with DRE (p=0.038)

DISCUSSION

Epilepsy has been considered one of the most common comorbidities among children with CP. The presence of epilepsy in CP, especially if refractory, significantly affects neurodevelopment and quality of life. The prevalence of epilepsy in CP has been reported in the literature varies widely; ranging from 15 to 90% (2-4). In the present study, 74% of the CP patients had epilepsy. Prevalence of epilepsy in our cohort was higher than in previous reports from different parts of our country, ranging between 50-57% (9-12). However, a similar rate of epilepsy was reported in the study of Bearden et al. (13), the prevalence of epilepsy was also found as high as 77%. These differences between the studies may be due to the different methodology, sample size, the average age of the patients at the enrollment, and variable duration of follow-up periods. Such a high percentage of patients with CP and concomitant epilepsy can be explained by the higher rate of severe SP patients are often referred to tertiary-center hospitals.

Numerous studies have investigated potential risk factors for epilepsy development in children with CP. The history of neonatal seizures is one of the most emphasized risk factors (3, 9-11). Our study revealed that neonatal seizure history was statistically higher in the epilepsy group compared to the patients without epilepsy, which is consistent with the previous literature. Additionally, neonatal seizures were more common in the DRE (42%) group than in patients with controlled epilepsy (19%). A similar relationship was also indicated by Mert et al.(9), children with neonatal seizures were 3.3 times more likely to have a poor epilepsy prognosis. Data on perinatal risk factors that may contribute to the occurrence of epilepsy in children with CP are relatively conflicting. Some of the studies revealed prematurity and low birth weight as possible risk factors for both epilepsy and CP (3, 4). In contrast, our study demonstrated that the percentage of term delivery and normal birth weight was higher in CP patients with epilepsy compared to those without epilepsy. Similar to our report, Zelnik et al. (14) showed that epilepsy was more common in term infants than in preterms. These results can be attributed to the fact that epilepsy is mostly caused by gray matter lesions, which are more common in full-term infants, while white matter lesions are more frequent in premature babies. In the study of Maksoud et al. (15), low Apgar scores were associated with an increased risk of epilepsy in CP in particular with DRE. In the current study, there was no significant difference between patients with and without epilepsy in terms of sex, parental consanguinity, and mode of delivery (p>0.050). Similar to our results, Gurkan et al. (11) found no significant association between epilepsy development and history of NICU hospitalization. In our study, six of seven patients with a history of neonatal hypoglycemia had epilepsy during follow-up. A similar relationship was also reported by Indian authors, as epilepsy occurred in 14 of the 30 (46.7%) CP children with a history of neonatal hypoglycemia (16). In children with CP, the perinatal insults are multi-factorial and further worsened by secondary injury to the brain such as hypoglycemia.

Our data showed that epilepsy was particularly more frequent in children with spastic tetraplegic CP, while it was less common in patients with dyskinetic or diplegic CP. Tetraplegic CP has been frequently reported to be a risk factor for epilepsy in previous studies (3, 15, 17). Most of our patients with DRE had tetraplegic CP. This is most likely linked to the higher rate of individuals with spastic quadriplegia in cerebral palsy populations in general, who are mostly affected by diffuse brain injury. However, in the study of Singhi et al.(18), the rate of epilepsy was the highest among patients with spastic hemiplegia (65.9%). Mert et al. (9) reported no significant difference between the type of CP and epilepsy development. These variations between studies can be attributed to the applied methodologies and sample size.

Similar to previous reports, the onset of epilepsy in the current study occurred at a young age (13 months) and more than half of our patients had their first seizures during the first two years of life (11, 16). In addition, the median age of seizure-onset was earlier in patients with DRE (7 months) than in the controlled epilepsy group (24 months). Some of the studies also mentioned that the age at seizure-onset might differ depending on the CP type.

Several reports showed a significant relationship between intellectual disability, motor impairment and epilepsy development (3, 13, 17). Although no statistical difference was detected between the level of motor and cognitive dysfunction and the development of epilepsy in our study, we found an association between these variables and intractable epilepsy. Patients with DRE were more likely to have higher GMFCS scores and moderate/severe cognitive impairments compared to the controlled epilepsy group. Contrary to our findings, Maksoud et al. (16) found an insignificant association between GMFCS score and intractable epilepsy.

Regarding MRI data, white matter predominance injury was the most common pathology (49%) in our entire cohort, while gray matter involvement was more frequent in the epilepsy group.

This finding was not surprising, as it is well known that cortical involvement plays a role in epileptogenesis.

With respect to the characteristics of epilepsy, the majority of individuals in our cohort had generalized epilepsy with a predominance of generalized tonic/tonic-clonic seizures (62%). Similarly, Gurkan et al. found generalized tonic-clonic seizures (46.6%) as the most frequent seizure type among their study population (13). However, in another report from our country, focal seizures were predominant (48.2%), probably due to their study consisted 42.9% of spastic hemiplegics (9). Focal seizures have been reported as one of the most important predictive factors of intractable epilepsy in children. However, we found no statistical difference in terms of seizure type and the subgroups of DRE and controlled epilepsy. The literature evaluating the predictive importance of EEG in CP patients with DRE is scarce. We detected multifocal epileptic discharges and a history of hypsarrhythmia or ESES more frequently in the DRE group. In the study of Tokatly Latzer et al, focal, multifocal discharges, and focal background slowing has been reported as predictive EEG abnormalities of intractable epilepsy (19). Another report acknowledged hypsarrhythmia as a poor prognostic factor (3).

Our study has some limitations, including the retrospective nature, relatively small sample size, and heterogeneity of the etiological factors of CP, limiting the statistical power. Other mentioned predictive factors for epilepsy development, such as family history of epilepsy or having a low Apgar score were not included in our analysis, due to the large size of missing data.

CONCLUSIONS

In summary, our study revealed that the frequency of epilepsy is higher than most reports. Epilepsy is common in certain forms of CP. The history of neonatal seizures appears to be the most significant risk factor for both epilepsy development and poor epilepsy prognosis in patients with CP. While term gestational age and normal birth weight were associated with epilepsy development, mode of delivery and the presence of consanguinity were not found to be risk factors in our cohort. Determination of potential risk factors is important in predicting the development of epilepsy in patients with CP, as it may provide closer follow-up of patients at high risk. Particular attention should be paid to the early identification and treatment of comorbid epilepsy in children with CP.

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