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Original Article

Brain magnetic resonance imaging findings and their relationship with prognosis in children with focal epileptic encephalographic discharges

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ABSTRACT

Objective: This study aimed to evaluate the relationship between normal brain magnetic resonance imaging (MRI) findings and prognosis in children with focal epileptic disorder on electroencephalography (EEG) without an epileptic syndrome.

Material and Methods: Data from patients aged 0-18 years, who were followed up with a diagnosis of epilepsy at the pediatric neurology clinics over the last 5 years, were retrospectively reviewed. Patients with focal epileptic disorder on EEG were selected. Those with an epileptic syndrome were excluded from the study. The patients' demographic characteristics, seizure types, etiologies, brain MRI findings, seizure focus, treatment methods, and seizure control were analyzed. Patients were divided into two groups based on their brain MRI findings (normal and abnormal) and compared in terms of treatment resistance, number of medications, and seizure control.

Results: The mean age of the 100 patients included in the study was 8±4.32 years, with an equal gender distribution (50% female, 50% male). Generalized seizures were observed in 72% of patients, while 28% had focal seizures. Seizure freedom was achieved in 60% of cases, and treatment resistance was noted in 23%. Cranial MRI revealed structural abnormalities in 67% of patients, with the majority (84%) showing sequelae-related changes, including hypoxic-ischemic sequelae (16%), encephalomalacia (12%), and structural malformations (10%). Although treatment resistance (28.8% vs. 12.1%) was higher and seizure freedom (56.7% vs. 66.7%) was lower in patients with abnormal MRI findings compared to those with normal MRI, these differences were not statistically significant (p =0.150 and p=0.310 respectively) . However, perinatal (p=0.013) and postnatal complications (p=0.042) were significantly more frequent in patients with abnormal MRI findings.

Conclusion: In children with focal epileptic disorder on EEG, normal brain MRI findings do not predict a better prognosis in terms of seizure control and treatment resistance. Other factors affecting treatment resistance in this population need to be investigated in more detail.

Keywords: Child, Epilepsy, Magnetic Resonance Imaging

INTRODUCTION

Epilepsy is a common neurological disorder that requires a precise understanding of its underlying etiology to guide appropriate management and improve patient outcomes. Identifying the cause of seizures is crucial, as it directly influences treatment decisions and prognosis. Key prognostic factors include etiology, EEG abnormalities, seizure type, the number of seizures before treatment initiation, and the early response to medication (1). Cranial magnetic resonance imaging (MRI) is the preferred imaging modality for assessing epilepsy, given its high sensitivity in detecting structural abnormalities that may contribute to epileptic activity. Common structural etiologies identified on MRI include cortical malformations, gliotic changes, and other focal lesions. However, epilepsy can also result from nonstructural causes, and in some cases, the etiology remains unknown despite comprehensive evaluations (2).

In pediatric epilepsy, interictal focal discharges observed on EEG are strongly associated with focal structural abnormalities on MRI. These findings highlight the complementary role of EEG and MRI in the diagnostic evaluation of epilepsy. However, some patients with focal epileptiform EEG activity have normal MRI findings, raising questions about the underlying mechanisms and their impact on clinical outcomes. Determining whether

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the presence or absence of structural abnormalities influences seizure control, treatment response, or long-term prognosis is essential for optimizing patient management.

Since epilepsy prognosis is closely related to its etiology, the use of MRI is expected to provide valuable insights into the likelihood of achieving seizure freedom and the potential risk of breakthrough seizures, due to its strong ability to determine the underlying cause (3,4).

Symptomatic etiology has traditionally been considered a negative predictor in epilepsy (1). However, little information is known about how patient characteristics and treatment patterns in those with lesional epilepsy compare to those with nonlesional epilepsy. Moreover, recent findings suggest that the distinction between lesional and functional (or non-lesional) epileptogenesis is becoming increasingly less clear (5). This challenges the expectation of significant prognostic differences between the two groups.

This study aimed to assess the prognostic significance of cranial MRI findings in children with focal epileptiform EEG activity. By analyzing differences in seizure control, treatment response, and long-term outcomes between patients with normal and abnormal MRI findings, it was aimed aim to provide clinically relevant insights to improve patient care and management in clinical practice.

MATERIALS and METHODS

The medical records of pediatric patients (0–18 years) diagnosed with epilepsy were retrospectively reviewed from the pediatric neurology outpatient clinic. The study was conducted between 2018 and 2021. A total of 100 patients were included in the study. The study included patients who had undergone both cranial MRI and EEG. Only those diagnosed with nonsyndromic epilepsy and exhibiting focal epileptiform discharges on interictal EEG were included, while patients with generalized epilepsy, syndromic epilepsy, or incomplete data were excluded.

Data extracted from medical records included patient age, gender, perinatal and postnatal complications, history of febrile seizures, prolonged febrile seizures, family history of epilepsy, epilepsy duration, age at seizure onset, seizure types, seizure control, treatment resistance, number of antiseizure medications used, physical examination findings, EEG findings, and cranial MRI results. Based on MRI findings, patients were classified into two groups: those with structural abnormalities and those with normal MRI results (non-structural). Seizure control and treatment resistance were compared between these two groups.

Perinatal problems were defined as conditions that affect development, including premature birth, low birth weight, birth trauma, neonatal infections, respiratory issues, hypoglycemia, hyperbilirubinemia, and congenital anomalies in infants. In mothers, perinatal problems included gestational diabetes, preeclampsia, bleeding, infections, amniotic fluid abnormalities, and early rupture of membranes. Postnatal problems were defined as conditions such as hyperbilirubinemia, encephalitis, meningitis, sepsis, septic shock, neonatal stroke, and asphyxia (including drowning or foreign body-related issues).

EEG recordings were conducted using an 18-channel system, with electrodes placed according to the international 10-20 system. The EEG data were interpreted by two neurologists.

Seizure types were classified as focal or generalized. Treatment resistance was defined as the persistence of seizures despite treatment with at least two antiepileptic drugs (AEDs) at appropriate doses.

Seizure control was defined as the absence of seizures for at least six months.

Treatment resistance in epilepsy is defined as the failure to achieve sustained seizure control despite adequate trials of at least two antiepileptic drugs (AEDs) administered at appropriate doses and for an adequate duration (6).

Statistics analysis:

Statistical analyses were conducted IBM Statistical Package for the Social Sciences, version 23.0 (SPSS Inc., Armonk, NY, IBM Corp., USA). Normality of the data was assessed using the Kolmogorov-Smirnov test. Parametric data were presented as mean and standart deviation values, while categorical variables were expressed as frequency and percentages. The Chi-square test was employed to compare categorical data. Comparisons between groups were made using independent samples t-test and Mann-Whitney U-test. A significance level of $p < 0.050$ was considered statistically significant.

Ethics committee approval was received from the KTU University Clinical Research Ethics Committee dated 27.12.2017-2017/2. The study has been conducted in accordance with the Helsinki Declaration.

RESULTS

General data of patients

A total of 418 patients diagnosed with epilepsy were reviewed. Of these, 318 patients who did not meet the inclusion criteria or had insufficient data were excluded from the study, leaving 100 patients with focal epileptic activity on EEG. The mean age of the patients was 8±4.32 years, with an equal gender distribution of 50% female and 50% male.

Among the patients, 29% had prenatal features, while 27% exhibited postnatal characteristics. Febrile seizures were reported in 21% of the patients, with 4% experiencing prolonged febrile seizures, and 13% having a family history of epilepsy.

Regarding seizure types, 72% had generalized onset seizures, while 28% had focal onset seizures, including 17% with focal

Table I: Comparison of clinical and demographic characteristics between patients with structural and non-structural MRI findings

	Structural n=67 (%)	Non-structural n=33 (%)	p
Age (mean months)	48.14±4.6	55.07±3.8	0.261*
Gender (F/M)8	32/34	18/16	0.834†
Perinatal problem	26 (38.8)	3 (9.1)	0.013†
Postnatal problem	23 (34.3)	4 (12.1)	0.042†
Febrile seizure	11 (16.4)	10 (30.3)	0.142†
Prolonged febrile seizure	3 (4.5)	1 (3)	1.000†
Epilepsy in Family	9 (13.4)	4 (12.1)	1.000†
Age of first seizure ≤5 >5	 52 (77.6) 15 (22.4)	 19 (57.6) 14 (42.4)	0.131†
Focal Seizure	21 (31.3)	7 (21.2)	0.214†
Epilepsy duration m (mean)	53.5	45.06	0.170†
Treatment resistance	19 (28.8)	4 (12.1)	0.150†
Seizure control with one ASM	34 (50.7)	23 (69.7)	0.060†
Seizure freedom	38 (56.7)	22 (66.7)	0.310†

:** *Independent samples t-test.* **†:** *Chi-square test,* ***ASM: *Anti-seizure medicine,* ***F:*** *female,* ***M:*** *male,* ***m:*** *month,* ***MRI:*** *Magnetic Resonance Imaging*

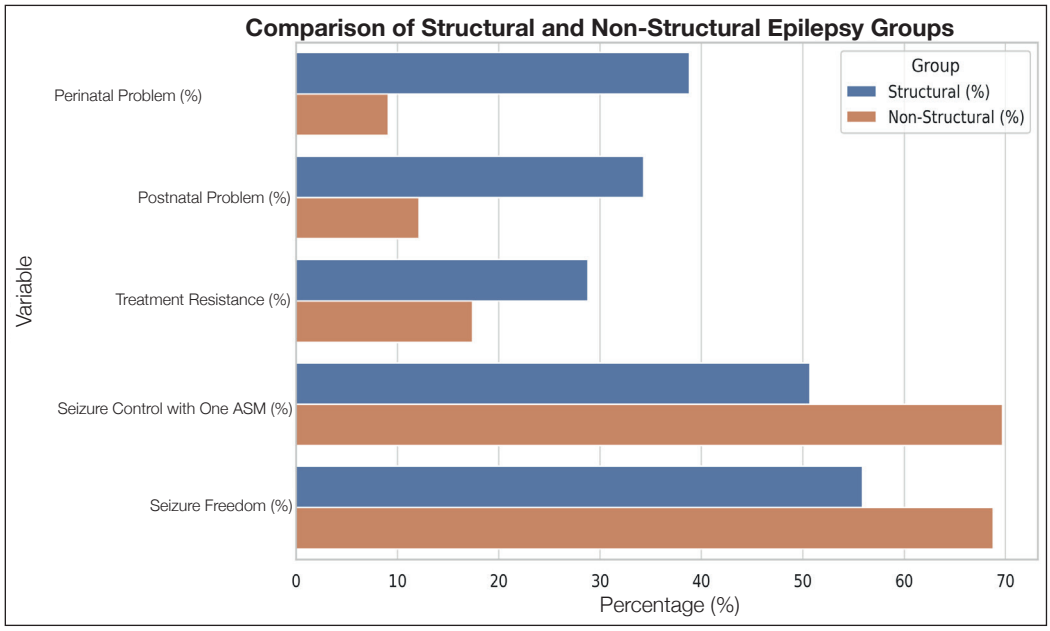

Figure 1: Comparison of structural and nonstructural epilepsy groups.

onset and awareness, 8% with focal onset and impaired awareness, and 3% with focal to bilateral tonic-clonic seizures.

Seizure freedom was achieved in 60% of the patients, while 9% experienced daily seizures, 4% had seizures weekly, 6% monthly, and 21% less frequently than once a month. Treatment resistance was observed in 23% of the patients, and treatment was discontinued in 4%.

Regarding antiseizure medication, 53% of patients were on monotherapy, 23% on dual therapy, 12% on triple therapy, and 8% on more than three medications. Valproic acid was the most commonly prescribed drug in monotherapy (24%), followed by carbamazepine (10%) and levetiracetam (10%).

Frontal lobe seizures were reported in 18% of patients, temporal lobe seizures in 15%, occipital lobe seizures in 5%, and parietal lobe seizures in 3%. However, seizure localization could not be determined in 59% of patients.

Comparison of structural and nonstructural groups

Imaging results revealed normal findings in 33% of patients. Among the remaining 67%, cranial MRI identified sequelae of hypoxia in 16%, encephalomalacia in 12%, structural

malformation in 10%, sequelae of hypoglycemia in 8%, gliosis in 6%, cerebral atrophy in 3%, infarcts in 2%, arachnoid cysts in 2%, cortical dysplasia in 2%, and sequelae of encephalitis in 2%. Additionally, other causes, including mesial temporal sclerosis, hemorrhage, tuberous sclerosis-associated hamartomas, and sequelae of kernicterus, were identified in 4% of cases.

There were no significant differences between the structural and nonstructural groups in terms of mean age, gender distribution, history of febrile seizures, history of prolonged febrile seizures, age at first seizure, presence of focal seizures, duration of epilepsy, or family history of epilepsy. In the nonstructural group, treatment resistance was lower, and seizure control with a single antiseizure medication (ASM) and seizure freedom was higher, but these differences were not statistically significant (Figure 1, Table I). Perinatal and postnatal problems were found to be statistically significantly more common in the group with cranial MRI abnormalities (Table I). Of the 33 patients with normal cranial MRI, 10 underwent high-resolution 3 Tesla cranial MRI due to persistent focal findings on EEG. Cortical dysplasia was detected in one patient, while the others had normal imaging results.

DISCUSSION

The study suggests that MRI findings may not be reliable predictors of prognosis in focal nonsyndromic epilepsy. No significant differences were observed between patients with and without MRI abnormalities in terms of treatment resistance, number of antiepileptic drugs, or seizure control. However, it is important to note that the p-value for seizure control with one antiseizure medication (ASM), which was $p = 0.060$, approached statistical significance and should be interpreted cautiously. Comparing MRI findings was essential to evaluate whether MRI, as the initial diagnostic tool, could offer insights into prognosis and treatment resistance. The results indicate that treatment resistance can persist in focal nonsyndromic epilepsy, even in the absence of MRI abnormalities. This may point to functional impairments that are not detectable by MRI in non-idiopathic focal epilepsies. Further functional studies using advanced imaging techniques, such as 3 Tesla MRI or functional MRI, are needed to investigate this possibility.

Treatment resistance was observed in 23% of all patients, with 28.8% in the group with cranial MRI findings and 17.4% in the group without. Park et al. (7) reported a higher treatment resistance rate of 40%, primarily in patients with structural brain abnormalities, such as hippocampal sclerosis and cortical malformations. This difference may reflect the impact of structural lesions on treatment outcomes, as patients with such conditions often show poorer seizure control. In contrast, our study suggests that patients without significant structural abnormalities may have a more favorable response to treatment, although this difference was not statistically significant. Given the borderline nature of the results, further research with larger sample sizes would be required to clarify whether these trends represent true effects. The treatment response, measured as seizure freedom, was found to be 68.6% in the structural group and 55.9% in the nonstructural group. In lesional epilepsy, the literature reports treatment response rates (seizure freedom) ranging from 24% to 60% (8,9). Several studies have linked treatment response to anomalies during early brain maturation, the nature of the underlying pathology, and the presence of detectable electrophysiological abnormalities in lesional epilepsy (7,8). The variations in response rates between studies may be attributed to differences in study design, borderline p-values in some cases, and the underlying etiology of epilepsy. This emphasizes the need for caution in interpreting findings from studies with small sample sizes or borderline statistical results.

In epilepsy, predictors of treatment resistance and poor prognosis typically include the presence of focal epilepsy and brain lesions (9,10). Based on this, it was expected that patients with focal epilepsies and normal MRI results would show lower treatment resistance and higher rates of seizure freedom. However, the findings of this study contradict this expectation. The existing literature on the prognosis of focal epilepsies is limited and often focuses on specific etiologies or surgical patient cohorts (11-13). For example, a cohort study of 64 patients undergoing surgery for focal epilepsy found that MRI status was a predictor of seizure freedom in a predictive model for drug-resistant focal epilepsy surgery patients (14). In contrast, a study involving 245 epilepsy cases revealed that cranial MRI identified an etiology in 62.8% of cases, but no difference in treatment response was observed between MRI-positive and MRI-negative groups (15). Furthermore, a study on MRI-negative patients undergoing epilepsy surgery found that one to two-thirds of resected specimens showed specific pathological lesions associated with epileptogenicity (16). These findings align with our study's observation that there was no significant difference in treatment resistance or seizure control between MRI-negative and MRI-positive groups.

Epilepsy is one of the most common neurological disorders, with focal seizures being the most prevalent type in childhood (17). Among focal seizures, focal impaired awareness seizures are the most frequent, accounting for 36% of all seizures (18). However, in our study, the rate of focal awareness seizures was lower, at 8%. This discrepancy may be attributed to the exclusion of patients with specific epileptic syndromes and combined focal and generalized epilepsy, as well as the selection of patients based on EEG findings rather than seizure type.

In our study, 70% of patients with focal nonsyndromic epilepsy exhibited generalized seizures. It is important to note that generalized motor symptoms can present in children with focal epilepsy (19). The higher rate of generalized seizures in our study may be due to inadequate seizure descriptions and limited observation of seizure onset. Moreover, focal interictal abnormalities can sometimes mimic focal epilepsy in patients with generalized epilepsy (18). Studies have shown that focal interictal abnormalities are present in 14% to 56% of patients

with generalized epilepsies, such as juvenile myoclonic epilepsy (19). However, we excluded patients with diagnoses of specific epileptic syndromes or those who showed generalized discharges on EEG.

Carbamazepine is generally the first-line treatment for focal epilepsy; however, in our study, valproic acid was the most commonly prescribed antiseizure medication. This may be due to the high prevalence of generalized seizures in our cohort, with some patients reporting focal seizures as generalized. Additionally, the safer side effect profiles of oxcarbazepine and levetiracetam compared to carbamazepine likely contributed to their increased use. These factors suggest a preference for broader-spectrum medications, but a better analysis of seizure type and patient characteristics is necessary for optimal treatment selection.

Temporal lobe seizures are generally reported to account for the majority (70%) of focal seizures, followed by frontal lobe seizures (20%) and seizures from other lobes (10%) (20). However, in our study, the most common seizures were frontal lobe seizures. This discrepancy in seizure distribution may stem from the selection of patients based on EEG and cranial MRI findings rather than seizure type. Additionally, the retrospective nature of our study, along with limited contributions from anamnesis data to seizure semiology, may have influenced the rates of diagnosis. In infants and children, EEG findings may not always identify the epileptogenic region due to factors such as brain immaturity, challenges in obtaining accurate medical history, and age-related differences in seizure presentation (21).

Among 10 patients with normal 1.5 Tesla cranial MRI but persistent focal abnormalities on EEG, follow-up 3 Tesla MRI revealed cortical dysplasia in one. Several studies highlight the superiority of 3 Tesla MRI (22). For instance, Sawaish et al. (23) identified a hippocampal lesion with 3 Tesla MRI that was undetected on 1 Tesla MRI. Similarly, Bachman et al. (24) demonstrated better lesion detectability with 3 Tesla compared to 1.5 Tesla in multiple sclerosis patients. However, a systematic review comparing 1.5 Tesla and 3 Tesla MRI suggests that while 3 Tesla MRI offers subjective improvements in lesion detection, finer anatomical details, and enhanced resolution, there is no conclusive evidence of increased diagnostic accuracy (25). Some studies have found that, despite the higher resolution and detailed imaging offered by 3T MRI compared to 1.5T MRI, there is no significant difference in diagnostic accuracy (26). Nevertheless, 3 Tesla MRI may offer practical advantages in certain cases. This suggests that while 3 Tesla MRI can provide enhanced imaging, its clinical benefit should be evaluated on a case-by-case basis.

Recent data suggest that functional imaging studies provide more informative insights than traditional MRI techniques in the evaluation of MRI-negative epilepsy. The role of functional imaging in detecting epileptogenic zones in patients with negative MRI results has become increasingly prominent. A comprehensive review discusses the integration of structural and functional imaging techniques, such as functional MRI (fMRI), single-photon emission computed tomography (SPECT), and positron emission tomography (PET), in the preoperative assessment of patients with drug-resistant focal epilepsy. The study emphasizes that in MRI-negative cases, these functional imaging modalities can identify hypometabolic or hyperperfused regions, aiding in the precise localization of the epileptogenic zone and improving surgical planning and outcomes (27). Multimodal neuroimaging has been shown to enhance the detection rate of structural and functional abnormalities, facilitating personalized treatment plans and improving diagnostic accuracy in the identification of the epileptogenic zone (28). These findings underscore the critical role of functional imaging in the comprehensive evaluation of patients with MRI-negative epilepsy, providing valuable insights that guide treatment decisions and ultimately improve patient outcomes.

CONCLUSION

Our study suggests that cranial MRI may not reliably predict prognosis in focal nonsyndromic epilepsy. Further large-scale studies are needed to determine whether patients with normal MRI findings have a better prognosis and to explore differences between those with and without MRI abnormalities. Future research should also include functional imaging to shed light on underlying mechanisms and improve prognostic predictions for this group, particularly those with refractory epilepsy.

Limitations

This study has several limitations that need to be acknowledged. First, the relatively small sample size may have limited the ability to detect significant differences in treatment resistance and seizure control between the structural and nonstructural groups, potentially affecting the robustness of the results. Additionally, the retrospective design of the study introduces certain biases, particularly due to reliance on patient history (anamnesis) for seizure type classification, rather than using video EEG, which may have compromised the accuracy of seizure type categorization. Another limitation is the imaging approach; while standard cranial MRI was used, the limited application of advanced techniques such as high-resolution 3 Tesla MRI and functional imaging may have resulted in missed diagnoses of subtle or early structural brain abnormalities, especially in patients with MRI-negative epilepsy. These imaging constraints could have impacted the comprehensive assessment of brain abnormalities and their correlation with seizure activity. To address these limitations, future studies with larger sample sizes, prospective designs, and the inclusion of advanced imaging modalities are essential to further explore and validate these findings.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. Ethics committee approval was received

from the KTU University Clinical Research Ethics Committee dated 27.12.2017-2017/2.

Contribution of the authors

Diler Durgut B: 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 patient follow-up, data management and reporting,Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***Kamaşak T:*** 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 necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***Kul S:*** Supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up. ***Acar Arslan E:*** 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 necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***Şahin S:*** 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 necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***Dilber B:*** 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 necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study. ***Cansu A:*** 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 patient follow-up, data management and reporting, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study.

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Conflict of interest

The authors declare that there is no conflict of interest.

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