# Clinically important intracranial abnormalities in children presenting with first focal seizure

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#### **ABSTRACT**

**Background.** Management of pediatric patients presenting with first seizure is challenging, especially with regards to emergent neuroimaging. The rate of abnormal neuroimaging findings is known to be higher in focal seizures than in generalized seizures, but those intracranial abnormalities are not always clinically emergent. In this study, we aimed to determine the rate and indicators for clinically important intracranial abnormalities that change acute management in children presenting with a first focal seizure to the pediatric emergency department (PED).

**Methods.** This study was conducted retrospectively in the PED at a University Children's Hospital setting. The study population consisted of patients aged between 30 days and 18 years with first focal seizure and who had emergent neuroimaging at the PED between the years 2001 and 2012.

**Results.** There were 65 eligible patients meeting the study criteria. Clinically important intracranial abnormalities requiring emergent neurosurgical or medical intervention were detected in 18 patients (27.7%) at the PED. Four patients (6.1%) underwent emergent surgical procedures. Seizure recurrence and the need for acute seizure treatment in the PED were significantly associated with clinically important intracranial abnormalities.

**Conclusions.** Neuroimaging study yielding of 27.7% shows that first focal seizure must be evaluated meticulously. From the emergency department's point of view; we suggest that first focal seizures in children should be evaluated with emergent neuroimaging, if possible with magnetic resonance imaging. Especially patients with recurrent seizures at presentation requires more careful evaluation.

**Key words:** children, first seizure, first focal seizure, emergent neuroimaging, important intracranial abnormalities, seizure recurrence.

Seizures are the most common neurological problem reported during childhood. It has been shown that 4-6% of children between the ages of 0-16 years have a seizure at least once during

their life, and seizures account for a major part of pediatric emergency department (PED) visits (1%).<sup>1</sup>

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priority must be to rule out a life-threatening intracranial condition and determine the need for emergent neurosurgical or medical intervention in order to prevent loss of time and labor, deferring non-urgent evaluation to a later time to be performed electively. With this aim, defining the patients who will benefit most from emergent neuroimaging is an important task. Guidelines published by Hirtz et al.2 in 2000 recommended emergent neuroimaging for first seizure in pediatric patients who had a persistent post-ictal neurologic deficit and/ or that could not return to baseline neurologic status, but the focal seizure was subject to non-emergent neuroimaging. A reassessment was published by Harden et al.8 in 2007, and focal seizure was considered as an indication for emergent neuroimaging. On the other hand, some authors recommend emergent neuroimaging in the first afebrile focal seizure based on the patient's age.9,10 Guidelines published from Ontario in 2015 recommend emergent neuroimaging in the first afebrile focal seizure.11

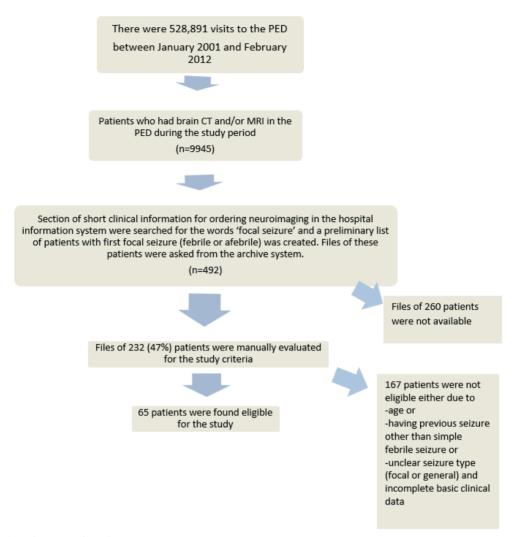
In this study, we aimed to determine the rate of clinically important intracranial abnormalities that change acute management in patients presenting with a first focal seizure and to investigate the clinical indicators and risk factors for emergent neuroimaging at the PED in this patient group.

## Material and Methods

This study was conducted retrospectively in the PED at a University Children's Hospital setting. The study was approved by the Ethics Committee of Hacettepe University (GO 14/577) and conducted in accordance with the latest version of the Declaration of Helsinki.

In the study, inclusion criteria were defined as; age between 30 days and 18 years, presenting with first focal seizure (no previous seizure other than SFS), receiving emergent neuroimaging (computed tomography-CT and/or magnetic

resonance imaging-MRI) at the PED before discharge. Thus; infants and children aged between 30 days and 18 years who presented with first focal seizure (febrile or afebrile) to the PED between January 2001 and February 2012 who had emergent neuroimaging were included. Patient history, physical examination, and clinical follow-up notes were manually written and archived as files on those dates; whereas laboratory tests and radiological results were recorded on the hospital information system. In our center, the first focal seizure is a criterion for emergent neuroimaging even in the absence of any other clinical alarming signs although there is no written local protocol. For obtaining study patients properly; first, the list of all patients who underwent brain CT and/ or MRI in the PED for any reason between the study dates were identified. Then, sections of short clinical information for ordering neuroimaging in the hospital information system were searched for the words 'focal seizure' and a preliminary list of patients with the first focal seizure was created. Files of these patients were obtained from the medical archive system, and after a detailed manual evaluation of these files, patients with first focal seizure who had undergone brain CT and/or MRI were included in the study. Exclusion criteria were; age younger than 30 days, incomplete basic information, unclear seizure type, and having a previous seizure other than a SFS. More detailed information for determining study patients is presented in Figure 1. The following information was obtained from the medical records of each patient and recorded on a standardized data collection form: Age, gender, associated symptoms, family history of seizure or epilepsy, developmental history, presence of any chronic systemic or neurological disease, physical and neurological examination findings, laboratory test results, treatment with anticonvulsants in the PED, neuroimaging findings, electroencephalogram (EEG) findings, final diagnosis, and antiseizure medication prescription for maintenance therapy (if present) and results in follow-up (if present).



**Fig. 1.** Identification of study patients.

We defined focal manifestations as a clinical seizure with motor components including head and eye deviation to one side, clonic and/or tonic movements, or loss of muscle tone in only one side of the body, with or without evolution to bilateral tonic clonic seizure in accordance with the International League Against Epilepsy (ILAE) guidelines.12 Focal seizures that are recorded to be more than one episode either just before coming to PED or during the period in the PED are considered as 'seizure recurrence' within 24 hours. According to International League Against Epilepsy (ILAE) guidelines, when the duration of seizure is ≥5 minutes patients are diagnosed and treated as status epilepticus SE.<sup>13</sup> However, for the scope of this study, status epilepticus (SE) was considered as a single seizure episode or multiple episodes lasting ≥30 minutes without recovery of consciousness/function in between episodes.

A complex febrile seizure was defined as a seizure associated with fever without evidence of intracranial infection or defined cause and has a focal onset and/or lasts longer than 15 minutes and/or occurs more than once in 24 hours in a child between six months and five years of age.<sup>14</sup>

Acute bacterial meningitis was defined as pleocytosis and/or the growth of a pathogen in cerebrospinal fluid (CSF).

#### Outcome Assessment

The principal outcome of our study was defined as clinically important intracranial abnormalities in brain imaging requiring emergent neurosurgical or medical intervention. We defined this based on the ILAE classification which was established in 2009 and is widely used for the evaluation of intracranial pathologies in terms of a clinical emergency, management, and follow-up (Table I).15 For our study, we considered clinically important intracranial abnormalities as Class IV and Class V lesions which are described as pathologies having therapeutic implications and those that need more immediate/urgent intervention. In this context, encephalitis/meningitis was classified as Class IV if empiric therapy was started prior to imaging and as Class V if so after imaging.<sup>16</sup>

## Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) for Windows 15.0 program was used for all data analyses in this study. Data was expressed as percentage, median, or mean ± standard deviation. The continuous variables were compared using a two-tailed t-test for the parametrically distributed data or the Mann-Whitney U test for the nonparametrically distributed data. The categorical variables were analyzed using a chi-square test. A p value of 0.05 or less was considered to be significant.

### Results

Between January 2001 and February 2012, 9945 patients who underwent neuroimaging in the PED were identified. After the evaluation of patient records and files, 65 patients who met the criteria were enrolled in the study (Fig. 1). The mean age of the patients was 56 ± 52.4 months (31 days to 195 months) and 43 (66%) of the patients were male. Although the number of patients with fever was 30 (46%), only 10 of them had a complex febrile seizure. Sixteen patients (24.6%) had an underlying chronic illness, either neurological or systemic. These included; cognitive/motor delays (n= 10), hydrocephalus (n= 1), brain tumor (n= 2), and other chronic systemic diseases (n= 3); hereditary spherocytosis (n= 1), cystinosis (n= 1), Down syndrome and atrioventricular septal defect (n=1). Demographic characteristics of the study patients are presented in Table II.

Abnormal neurological examination findings consisted of focal symptoms/signs in 27 (41%) of the patients (Table II). These were Todd paralysis in four patients, hemiparesis in one patient, unilateral central facial paralysis in one patient, tongue deviation to one side and asymmetric increased/decreased deep tendon reflexes (DTR) or unilateral pathological reflexes in the remaining patients. Other symptoms/signs such as drowsiness, lethargy, and hypo/hyperactive DTRs were present in 15 patients

Table I. Classification of neuroimaging findings (15).

Categories	Examples
Class I- Nonspecific	Periventricular leukomalacia, atrophy
Class II- Static remote lesions	Porencephaly, malformation of cortical development
Class III- Focal lesion responsible for the seizure that does not require immediate intervention but would be potentially amenable to epilepsy surgery	Focal cortical dysplasia or mesial temporal sclerosis
Class IV- Subacute or chronic process that has therapeutic implications and requires more immediate intervention or that has important diagnostic or prognostic implications	Brain tumor, leukodystrophies, metabolic disorder
Class V- Acute process that requires urgent intervention or need for additional urgent diagnostic evaluation and counseling	Hydrocephalus, acute stroke or hemorrhage, meningoencephalitis, metabolic cytopathy

and neurological examination was normal in 23 (35%) patients.

Sixty-two patients initially underwent brain CT, while the other three patients initially had brain MRI at the PED. A subsequent brain MRI was also performed in 19 patients after brain CT at the PED before discharge/admission. Overall neuroimaging at the PED revealed clinically important intracranial abnormalities requiring emergent neurosurgical or medical intervention in 18 patients (27.7%). The demographic, clinical characteristics and radiological results of these patients are presented in Table III. Brain CT and MRI of three of these patients are shown in Figures 2 and 3. In four patients, brain CT was normal, but MRI revealed clinically important intracranial abnormalities, namely three cases of meningoencephalitis and one cerebrovascular event (arterial occlusion).

Four patients (6.1%) underwent emergent surgical procedures (Table III). In addition to these four patients, the evaluation of a patient

**Table II.** General characteristics of the study patients (n = 65).

(n = 65).	
Age (months)*	$56 \pm 52.4$
1 - 6 months	9 (14)
6 - 12 months	6 (9)
12 months - 5 years	24 (37)
5 – 18 years	26 (40)
Male gender	43 (66)
Symptoms accompanying seizure	
Fever	30 (46)
Vomiting	26 (40)
Headache	10 (15)
Physical examination findings	
Any abnormal neurological findings	42 (64)
Focal symptoms/signs after seizure	27 (41)
Past medical history and family history	
Underlying illness	16 (24.6)
History of SFS	3 (4.6)
History of SFS in family	5 (7.7)
Family history of epilepsy	6 (9)

Data are presented as number (percentage), unless indicated otherwise. \*Mean±standard deviation; SFS: simple febrile seizure.

with a right focal seizure revealed the presence of a hemorrhagic cavernoma in the left frontal region, although he was not operated on until one month after admission.

In order to identify risk factors; we performed a comparison between the characteristics of the patients with clinically important intracranial abnormalities requiring emergent neurosurgical or medical intervention and other patients (those with normal imaging and nonemergent abnormalities) (Table IV). This comparison revealed that seizure recurrence in PED or within 24 hours, and the need for acute seizure treatment in PED were significantly associated with clinically important intracranial abnormalities (p; 0.004, 0.017, and 0.017 respectively).

Lumbar puncture (L/P) was performed in 23 patients (36.5%). Although the CSF cultures were all negative, other CSF findings were abnormal in four patients. In these patients, the final diagnosis was miliary tuberculosis

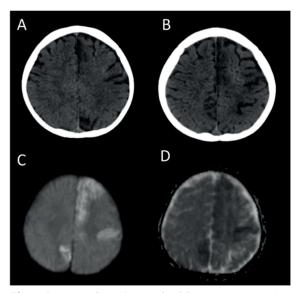
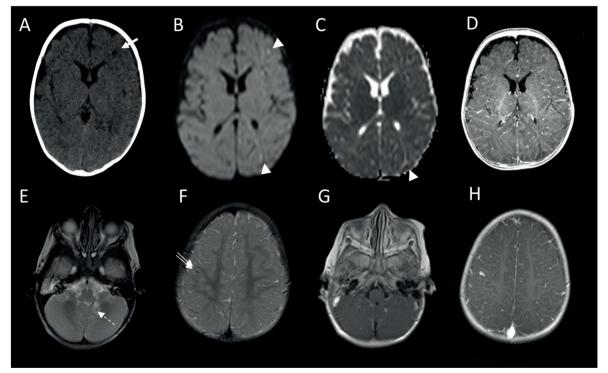


Fig. 2. Images of an 18-month-old patient presenting with a right focal seizure lasting about 2 minutes. Axial non-enhaced CT images (A, B) show cortical hypodense lesions which then were shown as acute cortical infarcts by diffusion restriction of cytotoxic edema on diffusion-weighted imaging (C, D) obtained an hour later. The patient was diagnosed with hereditary spherocytosis on further work-up.

and tuberculous meningitis in one patient, and meningoencephalitis in the other three patients.

Electroencephalogram was performed in 48/65 (73%) patients and there was an abnormality in 35/48 (73%) of them. Among these, epileptiform activity was present in 15 (31%) patients. Other abnormalities were seen in the remaining 23 patients such as irregular, asymmetric or slow background activity. Antiseizure medication was initiated in 41 (63%) patients.

After discharge from the PED, during the longterm follow-up, brain MRI was performed additionally for 14 patients, and none revealed any abnormalities necessitating emergent intervention. Considering 19 patients who underwent MRI at the PED after CT before discharge, a total of 33 patients had cranial MRI in addition to CT. Among these patients, there was a discrepancy between the CT and MRI results in 12 patients (36%) with normal CT findings despite abnormal MRI results. Eight of them were non-emergent abnormalities which could be important in long term followup, while four of them (12%) were clinically important intracranial abnormalities: Three cases of meningoencephalitis and one acute cerebrovascular event (arterial occlusion). On the other hand, the abnormality rate in the overall imaging including those performed during follow-up (brain CT and/or MRI) was 55%.



**Fig. 3.** Images of a child at the age of 5 months (upper row; A to D) and 15 month-old (lower row; E to H) child presenting to Pediatric Emergency Department with focal seizures. Nonenhanced CT of the patient shows nonspecific subtle left frontal periventricular hypodensity (A, arrow) while MRI obtained 6 hours later shows left frontal and parietal cortical tiny foci of diffusion restrictions and diffuse pial enhancement on diffusion-weighted imaging (B, C, arrowheads) and post-Gadolinium T1W image (D). Lower row shows nodular T2 hypointense lesions in the left medial cerebellar hemisphere (E, dashed arrow) and right frontal cortical (F, double arrow) which enhance on post-Gadolinium T1W series (G, H). Please note increased number of lesions are seen on post-contrast imaging. These patients received diagnosis of meningoencephalitis (upper row) and CNS tuberculosis (lower row) lesions.

 Table III. Patients with clinically important intracranial abnormalities requiring emergent neurosurgical or medical intervention.

Patient	Age, gender	Patient Age, gender 6: 11: 20	Seizure characteristics**	Brain CT	Seizure characteristics** Brain CT Brain MRI	Final diagnosis
1*	2 years, M	Hypoactive DTRs in	LFS, one episode, 20 min.		Brain abscess, 4 cm	Brain abscess.
		lower extremities			diameter in the right frontoparietotemporal region	Craniotomy and abscess drainage were performed.
7	11 years, M	Positive meningeal irritation signs, drowsiness	LFS, multiple seizures, focal to bilateral tonic clonic seizure, 15 min.	Normal	Cerebral edema, encephalitis	Encephalitis
e	45 days, F	Positive Babinski sign on the left side, hyperactive DTRs	LFS, one episode, 4 min.	Intraparencyhmal hematoma in right temporal region	ı	Late hemorrhagic disease of the newborn
4	16 years, M	Deviation of tongue to the left side	RFS, one episode, 3 min.	Edema and hypodense lesions in left parietal region and cerebellar hemispheres	New lesions in left parietal region and cerebellar hemispheres	Non-Hodgkin lymphoma and secondary cerebellar PNET in follow-up, progression in the mass leading to brain edema
ſŲ	15 months, M	15 months, M Irritability (+), drowsiness (+)	RFS, LFS, multiple seizures, 5 min.	Normal	Diffuse cortical swollen lesions, meningoencephalitis	Meningoencephalitis
*9	4 years, M	Hemiparesis on the right side of the body	RFS	A mass lesion in the left frontal region, 5 cm diameter	Acute hemorrhage into cavernoma in the left frontal lobe, 4.5 cm in diameter	Cavernoma Craniotomy and excision were performed.
*	4 years, M	Todd paralysis on the right side	RFS, multiple seizures, 60 min.	Chiari Type- 1 malformation, chronic compensated hydrocephalus, third ventriculostomy	Chiari Type- 1 malformation, acute deterioration of CSF circulation, left parietooccipital polymicrogyria	Acute deterioration of CSF circulation, tap procedure was performed.

CSF: cerebrospinal fluid, CT: computed tomography, DTR: deep tendon reflexes, F: female, M: male, min: minutes, MRI: magnetic resonance imaging, LFS: left focal motor seizure, \*Patients who needed emergent surgical intervention. \*\*Accurate information for seizure duration was not available in some patients.

Table III	Table III. Continued.					
Patient number	Age, gender	Neurological exam findings	Seizure characteristics**	Brain CT	Brain MRI	Final diagnosis
∞	5 months, F	Hyperactive DTRs at the right side	RFS, multiple seizures, 30 min.	Normal	Widespread lesions, dominant in the left cerebral hemisphere, compatible with meningoencephalitis	Meningoencephalitis
0,	18 months, F	Central facial paralysis on the right side (newly diagnosed), hemiparesis on the right side (previously present)	RFS, one episode, 2 min.	Acute and early subacute infarction in right parietal and left paramedian regions and chronic ischemic lesions in the left cerebral hemisphere	Ischemic infarct	Hereditary spherocytosis, cerebrovascular event
10	7 months, M Drowsiness	Drowsiness	LFS, multiple seizures	Hemorrhage in right temporal region 22 mm in diameter	Hyperintensity in bilateral Herpes simplex temporal lobes consistent encephalitis with herpes simplex encephalitis	l Herpes simplex encephalitis
11	3 years, M	Disturbed cooperation, hyperactive DTRs	RFS, one episode, 1 min. Normal	Normal	Diffuse meningeal enhancement consistent with encephalitis	Encephalitis
12	15 months, F	15 months, F Decreased spontaneous movements on the left upper and lower extremity	LFS	4 mm lesion in diameter in the right frontal lobe	Infra and supratentorial intense meningeal linear and nodular inflammation	Tuberculous meningitis, miliary tuberculosis
13	4 months, F	Lethargy	RFS, LFS, multiple seizures, 4 min.	Low density area in the left frontal region	Diffuse cortical and subcortical acute ischemic lesions predominantly in the left hemisphere compatible with encephalitis	Encephalitis

CSF: cerebrospinal fluid, CT: computed tomography, DTR: deep tendon reflexes, F: female, M: male, min: minutes, MRI: magnetic resonance imaging, LFS: left focal motor seizure, PNET: Primitive Neuro-Ectodermal Tumor, RFS: right focal motor seizure, \*Patients who needed emergent surgical intervention. \*\*Accurate information for seizure duration was not available in some patients.

Table III	Table III. Continued.					
Patient number	Age, gender	Neurological exam findings	Seizure characteristics**	Brain CT	Brain MRI	Final diagnosis
14	2 years, M	Normal in the acute phase, left hemiplegia was apparent during follow-up	LFS, multiple seizures, 3 min.	Normal	Occlusion in the right middle cerebral artery	Cerebrovascular event, infarction
15	18 months, M	18 months, M Decreased movements against gravity on the right extremities, Todd paresis	RFS, multiple seizures	A mass lesion with surrounding edema and internal microcalcifications, 38x30 mm in diameter, in the left parietal lobe	A large cavernoma, 43x33 mm in diameter, with hemorrhage and surrounding edema in the left parietal region	Hemorrhagic cavernoma
16	5.5 years, M	No pathologic findings	LFS, multiple seizures, 5 min.	Linear fracture in the right parietal bone and accompanying cerebral edema	1	Cerebral edema and posttraumatic seizure
17*	4 months, M Irritability	Irritability	RFS, multiple seizures, 5 min.	Right subdural collection, midline shift, compression in the lateral ventricles		Right subdural empyema, craniotomy, and drainage were performed.
18	6 years, F	Disturbed consciousness, bilateral spontaneous positive Babinski sign, clonus at the right lower extremity	Disturbed consciousness, LFS, multiple seizures, 3 bilateral spontaneous min. positive Babinski sign, clonus at the right lower extremity	Diffuse leptomeningeal contrast enhancement and findings attributable to increased intracranial pressure	1	Meningoencephalitis, cochlear partition abnormality

CSF: cerebrospinal fluid, CT: computed tomography, DTR: deep tendon reflexes, F: female, M: male, min: minutes, MRI: magnetic resonance imaging, LFS: left focal motor seizure, PNET: Primitive Neuro-Ectodermal Tumor, RFS: right focal motor seizure, \*Patients who needed emergent surgical intervention. \*\*Accurate information for seizure duration was not available in some patients.

**Table IV.** Comparison of patient characteristics based on presence of clinically important intracranial abnormalities by neuroimaging (brain CT and/or MRI).

	Patients with clinically important intracranial abnormalities on neuroimaging	Other patients N=47	р
Age (months), median (range)	N=18 21.5 (1.5-195)	53 (1-188)	0.322
Male gender	12 (66)	31 (66)	0.957
History	(**)	- ()	
Fever	6 (33)	24 (51)	0.199
Vomiting	8 (44)	18 (38)	0.651
Chronic disease	7 (38.9)	9 (19.1)	0.098
Seizure characteristics			
Seizure duration (min.), median (range)	3 (0.1-60)	5 (0.5-70)	0.211
Number of seizure episodes/day, median (range)	2 (1-7)	1 (1-7)	0.073
Patients with >1 seizure episode/day	11 (68.8)*	20 (42.6)	0.070
Focal symptoms/signs after seizure	10 (55.6)	17 (36.2)	0.156
Acute seizure treatment in PED	12 (66.7)	16 (34)	0.017
Seizure recurrence in PED	12 (66.7)	13 (27.7)	0.004
Seizure recurrence within 24 hours	13 (72.2)	18 (39.1)	0.017

Data are presented as number (percentage), unless indicated otherwise. p values less than 0.05 are printed in bold. CT: computed tomography, MRI: magnetic resonance imaging, min.: minutes, PED: pediatric emergency department. \*Information regarding number of seizure episodes were missing in two patients in this group.

#### Discussion

In this study, pediatric patients who presented with a first focal seizure and had neuroimaging in the PED were evaluated, and the requirement for emergent neuroimaging from an emergency department point of view was assessed. The rate of clinically important intracranial abnormalities was 27.7% whereas the total abnormality rate in neuroimaging was 55%. Furthermore, the rate of patients who needed emergent surgical intervention was 6.1%. Seizure recurrence in PED or within 24 hours and the need for acute seizure treatment in PED were significantly associated with the presence of clinically important intracranial abnormalities in neuroimaging.

The need for emergent neuroimaging and its effect on the management of the first seizure in children have been discussed previously.<sup>2-11,17</sup> In general, it is suggested that emergent neuroimaging is not necessary for

first seizure patients. However, regarding 'first focal seizure' different approaches have been suggested in the literature. Some authors recommend emergent neuroimaging<sup>8,11</sup> whereas some authors recommend it only if there are any predisposing conditions or if the age of the patient is younger<sup>3,9,10</sup> and some further recommend non-emergent imaging.2 Sharma et al.9 reviewed 500 children with new onset afebrile seizure, of whom 167 (33%) presented with documented focal features. After excluding patients with predisposing conditions, they found that 12.7% of the focal seizure patients had clinically significant abnormal imaging findings, mostly at younger ages, and suggested emergent imaging for focal seizure patients if the age is under 33 months.9 In a recent study, Amagasa et al.<sup>18</sup> found that focal seizure, prolonged seizure, and seizure cluster (similar to ours') were risk factors for CT or MRI abnormalities. The only study in the literature that included solely first afebrile

seizure patients with focal manifestations with quite wide exclusion criteria such as underlying chronic disease, altered mental status, acute trauma, etc., found the rate of clinically urgent intracranial pathology as 4.1%, with hemorrhage and infarction being the most common.<sup>10</sup> In that study, the authors suggested emergent neuroimaging for focal seizure patients under the age of 18 months. Recently Brugman et al.16 published a study about the necessity of urgent brain CT for the first seizure in which they used the same case classification system as ours'. In that study, predictors for clinically important intracranial pathologies were found as persistent post-ictal abnormal neurological state and a new post-ictal focal finding however focal onset failed to reach statistical significance. Compared with most of these studies, in our study the rates are quite higher which may be due to several factors. Since we aimed to assess general risk factors for clinically important intracranial abnormalities in first focal seizure not only in previously healthy children but for all pediatric patients (30 days-18 years) admitted to the PED, we did not exclude patients with fever or chronic underlying conditions. Our hospital is a tertiary referral hospital localized in the center of the country and an important part of the patients admitted to the PED have underlying chronic conditions. Therefore, our cohort might represent a more severe and complicated patient group than the general population. The rate of 27.7% that we found for clinically important intracranial abnormalities in emergent neuroimaging supports the need for emergent neuroimaging in this patient group. The differences between several previous studies and our study may be related to the differences both in patient inclusion/exclusion criteria and the description of "clinically important abnormalities".

In this study, seizure recurrence in PED or within 24 hours and the need for acute seizure treatment in PED were significantly associated with clinically important intracranial abnormalities. Our comparison also revealed that the median number of seizure episodes/

day and rate of patients with multiple seizure episodes/day were higher in the group with clinically important intracranial abnormalities although results were not statistically significant, most likely due to the low number of cases (Table IV). Here we note that seizure recurrence at the PED or multiple focal seizures at presentation should alert the clinician for emergent neuroimaging at the PED. There are a few studies pointing to the number of seizures at the presentation of the first seizure.<sup>3,18</sup> Other than emergent imaging, recurrence of seizure also supports the need for a longer follow-up at the PED or admission to the wards.19

In the current study, there was a discrepancy between the yields of CT and MRI results in 12 patients (36%) with normal CT and abnormal MRI results. Of note, four of 12 patients (12%) had clinically important intracranial abnormalities; three meningoencephalitis cases and an arterial ischemic infarct. In the study by Sharma et al.9, among the patients whose brain CT was normal, 43% underwent brain MRI and clinically significant abnormalities were detected in 3.7% of them. In another study that included patients under two years of age (excluding newborns) presenting with first afebrile seizure, among the patients with normal CT, the rate of abnormality in the MRI was 33%.19 Most of these abnormalities were not urgent but important for the patient's prognosis and long-term management, however, in one patient MRI revealed a watershed infarct that required acute management similar to our study.19 As an imaging modality, with superior soft tissue contrast, MRI shows minor developmental malformations, white matter lesions, parenchymal lesions, neurocutaneous disease lesions, and thrombotic cerebrovascular events, and pathologies of posterior fossa better than CT. Requirement for anesthesia, especially in young children, and higher cost represent the key disadvantages of MRI. However, CT offers the advantages of widespread availability, speed, low cost, and superiority in acute bleeding and calcification as well as fractures; yet, with the major disadvantage of radiation

exposure. In the guidelines published by ILAE, it is mentioned that MRI is superior to CT in patients presenting with seizures, although CT can be considered a screening method when MRI is not available or cannot be performed.<sup>15</sup> In the same report, it is also noted that in cases of recurrent seizures, abnormal neurological examination, or for better description of the abnormalities seen in CT, brain MRI can be performed. Similarly, it has been mentioned in other studies that an MRI should be the preferred neuroimaging modality in children presenting with first afebrile seizure although it may not be available or applicable for emergent cases.7,11 From the view of the management at the PED; we suggest a faster MRI protocol including fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging designed for prompt diagnosis and treatment, especially in the early phase of vascular infarcts.

The present study has some limitations, mainly due to its retrospective nature and small sample size. As shown in Figure 1, we were unable to reach all patient files for manual review, most likely due to the shortcomings in the archive system during those dates. This was the major handicap that led to a small sample size despite the fact that our center is a reference hospital. Other than these factors, although first focal seizure was a strict criterion for performing emergent neuroimaging in our center, our method for patient selection may have created a possible bias and a small portion of patients may have been missed. Also, some seizures with a very short focal onset may be overlooked as general seizures and hence not listed as focal seizures.

In this study, pediatric patients with first focal seizure were evaluated, and the yield of neuroimaging studies for clinically important intracranial abnormality was 27.7%. This shows that focal seizures must be evaluated

meticulously. From an emergency department point of view, we suggest that first focal seizures in pediatric patients should be evaluated with emergent neuroimaging, if possible with a dedicated MRI protocol. Especially those with recurrent seizures at presentation should be subject to more careful evaluation. Prospective studies in these patient groups are needed and will contribute more to identifying the risk factors.

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## **Ethical approval**

Ethical approval was obtained from the Ethics Committee of Hacettepe University (GO 14/577).

#### **Author contribution**

The authors confirm contribution to the paper as follows: study conception and design; TK, ÖT, GT; data collection; TK, BK; analysis and interpretation of results; TK, ÖT, GT, KKO, GH, DY; draft manuscript preparation; TK, ÖT. All authors reviewed the results and approved the final version of the manuscript.

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## Conflict of interest

The authors declare that there is no conflict of interest.

#### REFERENCES

- Roth HL, Drislane FW. Seizures. Neurol Clin 1998; 16: 257–284. https://doi.org/10.1016/s0733-8619(05)70064-5
- Hirtz D, Ashwal S, Berg A, et al. Practice parameter: evaluating a first nonfebrile seizure in children: report of the quality standards subcommittee of the American Academy of Neurology, The Child Neurology Society, and The American Epilepsy Society. Neurology 2000; 55: 616-623. https://doi. org/10.1212/wnl.55.5.616
- 3. Bautovich T, Numa A. Role of head computed tomography in the evaluation of children admitted to the paediatric intensive care unit with new-onset seizure. Emerg Med Australas 2012; 24: 313-320. https://doi.org/10.1111/j.1742-6723.2012.01561.x
- 4. Dayan PS, Lillis K, Bennett J, et al. Prevalence of and risk factors for intracranial abnormalities in unprovoked seizures. Pediatrics 2015; 136: e351-e360. https://doi.org/10.1542/peds.2014-3550
- Mathur S, Southern K, Sharma M. Significant findings on cranial CT scan after a first unprovoked seizure in children from North India. J Trop Pediatr 2007; 53: 428-430. https://doi.org/10.1093/tropej/ fmm055
- Shinnar S, O'Dell C, Mitnick R, Berg AT, Moshe SL. Neuroimaging abnormalities in children with an apparent first unprovoked seizure. Epilepsy Res 2001; 43: 261-269. https://doi.org/10.1016/s0920-1211(00)00206-0
- Al-Shami R, Khair AM, Elseid M, et al. Neuroimaging evaluation after the first afebrile seizure in children: A retrospective observational study. Seizure 2016; 43: 26-31. https://doi.org/10.1016/j. seizure.2016.10.008
- 8. Harden CL, Huff JS, Schwartz TH, et al. Reassessment: neuroimaging in the emergency patient presenting with seizure (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2007; 69: 1772-1780. https://doi.org/10.1212/01.wnl.0000285083.25882.0e
- 9. Sharma S, Riviello JJ, Harper MB, Baskin MN. The role of emergent neuroimaging in children with new-onset afebrile seizures. Pediatrics 2003; 111: 1-5. https://doi.org/10.1542/peds.111.1.1
- Aprahamian N, Harper MB, Prabhu SP, et al. Pediatric first time non-febrile seizure with focal manifestations: is emergent imaging indicated? Seizure 2014; 23: 740-745. https://doi.org/10.1016/j. seizure.2014.06.003

- 11. Critical Care Services Ontario (CCSO). Provincial guidelines for the management of epilepsy in adults and children epilepsy implementation task force. Available at: https://epilepsyontario.org/wpcontent/uploads/2015/03/Provincial-Guidelinesfor-the-Management-of-Epilepsy-in-Adults-and-Children\_Janurary-20151.pdf
- Fisher RS, Cross JH, French JA, et al. Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. Epilepsia 2017; 58: 522-530. https://doi.org/10.1111/ epi.13670
- Trinka E, Cock H, Hesdorffer D, et al. A definition and classification of status epilepticus-Report of the ILAE Task Force on Classification of Status Epilepticus. Epilepsia 2015; 56: 1515-1523. https:// doi.org/10.1111/epi.13121
- Berg AT, Shinnar S. Complex febrile seizures. Epilepsia 1996; 37: 126-133. https://doi. org/10.1111/j.1528-1157.1996.tb00003.x
- 15. Gaillard WD, Chiron C, Cross JH, et al; International League Against Epilepsy, Committee for Neuroimaging, Subcommittee for Pediatric. Guidelines for imaging infants and children with recent-onset epilepsy. Epilepsia 2009; 50: 2147-2153. https://doi.org/10.1111/j.1528-1167.2009.02075.x
- Brugman J, Solomons RS, Lombard C, Redfern A, Du Plessis AM. Risk-stratification of children presenting to ambulatory paediatrics with first-onset seizures: should we order an urgent CT brain? J Trop Pediatr 2020; 66: 299-314. https://doi.org/10.1093/tropej/ fmz071
- 17. Teng D, Dayan P, Tyler S, et al. Risk of intracranial pathologic conditions requiring emergency intervention after a first complex febrile seizure episode among children. Pediatrics 2006; 117: 304-308. https://doi.org/10.1542/peds.2005-0759
- 18. Amagasa S, Uematsu S, Tsuji S, Nagai A, Abe Y, Kubota M. Identification of children with first afebrile seizure for whom neuroimaging is unnecessary. Seizure 2021; 93: 140-144. https://doi.org/10.1016/j.seizure.2021.10.022
- Hsieh DT, Chang T, Tsuchida TN, et al. New-onset afebrile seizures in infants: role of neuroimaging. Neurology 2010; 74: 150-156. https://doi.org/10.1212/ WNL.0b013e3181c91847