



# First Afebrile Seizure in Children: Which Patients Require Emergent Neuroimaging?

## Çocuklarda İlk Afebril Nöbet: Acil Kraniyal Görüntüleme Hangi Hastalarda Gerekli?

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### Abstract

**Introduction:** The aim of this study was to investigate the frequency of intra-cranial pathology in children presenting to emergency department with a first afebrile seizure and to determine patients at high risk for abnormal neuroimaging.

**Methods:** The medical files of 173 children who presented to the emergency department with a first afebrile seizure and underwent neuroimaging within 24 hours of presentation were retrospectively evaluated. We defined clinically emergent intracranial pathology as any lesion requiring immediate medical or surgical intervention. The relationship of age, seizure characteristics, predisposing conditions, presence of new-onset neurologic deficits, and baseline neurological status with neuroimaging findings were compared.

**Results:** There were 103 males (59.5%) and 70 females. The mean age was 80±60.4 months (1-204). Of the 173 children, 87 (50.3%) had a computed tomography scan, 50 (28.9%) had magnetic resonance imaging, and 36 (20.8%) underwent both magnetic resonance imaging and computed tomography. Neuroimaging results were abnormal in 24.3% of patients whereas 5.2% had an emergent intracranial pathology. The conditions associated with abnormal neuroimaging were: 1) focal seizures, 2) new-onset neurological deficits 3) pre-existing neurological abnormalities, 4) predisposing conditions, and 5) being younger than 24 months of age.

**Conclusion:** Planning emergency neuroimaging in children with a first afebrile seizure seems rational if the child is younger than 24 months of age, has focal seizure(s), abnormal neurologic status prior seizure, new-onset neurological symptoms, or predisposing conditions.

**Keywords:** Children, first afebrile seizure, neuroimaging abnormality

### Öz

**Amaç:** Bu çalışmanın amacı ilk kez afebril nöbet geçirerek çocuk acil servisine getirilen çocuklarda nöroradyolojik bozukluk saptanma sıklığının ve hangi hastalarda bu riskin daha yüksek olduğunun belirlenmesidir.

**Yöntemler:** Çocuk acil servisinde ilk afebril nöbet nedeniyle izlenen ve ilk 24 saat içinde kraniyal görüntüleme yapılmış olan 173 hasta geriye dönük incelendi. Görüntüleme sonucunda acil medikal ya da cerrahi girişim gerektiren lezyonlar klinik olarak acil intrakraniyal patoloji olarak tanımlandı. Yaş, nöbet özellikleri, nöbet açısından predispozan faktör varlığı, nöbet sonrası yeni nörolojik bozukluk olması ve nöbet öncesinde bazal nörolojik bozukluk olması ile nöroradyolojik bulgular arasındaki ilişki karşılaştırıldı.

**Bulgular:** Hastaların 103'ü (%59,5) erkek, 70'i (%40,5) kız idi. Ortalama 80±60,4 ay (1-204 ay) idi. Hastaların %50,3'üne (87/173) bilgisayarlı tomografi, %28,9'una (50/173) manyetik rezonans, %20,8'ine (36/173) bilgisayarlı tomografi ve manyetik rezonans görüntüleme yapıldı. Olguların %24,3'ünde nöroradyolojik bozukluk saptandı. Acil intrakraniyal patoloji saptanma oranı ise %5,2 idi. Parsiyel tipte nöbet geçiren, yeni nörolojik defisit saptanan, nöbet öncesinde bazal nörolojik bozukluğu olan, öyküsünde nöbet açısından predispozan faktör saptanan ve 24 ay ve altında olan hastalarda nöroradyolojik bozukluk sıklığı anlamlı yüksek saptandı.

**Sonuç:** İlk kez afebril nöbet geçirme nedeniyle acil servise başvuran hastalar arasında 24 ay ve altında olan, parsiyel nöbet geçiren, bazal nörolojik bozukluğu olan, nöbet sonrası yeni nörolojik bulgusu olan ya da öyküde predispozan faktörü saptanan hastalarda acil kraniyal görüntüleme planlanması akılcı görünmektedir.

**Anahtar Kelimeler:** Çocuk, ilk afebril nöbet, nöroradyolojik bozukluk

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## Introduction

The aim of emergent neuroimaging in patients with a first afebrile seizure is to determine a severe cranial pathology that may require immediate intervention and treatment. In adult patients, the prevalence of abnormal neuroimaging (stroke, hemorrhage, neoplasm, etc.) ranges from 34% to 45% in different studies.<sup>1,2</sup> Due to this large proportion of structural lesions, emergent cranial computed tomography (CT) is recommended for adult patients with a new onset seizure. In pediatric patients, this rate is indicated to be between 0% and 21% in different studies.<sup>2-5</sup> CT identifies imaging abnormalities in 7-24% of children but alters immediate medical management in only a minority.<sup>4,6,7</sup> The American Academy of Neurology states that there is insufficient evidence to support a recommendation at the level of standard or guideline for the use of routine neuroimaging in children with a first afebrile seizure.<sup>8</sup> Therefore, emergent neuroimaging is indicated for selected cases according to history and physical examination considering potential risks of radiation, sedation and contrast agent.<sup>3,8-10</sup> However, in routine practice, children presenting to emergency department (ED) with a first afebrile seizure are often evaluated with cranial imaging, especially CT. Many factors, such as parental stress and tension, physicians' fear of legal issues that could arise after an incorrect diagnosis and abstaining from life-threatening consequences, are likely to be effective in this decision.

The aim of this study was to investigate the frequency of abnormal neuroimaging in children presenting to pediatric ED with a first afebrile seizure and to determine patients at high risk especially for clinically emergent intracranial pathology.

## Materials and Methods

The study was performed in a pediatric ED in a tertiary care training hospital with approximately 100.000 annual ED patient visits in İstanbul, Turkey. Patients aged between 1 month and 18 years, who presented to ED with a first afebrile seizure and underwent neuroimaging [CT and/or magnetic resonance imaging (MRI)] within 24 hours, were retrospectively evaluated. A total of 239 patients were admitted to ED with a first afebrile seizure within three years. One hundred seventy-three of these patients, who met our criteria, were included in the study. Demographic features, predisposing conditions (high risk factors for seizure such as neonatal hypoglycemia, perinatal asphyxia, bleeding disorders, malignancy, immune deficiency, previously known hydrocephalus or cranial tumor, recent head injury or operation), characteristics of the seizures (seizure type, duration, number of seizures), neurologic examination after seizure, baseline neurologic status, and neuroimaging results were recorded. Focal manifestations

and number and duration of seizures were based on the medical record. Patients <1 month or >18 years of age, with a diagnosis of febrile seizure, metabolic disorders (such as hypoglycemia, hyponatremia), or acute trauma were excluded from the study. The following definitions were used for the definitions and etiologic evaluations of the seizures according to the classification of epileptic seizures by the International League Against Epilepsy (ILAE)<sup>11</sup>:

**First unprovoked afebrile seizure:** One or multiple seizures within a twenty-four hour period with recovery of consciousness between episodes.

**Acute symptomatic:** Seizure in a previously neurologically normal child, within a week of an underlying etiology including central nervous system infection, encephalopathy, head trauma, cerebrovascular disease, and metabolic or toxic derangements.

**Remote symptomatic:** Seizure in the absence of an identified acute insult but with a history of a pre-existing neurological abnormality more than 1 week before.

**Idiopathic:** Seizure that is not symptomatic and occurred in a child with no prior neurological disorder or in a child in whom no neurological findings detected via physical examination.

Focal manifestations were defined as any transitory disturbance in motor function with focality such as eye and/or head deviation and isolated limb twitching. The patients were also considered to have focal manifestations if Todd's paresis was noted.

Neuroimaging findings were evaluated in 5 groups based on the ILAE guidelines for imaging children with new onset epilepsy<sup>6</sup> (Table 1). Acute lesions that require immediate medical or surgical interventions were considered as clinically emergent intracranial pathology.

The relationship of age, seizure characteristics, presence of risk factors for seizures, baseline neurologic disorders, and new-onset neurologic deficits after seizure (focal findings, papilledema, prolonged post-ictal period) with neuroimaging findings were compared. We also compared the relationship between the etiology of seizures and neuroimaging findings. Furthermore, patients younger than 24 months of age and older than 24 months of age were compared statistically according to seizure characteristics and neuroimaging findings.

## Statistical Analysis

Statistical analyses were conducted using the Statistical Program for the Social Sciences version 22 (IBM SPSS, Turkey). Descriptive variables were reported as percentages and mean  $\pm$  standard deviation data for categorical variables were analyzed using  $\chi^2$  or Fisher's exact tests and Continuity (Yates's) correction.

A p value of <0.05 was considered statistically significant. The study was approved by the institutional review board at İstanbul Medeniyet University Göztepe Training and Research Hospital.

## Results

This study included 173 children (103 boys and 70 girls) aged between 1 month and 204 months (mean: 80±60.4 months). One hundred twenty-one (70%) patients were older than 24 months of age. Of the 173 children, 87 (50.3%) had a CT scan only, 50 (28.9%) had MRI only, and 36 (20.8%) underwent both MRI and CT. Neuroimaging results were abnormal in 42 (24.3%) patients whereas 9 of 173 patients (5.2%) had a finding of emergent intracranial pathology requiring immediate intervention. Demographic, clinical, and neuroimaging findings of the patients are shown in Table 2.

All patients with emergent intracranial pathology had a focal seizure and new-onset neurological deficits. Brief summaries of patient presentations for those with emergent neuroimaging findings are shown in Table 3. In patients having both CT and MRI, 25% (9/36) of patients had abnormal MRI while CT was normal. Only one of these 9 children (11.1%) had a finding of emergent intracranial pathology on MRI that was not identified on CT. This patient had acute infarct.

The incidence of neuroimaging abnormalities was significantly low (6.7%) in patients with idiopathic etiology compared to that in patients with remote symptomatic (82.1%) and acute symptomatic group (100%) (p<0.01). There was no emergent intracranial pathology in patients with idiopathic etiology.

Class	Abnormality	Examples
1	Non-specific lesions	Periventricular leukomalacia, generalized cerebral atrophy, arachnoid cyst, venous anjioma, lipoma
2	Static-remote lesions	Porencephaly, other malformations of cortical development
3	Focal lesions responsible for the seizures but not requiring immediate intervention	Focal cortical dysplasia, mesial temporal sclerosis, focal encephalomalasia, focal calcification, old VP shunt
4	Subacute or chronic lesions that does not require immediate intervention but has important therapeutic or prognostic implications	Low-grade brain tumour, leukodystrophies, metabolic disorder
5*	Acute lesions requiring immediate medical or surgical intervention	New hydrocephalus, acute stroke or hemorrhage, encephalitis, meningitis, acute cerebral edema/herniation

\*Considered as clinically emergent intra-cranial pathology, VP: Ventriculo-peritoneal

The frequency of abnormal neuroimaging findings associated with seizures was high in patients younger than 24 months of age, had focal seizures, abnormal neurologic status prior to seizure, new neurological symptoms after seizure, and predisposing conditions (p=0.008, p=0.001, p=0.0001, p=0.0001 and p=0.0001, respectively; Table 4). There was no emergent intracranial pathology in patients with generalized seizure.

The frequency of abnormal neuroimaging findings was significantly high in patients younger than 24 months of age (p=0.008). Evaluation of the characteristics of patients according to age groups is shown in Table 5.

## Discussion

Afebrile seizures are one of the most common neurological emergencies among children. There are multiple causes of seizure, but new-onset epilepsy is the most common cause of a first afebrile seizure. The patient history and physical examination should direct the type and timing of laboratory and imaging studies.<sup>12</sup> The role of neuroimaging is not well defined in children presenting to ED with a first seizure. The prevalence of abnormal neuroimaging in different studies ranged between 7% and 24% and in 3-4% of them had immediate therapeutic significance.<sup>3,10,13,14</sup> In our study, the

**Table 2. Demographic, clinical, and neuroimaging findings of the patients**

	n	%
Age	≤24 months	52 30.1
	>24 months	121 69.9
Gender	Female	70 40.5
	Male	103 59.5
Seizure type	Focal	77 44.5
	Generalized	96 55.5
Duration of seizure	<5 min	116 67.1
	5-30 min	54 31.2
	≥30 min	3 1.7
Etiology of seizure	Remote symptomatic	28 16.2
	Acute symptomatic	10 5.8
	Idiopathic	135 78.0
Abnormal neurologic status prior seizure	21	12.1
New neurological symptoms after seizure	25	14.5
Predisposing conditions	23	13.3
Neuroimaging abnormality	42	24.3
Non-specific lesions (class 1)	14	8.1
Static-remote lesions (class 2)	6	3.5
Focal lesions (class 3)	9	5.2
Subacute or chronic lesions (class 4)	4	2.3
Acute lesions requiring immediate intervention (class 5)	9	5.2

prevalence of abnormal neuroimaging in children presenting to ED with a first afebrile seizure was 24.3% but only 5.2% of them had emergent intracranial pathology.

Shinnar et al.<sup>5</sup> evaluated 411 children with a first afebrile seizure in a prospective observational study. Neuroimaging studies were performed in half of the patients and 21% of them were abnormal whereas the incidence of lesions requiring acute intervention in children presenting with a first seizure was low (approximately 1%). Children with abnormal neurological examination and with partial seizures were more likely to have abnormal imaging. They concluded that neuroimaging should be considered in any child with a first seizure who does not have an idiopathic form of epilepsy.<sup>5</sup> Berg et al.<sup>15</sup> reported that the prevalence of abnormal

neuroimaging in children with newly diagnosed epilepsy was 12.7% but the incidence of lesions requiring acute intervention was low. Patients with neurologic deficits or partial seizures or focal electroencephalography (EEG) abnormalities were more likely to have abnormal neuroimaging. Therefore, they concluded that neuroimaging should be considered during the evaluation of children with newly diagnosed epilepsy, especially in those with neurologic deficits or partial seizures or focal EEG abnormalities that are not a part of an idiopathic localization-related epilepsy syndrome. In accordance with the literature, we have not found any neuroimaging abnormalities requiring immediate intervention in patients with idiopathic etiology.

Aprahamian et al.<sup>7</sup> recently published a large retrospective cohort of children with a first afebrile seizure with focal manifestations and they determined that the proportion of children with emergent intracranial pathology was 4.1%. In addition, they confirmed that patients younger than 18 months and those with Todd's paresis may be at a higher risk of having emergent intracranial pathology. In our study, the prevalence of neuroimaging abnormality was significantly high in patients with focal seizures than in patients with generalized seizures (41.6% vs. 10%). In addition, all patients with emergent intracranial pathology had focal seizures. In

Number	Age (month)	Gender	Type of seizure	New-onset neurological abnormality	Neuroimaging findings
1	204	F	Focal	Yes	VP shunt dysfunction
2	33	M	Focal	Yes	Acute infarct in the left frontal lobe and postcentral gyrus
3	14	M	Focal	Yes	Posterior fossa mass, effacement of the fourth ventricle (medullablastoma)
4	22	F	Focal	Yes	VP shunt dysfunction
5	3	M	Focal	Yes	Right subdural hemorrhage
6	156	F	Focal	Yes	VP shunt dysfunction
7	18	F	Focal	Yes	Subacute infarct in the right parietal and occipital lobes and thalamus with edema surrounding the lesion, and cerebellar atrophia
8	174	F	Focal	Yes	Intra-parenchymal hemorrhage in the left parietal lobe
9	98	M	Focal	Yes	T2 hyperintense lesions in right parietal and occipital lobes consistent with posterior reversible encephalopathy syndrome

VP: Ventriculo-peritoneal, F: Female, M: Male

**Table 4. Evaluation of patient characteristics according to neuroimaging findings**

		Neuroimaging findings		p	OR
		Abnormal n (%)	Normal n (%)		
<sup>1</sup> Gender	Female	20 (28.6%)	50 (71.4%)	0.365	
	Male	22 (21.6%)	81 (78.6%)		
<sup>1</sup> Age	≤24 months	20 (38.5%)	32 (61.5%)	0.008**	2.81
	>24 months	22 (18.2%)	99 (81.8%)		
<sup>2</sup> Duration of seizure	<5 min	28 (24.1%)	88 (75.9%)	0.217	
	5-30 min	12 (22.2%)	42 (77.8%)		
	≥30 min	2 (66.7%)	1 (33.3%)		
<sup>1</sup> Seizure type	Focal	32 (41.6%)	45 (58.4%)	0.001**	6.11
	Generalized	10 (10.4%)	86 (89.6%)		
<sup>1</sup> Seizure recurrence in 24 hours	Yes	18 (29.4%)	43 (70.5%)	0.318	
	No	24 (21.4%)	88 (78.6%)		
<sup>1</sup> Abnormal neurologic status prior seizure	Yes	15 (71.4%)	6 (28.6%)	0.001**	11.57
	No	27 (17.8%)	125 (82.2%)		
<sup>1</sup> New neurological symptoms after seizure	Yes	22 (88.0%)	3 (12.0%)	0.001**	46.93
	No	20 (13.5%)	128 (86.5%)		
<sup>1</sup> Predisposing conditions	Yes	20 (87.0%)	3 (13.0%)	0.001**	38.78
	No	22 (14.7%)	128 (85.3%)		

<sup>1</sup>Continuity (Yates) correction, <sup>2</sup>Chi-square test, \*\*p<0.01, OR: Odds ratio



other words, none of the patients with generalized seizures had emergent intracranial pathology. We detected emergent intracranial pathology in 11.7% of children with focal seizures. This rate is 3 times greater than the rate reported by Aprahamian et al.<sup>7</sup> which can be due to exclusion of patients with ongoing status epilepticus, altered mental status or signs of elevated intracranial pressure in that study. When evaluated based on age, while 38.5% of patients younger than 24 months of age had abnormal neuroimaging, only 18% of patients older than 24 months of age had abnormal neuroimaging in our study. This result is attributed to the fact that neuroimaging abnormalities are higher among those younger than 24 months of age.

Report of the Quality Standards Subcommittee of the American Academy of Neurology, the Child Neurology Society, and the American Epilepsy Society recommended that emergent neuroimaging should be performed in a child of any age who exhibits a postictal focal deficit (Todd's paresis) not quickly resolving, or who has not returned to baseline state within several hours after the seizure.<sup>8</sup> In a large retrospective study of children with new-onset afebrile seizure, 2 criteria were found to be associated with high risk for clinically significant abnormal neuroimaging: 1) presence of a predisposing condition (sickle cell disease, bleeding disorders, cerebral vascular disease, malignancy,

human immunodeficiency virus infection, closed-head injury, hydrocephalus), and 2) focal seizure if the patient is <33 months old. In high-risk patients, 26% had clinically significant abnormal neuroimaging compared with 2% of patients in the low-risk group.<sup>4</sup> Warden et al.<sup>2</sup> reported that neuroimaging results were always normal when the patient did not have an underlying high-risk condition (malignancy, neurocutaneous disorder, recent closed-head injury, or recent cerebrospinal fluid shunt revision), was older than 6 months, had sustained a seizure of 15 minutes or less, and did not have a history of a new-onset focal neurologic deficit. In our study, the rate of neuroimaging abnormality was 38.7 times greater in patients with predisposing conditions such as neonatal hypoglycemia, perinatal asphyxia, bleeding disorders, malignancy, immune deficiency, previously known hydrocephalus or cranial tumor, and recent head injury or operation.

Although it is known that MRI is the accepted imaging modality in children with seizures, CT is more common and technically easier than MRI in EDs. Additionally, CT mostly does not require sedation which is an advantage in EDs. In our study, among patients who had both CT and MRI, 25% (9/36) had abnormal MRI while CT was normal. This confirmed that MRI was superior to CT. However, only one of these 9 children had a finding of emergent intracranial pathology on MRI that was not identified on CT. This patient had an acute infarct and had a new-onset focal neurologic deficit that alerted us.

### Study Limitations

Our study has a few limitations. It was a retrospective study and the clinical data were assessed by ED chart review. Since the seizure type and other features were reported by parents or witnesses, identification of this data may be overlooked. Besides, neuroimaging of the patients were decided according to ED clinician's preference. We did not know the prospective follow-up of the patients who were discharged from the ED without neuroimaging and, whether neuroimaging abnormality was detected then.

### Conclusion

In our study, the prevalence of abnormal neuroimaging in children presenting to the ED with a first afebrile seizure was 24.3% but only 5.2% of them had emergent intracranial pathology. We recommend that emergent neuroimaging should be performed in children with focal seizure(s), new-onset neurological deficits, pre-existing neurological abnormalities, or predisposing conditions. Children younger than 24 months of age are also at a high risk for abnormal neuroimaging. Although MRI is the accepted imaging modality in children with seizures, CT may be an option in cases if MRI is technically not possible.

**Table 5. Evaluation of the characteristics of the patients according to age groups**

	Age group		P
	≤24 months n (%)	>24 months n (%)	
<sup>1</sup> Gender			
Female	21 (40.4%)	49 (40.5%)	1.000
Male	31 (59.6%)	72 (59.5%)	
<sup>2</sup> Duration of seizure			
<5 min	45 (86.5%)	71 (58.7%)	0.001**
5-30 min	6 (11.5%)	48 (39.7%)	
≥30 min	1 (1.9%)	2 (1.7%)	
<sup>2</sup> Seizure type			
Focal	28 (53.8%)	49 (40.5%)	0.105
Generalized	24 (46.2%)	72 (59.5%)	
<sup>1</sup> Seizure recurrence in 24 hours	33 (63.5%)	28 (23.1%)	0.001**
<sup>1</sup> Abnormal neurologic status prior seizure	9 (17.3%)	12 (9.9%)	0.267
<sup>1</sup> New neurological symptoms after seizure	12 (23.1%)	13 (10.7%)	0.060
<sup>1</sup> Predisposing conditions	9 (17.3%)	14 (11.6%)	0.438
<sup>1</sup> Abnormal neuroimaging	20 (38.5%)	22 (18.2%)	0.008**

<sup>1</sup>Continuity (Yates) correction, <sup>2</sup>Chi-square test, \*\*p<0.01

## Ethics

**Ethics Committee Approval:** Ethics Committee of Istanbul Medeniyet University Göztepe Training and Research Hospital, approval number: E/20.

**Informed Consent:** The study design was retrospective observational study.

**Peer-review:** Internally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: G.E.B., E.Y.K., S.S., Concept: G.E.B., Design: G.E.B., Data Collection or Processing: G.E.B., E.Y.K., S.Ö., Analysis or Interpretation: Ş.Ö., Literature Search: G.E.B., E.Y.K., Writing: G.E.B., E.Y.K.

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