




FULL-LENGTH ORIGINAL RESEARCH

The importance of acknowledging diagnostic uncertainty in patients with new-onset paroxysmal spells

Tarek El Halabi¹  | Maya Dirani¹ | Wassim Nasreddine¹  | Ghassan Hmaïmess² | Sandra El Sabbagh³ | Jaafar Wazne⁴ | Hassan Toufaily⁵ | Dana Hasbini⁴ | Ahmad Beydoun¹ 

¹Neurology Department, American University of Beirut Medical Center, Beirut, Lebanon

²Department of Pediatrics, Saint George Hospital University Medical Center, University of Balamand, Beirut, Lebanon

³Department of Pediatrics, Hotel Dieu de France Hospital, Beirut, Lebanon

⁴Rafic Hariri University Hospital, Beirut, Lebanon

⁵Labib Medical Center, Beirut, Lebanon

Correspondence

Ahmad Beydoun, Department of Neurology, American University of Beirut Medical Center, Riad El-Solh, PO Box 11-0236, Beirut 1107 2020, Lebanon.
Email: ab29@aub.edu.lb

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Abstract

Objective: The aims of this study were to evaluate the frequency of paroxysmal spells of indeterminate nature (PSIN) in a large cohort of children and adults with suspected new-onset seizures, to evaluate the reasons for including patients in this category, and to calculate the rate of erroneous diagnoses if the epileptologists were compelled to label those events as epileptic seizures or nonepileptic paroxysmal spells.

Methods: Patients identified for this study participated in a prospective study evaluating patients with suspected new-onset unprovoked seizures. The workup included a detailed history and a thorough description of the spells, a 3-hour video EEG recording, and an epilepsy protocol brain MRI. Based exclusively on a detailed description of the ictal events, two epileptologists were asked to independently classify each patient into those with a definite diagnosis of unprovoked seizures or a definite diagnosis of a nonepileptic paroxysmal spells (group 1) and those with PSIN (group 2).

Results: A total of 1880 consecutive patients were enrolled with 255 (13.6%) included in the PSIN group. Patients with PSIN were significantly younger than those with a definite diagnosis, and PSIN were significantly more frequent in children with developmental delay. The most common reason for including patients in the PSIN group was the inability to categorically discriminate between a seizure and a nonepileptic mimicker. When the raters were compelled to classify the spells in the PSIN group, the frequencies of erroneous diagnoses ranged between 32% and 38%. The final diagnoses on those patients were made based on the results of the EEG, MRI, and follow-up visits.

Significance: Our data indicate that a diagnostic category of PSIN should be recognized and ought to be used in clinical practice. Acknowledging this uncertainty

Tarek El Halabi and Maya Dirani contributed equally to the manuscript.

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will result in lower frequencies of erroneous diagnoses, possible stigma, and potential exposure to unnecessary antiseizure medications.

KEYWORDS

epileptic seizures, nonepileptic spells, paroxysmal spells, prospective study, unclassified spells

1 | INTRODUCTION

It is well established that the diagnosis of seizures is based on a detailed description of the paroxysmal spells obtained from the patient and/or a reliable witness.^{1,2} The EEG in isolation cannot be used to establish the diagnosis of seizures (unless the patient experienced a seizure during the recording) but can be useful in corroborating the diagnosis and in defining the electroclinical syndrome. Similarly, neuroimaging cannot be used to diagnose seizures but can be very valuable in identifying the underlying pathological substrate.

Diagnosing a seizure based on a detailed semiological description of the spell(s) is usually straightforward. However, differentiating between a seizure and a nonepileptic spell can occasionally be challenging, especially in patients with new-onset paroxysmal spells. This uncertainty can be due to several factors including a sketchy description of the spells, spells that were only partially witnessed, unreliable witnesses, and atypical features of the spells. In such cases, an attempt to categorically establish a diagnosis of seizure or a nonepileptic paroxysmal spell is prone to errors and, therefore, misdiagnosis.³⁻⁶ If a nonepileptic spell is erroneously diagnosed as a seizure, this can result in major negative impacts on patients, including driving restriction, loss of employment, stigma, and poorer quality of life.¹ Moreover, it may lead to unnecessary exposure to antiseizure medications (ASM), which can be associated with significant adverse events.⁷

The aim of this prospective study was to evaluate the frequency of paroxysmal spells of indeterminate nature (PSIN) in a large cohort of children and adults referred for suspected new-onset seizure(s). The secondary aims were to investigate the reasons as to why those spells were labeled as PSIN, to stratify their frequencies according to age groups and to the presence or absence of developmental delay, and to calculate the rate of erroneous diagnoses if the epileptologists were compelled, only based on the description of the ictal events, to label the spell as an epileptic seizure or a nonepileptic paroxysmal spell.

2 | METHODS

Patients identified for this study participated in an ongoing prospective study that started more than 9 years

Key point

- The initial diagnosis remained uncertain in 13.6% of patients presenting with new-onset paroxysmal spells
- Acknowledging this uncertainty lowers the frequencies of erroneous diagnoses, stigma, and exposure to unnecessary antiseizure medications
- Following appropriate workup and with clinical follow-up, this uncertainty will resolve in most cases

ago, enrolling children (6 months-17.9 years) and adults (18 years and older) with suspected new-onset unprovoked seizure or newly diagnosed epilepsy. This is a centralized study conducted at the American University of Beirut Medical Center (AUBMC) in association with the Lebanese Chapter of the International League against Epilepsy. Adult and pediatric neurologists from all five provinces (Qadaa) of Lebanon are referring all their patients (6 months and older) with a suspected single unprovoked seizure or suspected newly diagnosed epilepsy to the AUBMC where a full clinical evaluation and extensive workup are performed. Patients with acute symptomatic seizures, those with a history of alcohol or drug abuse, children with febrile seizures, and pregnant women were excluded.

The workup included a detailed history and a thorough description of the spells obtained from the patient and an eyewitness, a complete physical and neurological examination, a 3-hour sleep-deprived video EEG recording interpreted by two experienced epileptologists along with an epilepsy protocol brain MRI interpreted by a neuroradiologist blinded to the patient's history. The history and semiological description of the spells were either obtained by both raters interviewing the patient/witness at the same time or by concomitantly but independently evaluating the history obtained by a well-trained research physician. The results of the workup on each patient were conveyed to the referring physician who decided on whether to initiate treatment and on the choice of ASM. Patients were subsequently

evaluated every 6 months with additional visits scheduled as needed based on recurrence of the spells or adverse events.

2.1 | Brain MRIs

MRI examinations were performed on a 1.5 Tesla or 3 Tesla MRI (Ingenia, Philips). The MRI scanning protocol included a 3D sagittal thin cuts T1 to detect and identify subtle cortical malformations, 3D fast fluid-attenuated inversion recovery (FLAIR) of the whole brain with multiplanar reconstruction, and axial and coronal inversion recovery to detect migration anomalies, and subtle gray-white matter blurring.

2.2 | Classifications of patients

Based exclusively on the initial detailed description of the ictal event(s) obtained from the patient and an eyewitness and prior to evaluating the EEG or MRI results, two epileptologists (AB and WN) with more than 25 years' experience in pediatric and adult epilepsy were asked to independently classify each patient into one of two groups:

Group 1: Patients with a definite diagnosis of unprovoked seizure(s) or a definite diagnosis of a nonepileptic paroxysmal spell.

Group 2: Patients with PSIN. Patients were included in this group if the epileptologist could not confidently determine if the spell represented a seizure or a nonepileptic paroxysmal spell.

The epileptologists were asked to use a high confidence level (80% confidence level) when including a patient in group 1. Absent that threshold, the patient was included in group 2. The threshold of 80% was chosen since it represents a high degree of confidence and is similar to the threshold recommended by the Task Force on the operational classification of seizure types when classifying a seizure as having a focal or generalized onset.⁸ In case of disagreement between the two raters as to the category, the case was discussed in an attempt to reach an agreement. A patient included in group 2 by at least one of the epileptologists was considered to be experiencing PSIN.

For each patient included in group 2, the epileptologists were asked to answer the following two questions:

1. What is the reason that prevented you from reaching a definite diagnosis? The choices included the consideration of an alternative diagnosis, spells of an atypical nature, partially witnessed or unwitnessed spells,

discordant description from different witnesses, and other reasons.

2. If you were compelled based only on the available description of the spell to label it as a seizure or nonepileptic paroxysmal spell, how would you categorize it?

Very few patients had videos of the spells at the time of initial evaluation. However, the epileptologists were not allowed to review those videos and were asked to solely base their diagnoses on the description of the spells. The final diagnoses of patients included in the PSIN category were made based on the results of the 3-hour video EEG recordings, epilepsy protocol brain MRI, follow-up visits, follow-up EEGs, and videos of the spells, when available.

2.3 | Educational levels of mothers of children included in the study

In this study, the initial diagnoses made by the epileptologists were solely based on a detailed description of the semiological features of the event. Consequently, one possible reason for a spell to be labeled as PSIN could be related to the inability of eyewitnesses to provide the physician with a meticulous and detailed narrative of the clinical features that occurred during the spell. As a result, we aimed to determine whether the frequency of PSIN was higher when obtained from witnesses with a low educational level compared to the frequency when obtained from those with a high educational level. In order to test that hypothesis, we obtained the educational levels of all mothers of children included in the study and from whom a description of the paroxysmal spell(s) was obtained. The educational levels consisted of the following categories: illiterate, elementary school, middle school, vocational school, high school, university, and higher studies.

2.4 | Analysis

A Kappa coefficient analysis was performed to measure agreement between the results of each reviewer for the classification of patients into one of the two groups. The following ranges were used for interpretation of the Kappa values: <0, no agreement; 0-0.20, slight; 0.21-0.40, fair; 0.41-0.60, moderate; 0.61-0.80, substantial; 0.81-1, almost perfect.⁹

We then compared the frequencies of patients with PSIN according to age, gender, and presence or absence of developmental delay in children. In addition, we calculated the frequencies of the various reasons that led the epileptologists to include patients in the PSIN category

and stratified those according to age groups (adults versus children).

Descriptive statistics for the whole group were obtained. Categorical and continuous variables were compared using the chi-square and the t test, respectively. All tests were 2-sided, and a significant *P*-value was set at <.05. SPSS V21 was used for all analyses.

3 | RESULTS

3.1 | Demographics

A total of 1880 consecutive patients (1084 males and 796 females) were included in this study (mean age = 18.75 years, range: 6 months to 91 years). There were 1254 children (66.7%) and 626 adults (33.3%). Developmental delay was diagnosed in 284 of the children (22.6%). The patients were followed for an average of 7.2 years (range: 4.9-8.9 years). The patients were referred from all five provinces of Lebanon, and their geographical distribution was very similar to the percentages of the Lebanese population residing in those provinces indicating that there was no referral bias from a particular region of the country.

3.2 | Classification of patients by the epileptologists

Rater 1 classified 215/1880 patients (11.4%) in the PSIN group, while rater 2 classified 236/1880 patients (12.6%) in that category (Table 1). Both raters classified 1821 out of 1880 patients (96.9%) into the same groups: 1625 patients were included in group 1 (patients diagnosed with either definite seizures or definite nonepileptic paroxysmal spell) and 196 in group 2 (patients with PSIN) (Table 1). The agreement between the two raters in classifying paroxysmal spells into one of the two groups was almost perfect (Kappa = 0.851). The raters disagreed in categorizing 59 patients, with those patients classified in the definite seizure or nonepileptic spell group by one rater and in the

PSIN group by the other (Table 1). Those 59 patients were thus included in the PSIN group, resulting in a total of 255 patients (13.6%) in that group.

3.3 | Comparison of demographic variables between groups 1 and 2

Patients categorized with PSIN were significantly younger (mean age = 15.0 years) than those with a definite diagnosis (mean age = 19.3 years) (Table 2). In addition, children were significantly more likely to present with PSIN (15.3%) compared to adults (10.1%) (Table 2). Within the pediatric population, those with developmental delay were significantly more likely to be categorized with PSIN (23.2%) compared to children with a normal development (13.0%) (Table 2).

3.4 | Reasons for including patients in the PSIN group

The most common reason for including patients in the PSIN group was the inability of the epileptologists to categorically discriminate based on the history alone between an epileptic seizure and a nonepileptic seizure mimicker (Table 3). In fact, 175 patients (68.6%) were included because of a possible “alternative diagnosis” which comprised syncope, nonepileptic paroxysmal movement disorders (including chorea, tics, stereotypies, mannerism, paroxysmal dyskinesias, jitteriness, tonic reflex seizures of early infancy, rhythmic behavioral disorders, self-gratification disorder, Sandifer syndrome, benign neonatal sleep myoclonus, Fejerman syndrome, and hyperkplexia),¹⁰ daydreaming episodes, breath-holding spells, nonepileptic psychogenic seizures, transient ischemic attacks, febrile seizures vs. seizures induced by febrile illnesses, parasomnias, and migraines. As expected, the alternative diagnoses that were considered in adults mostly consisted of syncopal episodes, transient ischemic attacks, and nonepileptic psychogenic seizures. In contrast, paroxysmal movement disorders, syncope, daydreaming

		Rater 2		
		Definite seizure or nonepileptic spell	PSIN	Total
Rater 1	Definite seizure or nonepileptic spell	1625	40	1665
	PSIN	19	196	215
Total		1644	236	1880

TABLE 1 Classification of patients into groups 1 or 2 by the two raters

TABLE 2 Comparison between patients diagnosed with PSIN versus those with a definite diagnosis

	Patients with PSIN	Patients with a definite diagnosis (seizure or NEPS)	P-value
Mean age (years)	15.0	19.3	.001
Gender			
Males (N = 1084)	143 (13.2%)	941(86.8%)	.583
Females (N = 796)	112 (14.1%)	684 (85.9%)	
Age			
Adults (N = 626)	63 (10.1%)	563 (89.9%)	.002
Children (N = 1254)	192 (15.3%)	1062 (84.7%)	
Development in children			
Delay (N = 284)	66 (23.2%)	218 (76.8%)	<.001
Normal (N = 970)	126 (13.0%)	844 (87.0%)	

Abbreviations: NEPS, nonepileptic paroxysmal spells; PSIN, paroxysmal spells of indeterminate nature.

TABLE 3 Reasons for including patients in the PSIN group stratified by age groups

	All	Adults	Children
Alternative diagnosis	175 (68.6%)	40 (63.5%)	135 (70.3%)
Syncope	42 (16.5%)	18 (28.6%)	24 (12.5%)
Movement disorders	40 (15.7%)	1 (1.6%)	39 (20.3%)
Daydreaming	22 (8.6%)	0	22 (11.5%)
BHS	19 (7.5%)	0	19 (9.9%)
Psychogenic seizures	15 (5.9%)	9 (14.3%)	6 (3.1%)
TIA	14 (5.5%)	11 (17.5%)	3 (1.6%)
Febrile seizures	11 (4.3%)	0	11 (5.7%)
Parasomnia	8 (3.1%)	0	8 (4.2%)
Migraine	4 (1.6%)	1 (1.6%)	3 (1.6%)
Atypical features	59 (23.1%)	11 (17.5%)	48 (25.0%)
Unwitnessed spells	18 (7.1%)	11 (17.5%)	7 (3.6%)
Discordant description of spells	2 (0.8%)	0	2 (1.0%)
Others	1 (0.4%)	1 (1.6%)	0
Sum	255	63	192

Abbreviations: BHS, breath holding spells; PSIN, paroxysmal spells of indeterminate nature; TIA, transient ischemic attack.

episodes, and breath-holding spells predominated in the pediatric age group. Other less common causes for classifying a patient into group 2 included episodes with atypical features (23.1%), unwitnessed spells (7.1%), and spells with discordant descriptions by eyewitnesses (Table 3). Unsurprisingly, the frequency of unwitnessed spells was substantially more frequent in the adult population.

3.5 | Educational levels of the children's mothers

There was no significant difference in the educational levels of mothers of children included in group 1 compared to those diagnosed with PSIN ($P = .75$). For instance, the

illiteracy rates were 3.2% and 2.2% for mothers of children with a definite diagnosis and those with PSIN, respectively. The corresponding frequencies for mothers with a university education were 26.0% and 29.0%, respectively.

3.6 | Final diagnoses in the PSIN group

Following the workup that included a 3-hour sleep-deprived EEG, an epilepsy protocol MRI, and clinical follow-up with repeated EEGs as needed, a definite diagnosis was reached in the majority of patients categorized in the PSIN group. Of the 255 patients initially included in that group, 12 were lost to follow-up. Of the remaining 243 patients, 107 (44.0%) were eventually diagnosed with

seizures, 82 (33.7%) with nonepileptic paroxysmal spells, and 54 (22.2%) remained in the PSIN group at last follow-up. When stratified by age groups, a definite diagnosis was reached in 144 out of 183 children (78.7%), with 80 (55.6%) ultimately diagnosed with seizures, and in 45 out of 60 adults (75.0%) with 27 (60.0%) eventually diagnosed with seizures. In 123/189 patients (65.1%), the diagnosis was established based on the results of the initial 3-hour video EEG recording and brain MRI, while for the remaining 66 patients, the diagnosis was reached after a mean of 12.4 months of clinical follow-up. A large proportion of patients who remained undiagnosed after workup and follow-up consisted of those who presented with a single unprovoked paroxysmal spell and who did not experience any recurrence off treatment during the follow-up period. The contributions of the EEG, MRI, and clinical follow-up in establishing the final diagnoses will be the subject of a separate publication.

3.7 | Diagnostic accuracy when the raters were compelled to classify spells in the PSIN group

When the raters were compelled to classify the spells of patients in the PSIN group solely based on the semiology of the events, rater 1 categorized them as seizures in 115 patients and as nonepileptic paroxysmal spells in 74 patients. The corresponding numbers for rater 2 were 99 patients and 90 patients, respectively. When compared to the eventual diagnoses reached on those patients, rater 1 was inaccurate in 60/189 (31.7%) of cases (Table 4A) while the diagnosis of rater 2 was incorrect in 72/189 (38.1%) of cases (Table 4B). The inaccuracy rate between both raters was not significantly different ($P = .2$).

Of importance, 16.9%-18.0% of patients in the PSIN group labeled as experiencing seizures by the

TABLE 4 (A) Agreement between initial and final diagnoses when rater 1 was compelled to classify events in the group of patients with paroxysmal spells of uncertain nature; (B) Agreement between initial and final diagnoses when rater 2 was compelled to classify events in the group of patients with paroxysmal spells of uncertain nature

		Final diagnoses	
		Seizures	NEPS
Rater 1 classification	Seizures	81 (42.9%)	34 (18.0%)
	NEPS	26 (13.8%)	48 (25.4%)
Rater 2 classification	Seizures	67 (35.4%)	32 (16.9%)
	NEPS	40 (21.2%)	50 (26.5%)

Abbreviations: NEPS, nonepileptic paroxysmal spells.

epileptologists were eventually diagnosed with nonepileptic paroxysmal spells (Table 4A and B). On the other hand, 13.8%-21.2% of patients in this group labeled by the raters as experiencing nonepileptic paroxysmal spells were ultimately diagnosed with seizures (Table 4A and B).

3.8 | Diagnostic accuracy of patients initially diagnosed with seizure or nonepileptic paroxysmal spell

After the workup and follow-up visits, only six out of the 1321 patients initially diagnosed with seizures by both raters were eventually diagnosed with nonepileptic paroxysmal spells, which amounted to an inaccuracy rate of 0.5%. None of the 304 patients initially diagnosed with nonepileptic paroxysmal spells were reclassified after workup and follow-up.

3.9 | ASM initiation in patients with PSIN

A total of 67/255 patients (26.2%) with PSIN were initiated on ASM treatment by their referring physicians before undergoing EEG or MRI. Out of those, 17 out of the 82 patients (20.7%) ultimately diagnosed with nonepileptic paroxysmal spells received treatment with an ASM for an average of 24.5 weeks (range: 0.5-182 weeks).

4 | DISCUSSION

The main finding of this study is that despite a detailed description of the semiology of the events, the initial diagnosis remained uncertain in 13.6% of patients with new-onset paroxysmal spells. This frequency was significantly higher in children (15.3%) compared to adults (10.1%) and in children with developmental delay (23.2%) compared to those with a normal neurodevelopment (13.0%).

The most common cause for including patients in the PSIN category in our study was the inability to categorically discriminate, based on the narration of the spell, between an epileptic seizure and one of its mimickers.¹¹⁻¹⁵ The difficulties in differentiating certain types of seizures from nonepileptic paroxysmal spells, especially in children and particularly in those with developmental delay, have been emphasized in several previous studies.¹⁶⁻¹⁹ Occasionally, the distinction between a seizure and a nonepileptic paroxysmal spell could only be established by capturing the habitual event on video EEG recording.²⁰ In addition, the fact that 196/255 patients (77%) were categorized as having PSIN by both raters strongly

suggests that the inclusion of patients in this category was not rater-specific and that in some cases, a meticulous account of the semiological features of a paroxysmal spell is not sufficient to allow the treating physician to positively decide if the event represented an epileptic seizure or a nonepileptic spell.

Only two previous studies, both conducted in the pediatric population, evaluated the frequency of uncertainty in the diagnosis of patients presenting with new-onset paroxysmal spells.^{6,21} In the first study,²¹ 178/881 children (20.2%) were diagnosed with spells of uncertain nature.²¹ The higher frequency of PSIN in that study compared to ours is probably a reflection of the rigid, predefined diagnostic criteria that had to be fulfilled for a diagnosis of seizures to be made.²¹ The second study reported uncertainty in the initial diagnosis of 90/684 children (13.2%),⁶ a frequency very comparable to the 15.3% found in the subgroup of children enrolled in our study. The authors, however, failed to provide the reasons underlying their clinical uncertainty.

In those two studies, a definite diagnosis in the group of children with PSIN was eventually reached in 30%–66% of patients.^{6,21} In contrast, we were able to conclusively reach a definitive diagnosis in 77.8% of our patients, with this higher frequency likely related to the long-term prospective nature of our study, the workup that included a 3-hour video EEG with sleep recording, an epilepsy protocol MRI and a close follow-up with clinic visits and repeat EEGs including prolonged recordings as clinically indicated.

Our study ascertains the importance of incorporating a diagnostic category labeled as PSIN when evaluating patients presenting with new-onset paroxysmal spells. Firstly, the importance of this category was demonstrated by a high inter-rater reliability, which is considered a prerequisite for an accurate diagnostic model.¹ Indeed, when two experienced epileptologists classified the 1880 patients solely based on a detailed description of the semiological features of the spells into those with a definite diagnosis (seizure or nonepileptic paroxysmal spell) or PSIN, the agreement factor was almost perfect. Secondly, the validity of the PSIN category was assessed by examining the misdiagnosis rate when this category was not acknowledged. In fact, when the epileptologists were compelled to categorize the spells experienced by patients in the PSIN category as epileptic or nonepileptic, this resulted in a misdiagnosis rate ranging from 31.7% to 38.1% across the two raters. Of greater importance is the fact that the raters would have misdiagnosed 17%–18% of patients in the PSIN group as experiencing seizures, whereas those patients were eventually diagnosed as experiencing nonepileptic spells. This erroneous diagnosis can result in an unnecessary exposure to ASM,²² a concern proven

in our study as 21% of patients in the PSIN category who were eventually diagnosed with nonepileptic spells were initially started and maintained on ASM for an average duration of six months. In addition to the exposure to the potential adverse events of ASM, this misdiagnosis can result in stigma for patients and in a large financial burden on the healthcare system estimated to be in the range of 29 million pounds annually in the United Kingdom.^{23,24}

The main problem when evaluating patients with paroxysmal spells is the absence of objective semiological variables with high enough sensitivities and specificities to differentiate between seizures and nonepileptic spells. It should be noted that the ILAE classifications of epileptic seizures and epilepsies assume that a diagnosis of seizure/epilepsy has been made and provide a scheme for the classification of the various types of seizures and epilepsies.^{8,25} However, the ILAE does not provide guidelines on how or when a diagnosis of seizure can be confidently made since there are no definite criteria to cover all the possible semiological manifestations of a seizure. Moreover, even the seizure classification involves some degree of uncertainty since the Task Force recommended for a clinician to have at least an 80% confidence level when deciding whether a seizure is of focal or generalized onset.^{8,25} If that confidence level is not reached, the seizure should be listed as a seizure of unknown onset.^{8,25} In our study, the epileptologists adopted a similar confidence level when deciding whether a paroxysmal spell represented a seizure or one of its mimickers. Absent that threshold, the spell was listed as a PSIN. The appropriateness of this approach was validated since only 0.5% of patients in group 1 (patients diagnosed with definite seizures or definite nonepileptic paroxysmal spells) were misdiagnosed compared to erroneous diagnoses ranging between 31.7% and 38.1% when the epileptologists were compelled, only based on the semiological features of the events, to decide whether patients in the PSIN category were experiencing seizures or nonepileptic spells. Those data indicate that in order to reduce the rate of misdiagnoses, physicians should take a detailed history of the semiological features of the spell and use a high level of confidence before committing to a diagnosis of seizure or nonepileptic paroxysmal spell.

In the absence of a diagnostic gold standard, some have tried to increase the reliability in diagnosing seizures with the use of specific diagnostic criteria.²⁶ In one study, three neurologists independently evaluated the semiologies of spells experienced by 100 patients (15 years of age and older) with a single new-onset paroxysmal spell and categorized each spell as epileptic or nonepileptic.²⁶ Although the use of the diagnostic criteria improved the overall kappa among the three reviewers from 0.58 to 0.73, a disagreement was still present for 12% of patients.²⁶ A similar study conducted in children

found that the interobserver agreement was only 0.41 when three experienced pediatric neurologists evaluated the nature of 100 paroxysmal spells based on a written history. This agreement improved only slightly to 0.45 when descriptive criteria were used.²⁷ Those results indicate that even the use of objective and descriptive criteria to diagnose seizures does not refute the fact that some patients will need to be categorized as experiencing PSIN. We elected to use the term “PSIN” over others such as “possible” or “probable” seizures since the former does not include the term “seizure” with all of its negative connotations and implications, especially that a substantial proportion of those patients will eventually be diagnosed with nonepileptic spells.

It might be argued that specific factors, including unwitnessed spells and a poor description of the paroxysmal spells, could have inflated the frequency of PSIN in our study. We, however, are confident that the impact of those factors was minimal. Actually, the partially witnessed or unwitnessed spells accounted for only 7.1% of patients categorized with PSIN. Moreover, the educational levels of mothers who provided us with the narrative of the paroxysmal spells experienced by their children were not different between children for whom a definite initial diagnosis was established compared to those diagnosed with PSIN. This finding strongly suggests that the frequency of patients presenting with PSIN is not related to an unreliable history or a poor description of the ictal event.

In conclusion, our data indicate that a diagnostic category of PSIN should be recognized and ought to be used in clinical practice. Acknowledging this uncertainty will result in a lower frequency of erroneous diagnoses, possible stigma, and potential exposure to unnecessary ASM. Patients and/or parents should be told that this uncertainty will resolve in most cases following an appropriate workup and with clinical follow-up. Meanwhile, patients or parents should be given instructions for seizure precautions until the nature of the spells is eventually clarified.

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CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

ETHICAL APPROVAL

The Institutional Review Board of the AUBMC approved this study, and all patients or their parents signed an informed consent form. Children between the ages of 7 and 17 years signed an assent form.

ORCID

Tarek El Halabi  <https://orcid.org/0000-0002-1197-1393>

Wassim Nasreddine  <https://orcid.org/0000-0001-6487-8259>

Ahmad Beydoun  <https://orcid.org/0000-0002-9047-1185>

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