Original Article

Paroxysmal Nonepileptic Events in a Pediatric Epilepsy Clinic
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Aims: We aimed to study the frequency, age, and gender distribution of paroxysmal nonepileptic events (PNEs) in children referred to epilepsy clinic with the diagnosis of epilepsy. We also evaluated the therapeutic implications of correct diagnosis and co-existence of true epilepsy in this population. Settings and Design: All new patients below 18 years attending the Pediatric epilepsy outpatient clinic of PD Hinduja hospital over 6 months were evaluated. Materials and Methods: Patients with history of paroxysmal events characterized by abrupt changes in consciousness or behavior or movement were included. They were assessed on description of events aided by recorded videos. If the diagnosis was not confirmed by this preliminary evaluation, further investigations were advised. Statistical Analysis Used: Chi-square/Fisher’s exact test was used to analyze differences between categorical variables and Kruskal–Wallis test between continuous variables. The data were analyzed by SAS University Edition. All significance tests were two-tailed with α<0.05. Results: Two hundred new patients presenting with paroxysmal events were enrolled over 6 months. After diagnoses, 19% of these children had PNEs, 80% had epileptic events, and 1% remained undiagnosed. Common nonepileptic events seen were physiological in patients below 5 years and psychogenic in older children. Thirty-four percent of patients with PNEs were on anti-epileptic drugs (AEDs). After confirming nonepileptic attacks, only 2.6% patients needed AEDs for coexisting epilepsy which was statistically significant (P < 0.001) change in treatment. Conclusions: Epilepsy mimics are common in children and are often misdiagnosed causing undue stress. Correct diagnosis leads to a drastic change in management like withdrawal of drugs, commencing new treatment if needed, and appropriate referrals.

Keywords: Epilepsy mimics, nonepileptic events, paroxysmal, pseudoseizures, psychogenic

INTRODUCTION
Paroxysmal nonepileptic events (PNEs) are disorders that mimic seizures but are not due to abnormal electrical discharges in the brain.[1] 10%–43% of patients monitored in video-electroencephalogram (VEEG) laboratories in literature have nonepileptic events.[2-13] Misdiagnosis is fraught with dire consequences such as unnecessary investigations, potentially harmful treatments, unwarranted restriction of activities, and parental over-anxiety. All these lead to serious psychosocial and financial burden on the family and society.

PNEs occur in all age groups ranging from neonates to adults. The differential diagnosis is broader in children than adults.[2-13] Majority of PNEs in adults are psychogenic while in children physiological as well as psychogenic events are seen, some being age
Specific. Physiologic events include sleep-related disorders (sleep myoclonus, parasomnias), shuddering attacks, breath-holding spells, and vasovagal syncope. PNEs should always be excluded in patients with drug-resistant epilepsy.\textsuperscript{[10]} The most helpful way to differentiate PNE from seizure is a detailed history and eye-witness description of the event augmented by an event video.\textsuperscript{[14,15]} Certain clinical cues clinch the diagnoses. VEEG is the gold standard for confirmation through high cost, availability and expert interpretation limits its use.\textsuperscript{[3-13]} Correct diagnosis leads to successful management, that is, discontinuing AEDs, commencing new treatment (movement disorders, migraine) and further referrals (cardiologist, psychiatrist).\textsuperscript{[6,9]} This ultimately saves on health resources and alleviates significant distress in affected families.

Though many studies on the prevalence of PNEs in VEEG units are reported in western literature, very few prospective, outpatient studies from developing countries and none from the Indian subcontinent to the best of our knowledge exist.\textsuperscript{[16,17]} Most studies reported in the literature are retrospective analysis of VEEG units which has limitations.\textsuperscript{[3-13]} Mild, infrequent, and straightforward cases are not advised VEEG. Retrospective studies are constrained by information from the medical records and recall of individuals. Events may not be recorded during the monitoring period. Hence, VEEG data is not a true indicator of the incidence of PNEs in the huge epilepsy population.

This study was a prospective, out-patient evaluation of proportion and etiology of PNEs among all new referrals to pediatric epilepsy clinic of a tertiary care hospital. We compared the demographic and clinical characteristics of PNEs between different age groups (less than 5 years, 5–12 years and more than 12 years). Therapeutic implications of correct diagnosis and 1 year outcome of patients with PNEs were assessed. The co-existence of true epilepsy and psychological co-morbidities in patients with psychogenic nonepileptic seizures was studied as well.

**Subjects and Methods**

All new patients attending the pediatric epilepsy clinic between 1st December 2015 and 31st May 2016 below 18 years of age were included if they presented with paroxysmal events and consented to take part in study. Using a proportion of 15.2% for PNEs from an earlier study, a sample size of 199 was considered to be satisfactory.\textsuperscript{[24]} Paroxysmal events were characterized by abrupt changes in consciousness or behavior or sensation or movements of limbs/body/eyes. Patients with incomplete clinical information or confirmed acute symptomatic seizures were excluded. The study was approved by the Institutional Review Board of the hospital. Appropriate informed consent and assent were obtained before enrolment.

All relevant data that is, demographics, medical history, event description, treatment, and investigations done were recorded in a predesigned form (attached). Patients were assessed for the diagnosis of paroxysmal events based on eye-witness description (family members/teacher) sometimes aided by videos. Past medical records including perinatal, development, and family history were recorded. Details of events which included age of onset, frequency, and duration of episodes, state of occurrence (awake/sleep), position during event (standing/sitting/lying down), and aggravating or relieving factors were noted. Event details like aura, eyes open or closed, tongue biting, awareness, responsiveness, speech, distractibility, post-ictal change, and event recall by patient were recorded. At times, imitation of the event by a family member or clinician was required to reach confirmation. A comprehensive examination and additional clinical scores like The Frontal Lobe Epilepsy and Parasomnias (FLEP) score were employed to distinguish parasomnias from frontal lobe epilepsy.\textsuperscript{[18]}

If the diagnosis was inconclusive by preliminary evaluation, investigations like EEG/VEEG, Electrocardiogram (ECG), Head-up tilt table test (HUTT), and neuroimaging were performed as required. VEEG is the gold standard investigation to confirm the diagnosis of PNEs.\textsuperscript{[19]} EEG correlates of the event, semiology of attack, and provocative methods like hyperventilation and suggestibility during VEEG were used to arrive at diagnosis. All children presenting with an unexplained fall also underwent an ECG for cardiac causes and HUTT.\textsuperscript{[20,21]} One of the two pediatric neurologists reviewed all reports and arrived at diagnosis and parents were explained the prognosis. Treatment and further referrals were advised accordingly. All children diagnosed with psychogenic nonepileptic seizures were referred to a child-psychologist for Childhood Behavior Checklist score (CBCL).\textsuperscript{[22]} Outcome at 1-year follow-up of these patients was assessed.

**Data analysis**

The data obtained were coded and entered into Microsoft Excel Worksheet. Quantitative data were presented as frequency (percentage) for categorical variables and as mean (±standard deviation) or median (range) for continuous variables. Chi-square/Fisher’s exact test was used to analyze differences between

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categorical variables. Kruskal–Wallis test was used to calculate differences between continuous variables. McNemar’s chi-square test was used to calculate if proportion of patients receiving AEDs was different before and after the correct diagnosis. The data were analyzed by SAS University Edition (SAS Institute Inc., Cary, NC, USA). All significance tests were two-tailed with $\alpha < 0.05$.

RESULTS

Two-hundred new patients meeting the inclusion criteria were enrolled prospectively for the study over 6 months. These children were further divided into three age groups: A-less than 5 years, B-five to 12 years and C-12 to 18 years of age. Seventy-eight (39%) fell in the group A, 90 (45%) in group B and 32 (16%) in group C [Table 1]. One-hundred twenty-seven (63.5%) were males and 73 (36.5%) were females. There was an uneven distribution of patients according to sex with high male preponderance in each group [Table 1].

Diagnoses could be reasonably achieved in 198 children. One-hundred sixty out of 200 (80%) were found to have epileptic events, 38 (19%) had nonepileptic events and 2 (1%) remain undiagnosed [Figure 1].

Twenty-two (28.2%) patients in group A, 10 (11.1%) in group B and six (18.7%) in group C had PNEs. Proportion of PNEs was significantly higher in patients below 5 years in this study (chi-square test, $P = 0.02$).

Concomitant epilepsy with PNEs was seen in three (1.5%) of 200 patients, one in group A and two in group C.

No significant gender predilection for PNEs was seen in our study (chi-square test, $P = 0.16$) [Table 2]. Although the proportion of males diagnosed with PNEs was higher in group II compared to groups I and III, this difference was not statistically significant ($P = 0.13$).

Physiological PNEs were seen in 33 patients, whereas psychogenic events were seen in five patients. Benign sleep myoclonus was overall the commonest PNE seen in seven (18.4%) patients. Commonest PNE seen was sleep myoclonus in group I (27.3%), psychogenic in group II (30%), and syncope in group III (50%).

Physiological PNEs were more common below 5 years, whereas psychogenic events and syncope were commoner above 5 years [Figure 2].

Median duration of symptoms before diagnosis was significantly different between the three groups with 6 (range 0–36) months in group I, 3 (range 0–12) months in group II, and 42 (range 6–108) months in group III ($P = 0.002$) [Table 2]. There was also a significant difference found in the median duration of treatment with AEDs before the diagnosis of PNEs, with a longer duration taken in group III compared to the other two groups ($P = 0.02$) [Table 2].

Other variables (sex, frequency, abnormal EEG, concomitant epilepsy, associated developmental delay, etc) were not significantly different between the three groups [Table 2].

FLEP score was used in one child with nocturnal events and suggested parasomnias.

Nineteen of 38 (50%) patients with nonepileptic events were diagnosed only by history of which home videos were available in nine. Twelve (31.6%) patients had EEG and other investigations (ECG, HUTT) in addition to history for confirmation. In seven patients (18.4%) diagnosis was established after VEEG which included five patients of psychogenic seizures, one each of benign myoclonus and benign torticollis. Classic features of psychogenic events leading to diagnosis were bizarre tremor-like movements, side to side head or body movements, prolonged attacks with eyes closed and resistance to eye opening, lack of injuries and precipitation with verbal suggestions and audience.[4,5,11-15] The EEG remained normal during these episodes.

![Figure 1: Final diagnosis of patients seen in epilepsy clinic](image_url)
Historical features to differentiate syncope from seizure were occurrence in upright posture, prior unpleasant situation like blood collection; premonitory symptoms of dizziness; pallor, temperature change, sweating, and brief tonic/clonic movements. Short duration of episodes, peri-ictal headache, and normal or brief post-ictal phase were noticed in all. In two cases with recurrent syncope, HUTT was advised. One patient underwent the test, result being positive for cardioinhibitory and vasodepressor response.

Thirteen of 38 patients diagnosed with PNEs (34.2%) were on AEDs at time of diagnosis which were discontinued in 12. Alternative medicines were started in two (migraine and benign paroxysmal vertigo). One patient with paroxysmal kinesiogenic dyskinesia was continued on carbamazepine. A statistically significant difference was noted for change in treatment before and after final diagnosis of PNE with \( P < 0.0001 \) calculated by McNemar’s chi-square test [Figure 3]. All patients with psychogenic events were referred to psychologist for evaluation and assessment of co-morbidities. CBCL was assessed in three of five but failed to detect a clinically significant stressor.\(^a\)

Follow-up could be done in 24 of 38 children (63%) with PNEs for duration of 12–18 months. Seventeen out of these 24(70%) had marked reduction or absence of episodes [Table 3].

**DISCUSSION**

PNEs, although common in childhood, are often misdiagnosed as epilepsy due to inadequate awareness about various differentials, poor history-taking and excessive reliance on investigations (e.g., epileptiform EEG abnormalities seen in 1–2% of normal children).\(^{6-13,23}\) Unlike PNEs seen in adults which are mostly psychogenic, pediatric PNEs comprise a broader differential. Often AEDs are started with no relief and hence PNEs should be considered in all drug-refractory
epilepsies. Events that are situational (standing, blood collection, audience) and those that can be interrupted (tics, self-gratification) are unlikely to be seizures.

In this study, 19% of new patients attending our clinic over 6 months had PNEs, 80% had true epilepsy and two remained undiagnosed. The proportion of PNEs amongst those with suspected epilepsy has varied widely (3.5% to 43%) in past studies. Although most studies are retrospective reviews of patients in VEEG labs, our study involved prospective recruitment of patients attending a pediatric epilepsy clinic. Our proportion is close to those reported by Kotagal (15.2%), Kutluay (23%), and Yilmaz (15.9%). To the best of our knowledge, only one prospective outpatient study in children reported a significantly low proportion (23%) with a final diagnosis of epilepsy. Perhaps, referral bias was responsible for these variations in the proportion of PNEs.

No significant gender predilection for PNEs was seen in our study though previous studies reported psychogenic nonepileptic seizures more in girls above 12 years and in boys below 12 years of age. This may be partly because we had relatively fewer children in the older age groups.

In our study, 86.7% had physiological nonepileptic events and 13.3% had psychogenic nonepileptic events. Although Kutluay showed 62% as physiological events, others reported comparatively lower percentage of physiological events (49.3%, 43.2%). Fewer patients in adolescence, wherein more psychogenic events occur, may be responsible for this difference in our cohort.

The proportion of PNEs was significantly higher in children below 5 years of age when compared to older children. All patients below 5 years had physiological or organic events, with sleep myoclonus (27.3%) being commonest. Higher occurrence of physiologic events in this age has been reported in past studies too.

Kotagal reported 96.2% physiological events and 3.8% psychogenic seizures, with parasomnias and stereotyped movements (19.2% each) as the commonest, whereas Park found normal infant behavior followed by benign sleep myoclonus as the commonest.

In patients between 5 and 12 years of age, 11.1% were diagnosed with nonepileptic events which was lesser compared to Kotagal (45.5%). Psychogenic seizures (30%) was the commonest in these children with male predominance (66.7%), which matched with other studies (36.1%, 52.9%).

For patients above 12 years, 18.7% had nonepileptic events, with syncope (50%) most frequent concordant

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Table 3: Follow-up of cases diagnosed as PNEs

| Condition                        | Total no. of cases | Follow-up | Events stopped/reduced/not observed |
|----------------------------------|--------------------|-----------|-------------------------------------|
| Breath-holding spells            | 5                  | 2         |                                     |
| Sleep myoclonus                  | 7                  | 5         | 3 stopped, 2 rare                   |
| Syncope                          | 5                  | 3         | 3 (1 underwent HUTT)                |
| NEAD                             | 5                  | 3         | 2 + 1 had reduced freq. on vit. C   |
| Movement disorder                | 3                  | 3         | 1 case of PKD had reduced freq. on CBZ |
| Migraine                         | 3                  | 2         | 0                                   |
| Tics                             | 2                  | 2         | 0                                   |
| Benign paroxysmal vertigo        | 2                  | 2         | 1                                   |
| Benign myoclonus of infancy      | 1                  | 1         | 1                                   |
| Shuddering attacks               | 1                  | 1         | 1                                   |
| Torticollis                      | 1                  | 0         | 0                                   |
| Parasomnia                       | 1                  | 0         | 0                                   |
| Cataplexy                        | 1                  | 0         | 0                                   |
| Self-gratification               | 1                  | 0         | 0                                   |
| Total                            | 38                 | 24        | 17                                  |

NEAD = nonepileptic attack disorders, PKD = paroxysmal kinesiogenic dyskinesia, CBZ = carbamazepine, HUTT = headup tilt table test
with the study by Park EG.\textsuperscript{5} However, psychogenic seizures were seen in just 33.3\% as opposed to the 83.3\% seen by Kotagal.\textsuperscript{14} When compared to Kotagal, where two-thirds of adolescents with psychogenic events were girls, we showed no gender predilection.\textsuperscript{8,9} This could be due to a small sample size with heterogeneous distribution by age and sex in our study.

History alone was sufficient for diagnosis in 50\% cases reiterating its value.\textsuperscript{14,15} However, VEEG was employed in 18.4\% patients and was long enough (few hours-six days) to capture at least one habitual event. Suggestibility was used for psychogenic seizures. We often use a tuning fork and verbal suggestion for provoking attacks though others have used sleep-deprivation, hyperventilation, photic-stimulation and saline injection.\textsuperscript{4,5,9}

One percent patients remained undiagnosed, whereas others have reported undiagnosed events as high as 14\%.\textsuperscript{14} In suspicious cases, it is better to withhold the diagnosis of epilepsy until all differentials are carefully considered rather than hastily labeling as “epilepsy.”

Coexistence of PNEs with epilepsy was seen in 7.9\% of our patients, whereas past studies reported 9\%–46\%.\textsuperscript{6,9,10} When epileptic seizures are controlled, psychogenic seizures become more apparent in some cases, perhaps out of the child’s attempt to seek more caregiver attention. The treatment strategy should address both disorders.

Significant difference was found in treatment before and after final diagnosis in patients with PNEs. Similar observation was made in other studies where 19\%–75\% of patients with PNEs were unnecessarily started on AEDs.\textsuperscript{5,6,8-10} Despite uncertainty in diagnosis, clinicians often start AEDs partly due to parental anxiety and lack of effective communication. Inadvertent use of AEDs in children can have potentially negative effect on learning and behavior. As the natural course of these events is spontaneous remission, AEDs may falsely appear to be effective. 70\% patients followed up at 1 year had a marked reduction or absence of episodes similar to Kotagal where 65\% were event-free at a median follow-up of 8 months.\textsuperscript{4}

Most studies have reported psychological co-morbidities in 50\%–70\% of patients with psychogenic nonepileptic seizures.\textsuperscript{24,25} Fewer patients with psychogenic seizures and subjective variation in assessment could attribute to lack of detection in our cases.

We had fewer adolescents as the sample was not uniformly distributed. The results do not represent actual incidence of PNEs in general population as this study was from a tertiary care clinic. We were not able to identify psychological co-morbidities in patients with psychogenic seizures probably due to small sample size and lack of control group to compare CBCL results.

Mimickers of epilepsy are common and diverse in children. Misdiagnosis often results in unnecessary treatment, further causing undue psychological and financial stress to the child’s family. Improving awareness among health-care professionals is crucial for early identification, referrals to specialists, and appropriate treatment. Further multi-centric studies on characteristics, diagnostic clues, management strategies, and outcomes of children with PNEs are needed for optimum care.

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Conflicts of interest
There are no conflicts of interest.

References
1. Benbadis S. The differential diagnosis of epilepsy: a critical review. Epilepsy Behav 2009;15:15-21.
2. Scheepers B, Clough P, Pickles C. The misdiagnosis of epilepsy: findings of a population study. Seizure 1998;7:403-6.
3. Desai P, Talwar D. Nonepileptic events in normal and neurologically handicapped children: a video-EEG study. Pediatr Neurol 1992;8:127-9.
4. Kotagal P, Costa M, Wyllie E, Wolgammuth B. Paroxysmal nonepileptic events in children and adolescents. Pediatrics 2002;110:e46.
5. Park EG, Lee J, Lee BL, Lee M, Lee J. Paroxysmal nonepileptic events in pediatric patients. Epilepsy Behav 2015;48:83-7.
6. Kurtluay E, Selwa L, Minecan D, Edwards J, Beydoun A. Nonepileptic paroxysmal events in a pediatric population. Epilepsy Behav 2010;17:272-5.
7. Bye AM, Kok DJ, Ferenschild FT, Vles JS. Paroxysmal non-epileptic events in children: a retrospective study over a period of 10 years. J Paediatr Child Health 2000;36:244-8.
8. Uldall P, Alving J, Hansen LK, Kiback M, Buchholt J. The misdiagnosis of epilepsy in children admitted to a tertiary epilepsy centre with paroxysmal events. Arch Dis Child 2006;91:219-21.
9. Yılmaz Ü, Serdaroğlu A, Gürkaş E, Hirfanoğlu T, Cansu A. Childhood paroxysmal nonepileptic events. Epilepsy Behav 2013;27:124-9.
10. Smith D, Defalla BA, Chadwick DW. The misdiagnosis of epilepsy and the management of refractory epilepsy in a specialist clinic. QJM 1999;92:15-23.
11. Wyllie E, Glazer JP, Benbadis S, Kotagal P, Wolgammuth B. Psychiatric features of children and adolescents with pseudoseizures. Arch Pediatr Adolesc Med 1999;153:244-8.
12. Benbadis SR, O’Neill E, Tatum WO, Heriaud L. Outcome of prolonged video-EEG monitoring at a typical referral epilepsy center. Epilepsia 2004;45:1150-3.
13. Kramar U, Carmant L, Riviello JJ, Stauffer A, Helmers SL, Mikati MA, et al. Psychogenic seizures: video telemetry observations in 27 patients. Pediatr Neurol 1995;12:39-41.
14. Prasad M, Babiker MO. Fifteen-minute consultation: when is a seizure not a seizure? Part 1, the younger child. Arch Dis Child Educ Pract Ed 2016;101:15-20.
15. Babiker MO, Prasad M. Fifteen-minute consultation: when is a seizure not a seizure? Part 2, the older child. Arch Dis Child Educ Pract Ed 2015;100:295-300.
16. Hindley D, Ali A, Robson C. Diagnoses made in a secondary care “fits, faints, and funny turns” clinic. Arch Dis Child 2006;91:214-8.
17. Srikumar G, Bhatia M, Jain S, Maheshwari MC. Usefulness of short term video-EEG monitoring in children with frequent intractable episodes. Neurol India 2000;48:29-32.
18. Manni R, Terzaghi M, Repetto A. The FLEP scale in diagnosing nocturnal frontal lobe epilepsy, NREM and REM parasomnias: data from a tertiary sleep and epilepsy unit. Epilepsia 2008;49:1581-5.
19. Cuthill FM, Espie CA. Sensitivity and specificity of procedures for the differential diagnosis of epileptic and non-epileptic seizures: a systematic review. Seizure 2005;14:293-303.
20. Udani V, Bavdekar M, Karia S. Head up tilt test in the diagnosis of neurocardiogenic syncope in childhood and adolescence. Neurol India 2004;52:185-7.
21. Lewis DA, Dhala A. Syncope in the pediatric patient. The cardiologist’s perspective. Pediatr Clin North Am 1999;46:205-19.
22. Dang HM, Nguyen H, Weiss B. Incremental validity of the Child Behavior Checklist (CBCL) and the Strengths and Difficulties Questionnaire (SDQ) in Vietnam. Asian J Psychiatr 2017;29:96-100.
23. Capdevila OS, Dayyat E, Kheirandish-Gozal L, Gozal D. Prevalence of epileptiform activity in healthy children during sleep. Sleep Med 2008;9:303-9.
24. Reilly C, Menlove L, Fenton V, Das KB. Psychogenic nonepileptic seizures in children: a review. Epilepsia 2013;54:1715-24.
25. Diprose W, Sundram F, Menkes DB. Psychiatric comorbidity in psychogenic nonepileptic seizures compared with epilepsy. Epilepsy Behav 2016;56:123-30.