

Behavioral Problems in Indian Children with Epilepsy

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Objective: To assess prevalence of behavioral problems in children with epilepsy.

Methods: This was a cross-sectional study of children with epilepsy, and normal controls enrolled between July 2013 to June 2015. Child Behavior Checklist (CBCL) was used as a tool to assess the behavior based on parents reported observation.

Results: There were 60 children with epilepsy in 2-5 years and 80 in 6-14 years age groups, and 74 and 83 unaffected controls, respectively. Mean CBCL scores for most of the domains in children of both age groups were significantly higher than controls. Clinical range abnormalities were mainly detected in externalizing

domain (23.3%) in 2-5 years, and in both internalizing (21.2%) and externalizing (45%) domains in children of 6-14 years. Younger age of onset, frequency of seizures and duration of disease had significant correlation with behavioral problems in both the age groups. Antiepileptic drug polytherapy was significantly associated with internalizing problems in older children.

Conclusion: Age at onset, frequency of seizures and duration of disease were found to be significantly associated with occurrence of behavioral problems.

Keywords: Child behavior checklist, Co-morbidity, Outcome.

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Children with epilepsy suffer from symptoms of disease, effect of therapy, risk of recurrence, impairment of brain function and development of behavioral problems [1]. Psychopathology has been reported to be associated with epilepsy [2,3]. Psychiatric disorders can occur in 50-60% of patients with epilepsy [4], and behavioral co-morbidities to the tune of 43% of cases [5]. Previous studies have reported that these children have problems of attention, hyperkinesias, thought, low self-esteem, anxiety and depression [6-10]. Further, cognitive and behavioral impairments can even occur following a single seizure, and antiepileptic drugs may also alter behavior to some extent [11].

Previous studies done in children with epilepsy have addressed a mixed age group (4-16 years) and shown variable results in different domains [12, 13]; using child behavior checklist (CBCL), a well standardized tool for detection of behavioral problems in epilepsy [14,15]. In the present study, we have assessed behavioral problems in two separate age groups (2-5 and 6-14 years) using standard CBCL tool for each group and have tried to find out the differences in pattern of occurrence of behavioral problems. Additionally, factors associated with development of these problems were also analyzed in both younger and older age groups.

METHODS

This was a cross-sectional study conducted on children with epilepsy who were recruited from the Epilepsy Clinic and/ or Out Patient Department (OPD) at Institute of Medical Sciences, Banaras Hindu University, Varanasi. Purposive sampling method was used for the selection of cases during the period of July 1, 2013 to June 30, 2015. The protocol of the study was approved by institutional ethical committee, and informed consent was obtained from the parents or authorized representative of each child.

Children of 2-14 years age group of both gender having idiopathic epilepsy, defined as history of occurrence of 2 or more episodes of unprovoked focal or generalized seizures having normal cranial CT/MRI scan and normal/ abnormal electroencephalogram (EEG) [16]. Controls were recruited from the OPD of Pediatrics who came for their routine health check-up and were found healthy, and they belonged to similar age group as of patients with epilepsy. *Exclusion criteria:* Patients with the diagnosis of symptomatic epilepsy syndromes, epileptic encephalopathy, febrile seizures, cerebral palsy, developmental delay, mental retardation, neurodegenerative and metabolic disorders, neurotuberculosis, and neurocysticercosis were excluded from the study.

Developmental delay was labelled on the basis of history and developmental assessment, and Binet-Kulshrestha Intelligence Scale was used for intelligent quotient (IQ) assessment in all cases. Moderate and severe developmental delay/mental retardation cases were excluded. Detailed information regarding age of onset, types of seizures (partial/generalized), frequency, duration of disease, antiepileptic medications, compliance to treatment, control of seizures and family history were recorded. The IQ was categorized as average when score was ranging between 90-109 and below average when it was between 75-89. The frequency of seizure was defined as per Sabbagh, *et al.* [17]. All patients were receiving antiepileptic drugs (phenytoin sodium/ sodium valproate/ carbamazepine/ clobazam) either as monotherapy or in combinations of two or three. Children who were admitted for acute control of seizures were assessed once it was controlled and they were discharged from the hospital. Controlled seizure was defined as cases who were seizure free for at least 6 months before assessment and those who had recurrence of seizures despite antiepileptic medications were considered as uncontrolled seizure. Revised Kuppaswamy scale was [18] was used for the assessment of socio-economic status.

Assessment for behavioral problems was done by a clinical psychologist. The native language of the study population was Hindi and the questions were translated from English version of CBCL by a language expert, and same questions were asked to each parent/caregiver and also to those who could not read, and the responses were recorded in the three-point scale of the Achenbach CBCL [19]. The CBCL (2001 version) included 100 items for 2-5 years age-group and 113 for 6-14 years age-group, and parents reported inventory was used for the study. Parents rated their child's behavior on a three-point Likert scales: 0 (not true), 1 (somewhat or sometimes true), and 2 (very true or often true) and took 30-45 min to complete. The scale has standardized normative scores for age and gender encompassing behavioral dimensions such as emotionally reactivity, anxious/depressed, somatic complaints, withdrawn, sleep problems, attention problems, and aggressive behavior in 2 to 5 year age group; and anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule breaking and aggressive behavior problems in the age group of 6-14 years. It also provided a total behavior problem score and two second-order factor scores for internalizing problems (emotionally reactive, anxious/depressed, somatic complaints, withdrawn and sleep problems) and externalizing behavior (attention problems and

aggressive behavior in younger age group and rule breaking and aggressive behavior in older children). Counseling was provided to children and families having clinical range abnormalities, and non-responders were referred to psychiatrist for pharmacotherapy.

Statistical analysis: Data were analyzed using SPSS software version 16.0 (Chicago, IL, USA). Student's *t*-test was used to compare the observations of patients with controls. Chi-square test was applied for comparisons of data of proportions. Yates correction was done wherever required and relative prevalence with confidence intervals were also calculated. Pearson's correlation coefficients were calculated for the factors such as age of onset, frequency of seizure and duration of disease and Spearman's correlation coefficient for antiepileptic drug polytherapy with the development of behavioral problems. A *P* value of <0.05 was considered as statistically significant.

RESULTS

A total of 140 children with epilepsy and 157 healthy controls in a similar age group were enrolled (**Fig. 1**), and were further sub-divided into two age-groups: 2-5 years (60 epilepsy and 74 controls) and 6-14 years (80 epilepsy and 83 controls). The mean (SD) age of onset of disease was 2.6 (1.8) years and 4.9 (2.3) years in 2-5 and 6-14 years age-group, respectively. There were 41 males in 2-5 years and 51 in 6-14 years age-groups in cases with epilepsy. In 2-5 years age group, 31(51.7%) received sodium valproate, 10 (16.7%) phenytoin sodium and 19 (31.7%) cases drugs in combinations (levetiracetam, carbamazepine/oxcarbamazepine, clobazam); The corresponding figures in 6-14 years age-group were 45 (56.2%), 10 (12.5%) and 25 (31.3%), respectively.

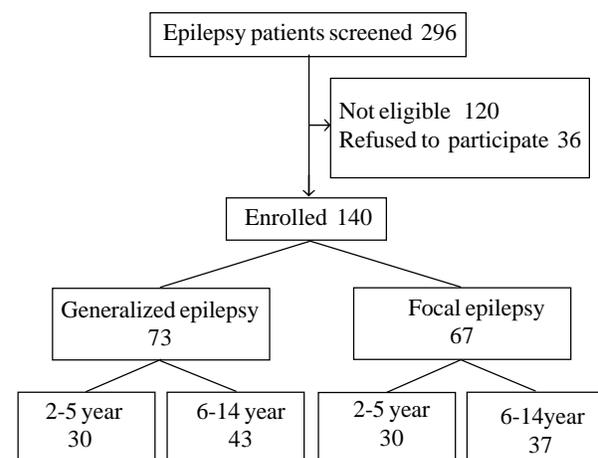


FIG. 1 Details of enrolment of the children with epilepsy.

There were no significant differences as regard to total behavioral problems between children on monotherapy as compared to polytherapy in both younger (10.5% vs 17.1%, $P=0.35$) as well as older age groups (35% vs 41.5%, $P=0.41$), respectively. A relatively higher percentage of children with below average IQ had total behavioral problems in comparison to those who had average IQ in both younger (18.6% vs 13.6%, $P=0.96$, relative prevalence (RP) 1.15, confidence interval (CI) 0.25- 5.30) as well as older age group (49% vs 34%, $P=0.15$, RP 1.03, CI 0.39-2.75), but the differences were found to be insignificant.

Thirty nine (65%) children in 2- 5 years group and 44 (55%) in 6-14 years had controlled seizures and the rest had uncontrolled seizures at the time of assessment. In younger age-group, there was no significant difference in the occurrence of behavior problems between children with controlled and uncontrolled seizures (2.5% vs 9.5%, $P=0.25$, RP 0.18, CI 0.48-12.37). However, in the older age group, children with uncontrolled seizures had higher incidence of behavior problems than children with controlled seizures (50% vs 18.1%, $P=0.003$; RP 2.44, CI 0.07-0.50). None of the parents of cases had any history of psychological problems. No significant differences in mean values of different domains were found in children on monotherapy *versus* polytherapy in both age groups. However, in the 6-14 years age-group, uncontrolled seizures were significantly ($P<0.05$) associated with internalizing behavioural problems.

Mean values of behavioral scores in patients with epilepsy aged 2-5 years were significantly higher as compared to control in the CBCL domains of emotional reactivity ($P=0.021$), withdrawn ($P=0.004$), attention problems ($P<0.001$), aggressive behavior ($P<0.001$), externalizing ($P<0.001$) and total behavior problems ($P<0.001$) (**Table I**). In the 6-14 years age group, all the domains showed significantly higher scores in patients than controls, except somatic complaints and thought problems (**Table II**). Further, 23.3% children with epilepsy of 2-5 years had externalizing behavior scores, and 21.2% and 45% of 6-14 years had internalizing and externalizing behavior scores in the clinical range, respectively (**Fig. 2**).

Age of onset of seizure had negative correlations with total behavior problems ($r= -0.289$, $P<0.05$) in 2- 5 years, and with internalizing ($r= -0.230$, $P<0.05$), externalizing ($r= -0.243$, $P<0.05$) and total behavior problems ($r= -0.339$, $P<0.01$) in 6-14 age groups. Frequency of seizure had positive correlations with externalizing ($r=0.41$) and total behavior problems ($r=0.37$) in younger age-group, and also in older age-group older ($r= 0.251$ and 0.410 ,

respectively). Duration of disease had positive correlations with internalizing behavior problems in both younger ($r= 0.307$) and older age groups ($r= 0.251$). Further, in older children, significant positive correlations were found for antiepileptic drug polytherapy ($r= 0.293$) with internalizing behavior problems.

DISCUSSION

In the present study, most of the behavior domains in children with epilepsy had higher mean scores than controls, but below the cut-off levels. Externalizing behavioral problems appeared to affect patients of both the age-groups, but internalizing behavior such as depression and anxiety were mostly limited to school-age children.

TABLE I CBCL T SCORES IN CONTROLS AND CHILDREN WITH EPILEPSY IN 2-5 YEARS-AGE GROUP

Domains	Controls(n=74)	Epilepsy(n=60)
†Emotionally reactive	53.4 (5.0)	55.5 (5.0)
Anxious/depressed	52.8 (3.5)	52.5 (3.4)
Somatic complaints	51.1 (3.2)	50.7 (2.5)
#Withdrawn	51.2 (3.2)	53.6 (5.9)
Sleep problems	50.6 (1.4)	50.9 (2.1)
*Attention problems	54.6 (5.1)	61.2 (6.2)
*Aggressive behavior	54.3 (4.3)	59.5 (6.7)
Internalizing problems	45.7 (7.6)	48.1 (7.6)
*Externalizing problems	51.4 (7.6)	60.2 (5.5)
*Total behavior problems	48.3 (9.1)	53.0 (5.5)

All values in mean (SD); * $P<0.001$; # $P=0.004$; † $P=0.021$.

TABLE II CBCL T SCORES IN CONTROLS AND CHILDREN WITH EPILEPSY IN 6-14 YEARS AGE-GROUP

Domains	Controls (n=82)	Epilepsy (n=80)	P value
Anxious/depressed	50.3 (2.4)	53.9 (5.7)	<0.001
Withdrawn/depressed	55.2 (5.2)	58.6 (8.6)	0.003
Somatic complaints	56.7 (6.4)	55.8 (7.2)	0.788
Social problems	53.7 (3.7)	57.2 (5.7)	<0.001
Thought problems	50.8 (2.3)	51.0 (3.6)	0.622
Attention problems	53.5 (3.9)	57.6 (6.0)	<0.001
Rule breaking behavior	53.4 (5.2)	55.1 (5.8)	0.021
Aggressive behavior	58.9 (7.9)	65.9 (9.6)	0.001
Internalizing problems	49.4 (7.6)	53.9 (10.1)	0.002
Externalizing problems	56.3 (7.1)	61.9 (8.5)	<0.001
Total behavior problems	50.9 (6.2)	56.6 (7.8)	<0.001

All values mean (SD).

WHAT IS ALREADY KNOWN?

- Children with epilepsy can develop behavioral problems in various domains.

WHAT THIS STUDY ADDS?

- Behavioral co-morbidities differ in children with epilepsy in different age-groups, with affection of externalizing behavior in younger children and both internalizing and externalizing behavior in older age-group.

Impaired attention, anxiety, depression, hyperkinetic, impulsivity, low self-esteem and thought problems are some of the co-morbidities reported earlier, mostly in mixed age-group of children [5-7,9]. In addition, educational underachievement has been also observed in these children [20]. Behavior problems may not only occur following idiopathic epilepsy but also due to secondary causes like neurocysticercosis [21]. Abnormal excitability and disrupted synaptic plasticity in the developing brain can result in epilepsy and subsequently behavior problems in these patients [22].

We did not observe any difference in the incidence of behavioral problems in children with below average IQ in comparison to cases with average IQ in both the age groups. It may be possible that effect of IQ was not distinctly seen because of lesser number of cases in the sub-groups. In contrast, Buelow, *et al.* [23] observed a higher risk of occurrence and mean problem scores in cases with low IQ as compared to patients having middle or high IQ groups, and all types of problems were found in children with low IQ. Similar to our findings, Powell, *et al.* [24] also observed no significant difference in behavior between children with epilepsy having decreased seizure-frequency as compared to those with good seizure-control.

A significant effect of age of onset, frequency of seizures and number of antiepileptic drugs in relation to behavioral problems have been reported earlier [5,10,17]. We found younger age of onset, and frequency of seizures were significantly associated with behavioral problems. In addition, duration of disease in both age groups and anti-epileptic drugs in older children also affected the internalizing problems. However, no difference in behavioural problems was observed between mono and polytherapy. In contrast, effect of polytherapy over behavioural problems was found by Datta, *et al.* [25] in their patients with epilepsy. It appears that multiple factors affect the behavioral domains in children with epilepsy. Further, it is likely that the child's psychological perception of the disease situation, especially in older children, could be another contributing factor to the patient's behavior during the course of illness. Thus, use of minimum number of anti-epileptic drugs for seizure-control should be aimed, to minimize the occurrence of behavioral impairment in these children.

The strength of the present study is the use of a standardized validated measurement tool, applied in two age-groups of population to observe the different behavioral pattern. However, it has certain limitations as findings are based only on parent-reported observations. We did not observe the effect of parental educational level and teacher-report of school-going children, which may limit the generalizability of the results up to some extent. Further, it would be also be pertinent to carry out follow-up assessments to document resolution of problems after discontinuation of treatment.

In conclusion, due attention should be given for recognition of behavioral co-morbidities in children with epilepsy. They need periodic assessment during epilepsy treatment and if abnormalities are detected, may need counseling and also adjustment on behalf of parents.

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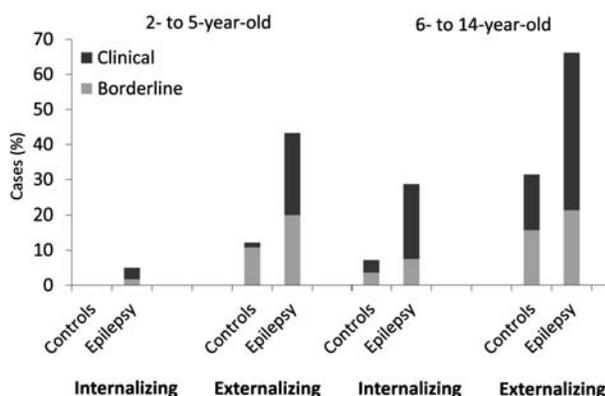


FIG. 2 Internalizing and externalizing behavioral problems in 2-5 and 6-14 years age-groups in controls and children with epilepsy.

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