

# Study of prevalence of epilepsy and its co morbidities in children with learning disabilities (LD)

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## Abstract

**Introduction:** There is higher association of learning disability (LD) in children with epilepsy. The study was done to find out the prevalence of epilepsy in children with learning disabilities and to examine the seizure factors and side effects of antiepileptic medications that place children at a higher risk of association with Learning Disability. **Methodology:** In this observational cross-sectional study, children of age group 8yr-15yr who were diagnosed as learning disabled on the basis of a comprehensive developmental, psycho-educational evaluation by the expert panel were enrolled randomly and evaluated for epilepsy. Study population of learning disabled children was divided in two groups-those with epilepsy and without epilepsy. Seizure variables like seizure control, seizure type, cause of seizure, medication status, age of onset, drugs, monotherapy v/s polytherapy were studied among these two groups. **Results:** Prevalence of epilepsy in children with LD was found to be 18%. A significant association of pregnancy related complications ( $p=0.009, df=2$ ), birth asphyxia ( $p=0.031, df=1$ ), neonatal seizures ( $p=0.031, df=1$ ) and meningitis ( $p=0.031, df=1$ ) was found in children diagnosed to have LD with epilepsy. Higher occurrence of gross ( $p=0.002, df=1$ ) and fine motor ( $p=0.031, df=1$ ) developmental delay and significantly lower IQ was found in children with LD & epilepsy, compared to children with only LD. **Conclusion:** Concurrence of epilepsy in learning disabled children puts them at higher risk for further academic problems. Epileptic seizures and various side effects of antiepileptic medications may affect the cognitive function. Referral for evaluation of LD must be advised in those epileptic children who have academic difficulties.

**Keywords:** Epilepsy in children, Dyslexia, Antiepileptic medications, Epilepsy comorbidities

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## Introduction

Learning Disability (LD) affects about 2-10% of the school-age population. They are characterized by an academic functioning that is below the level that would be expected at their age, Intelligent Quotient (IQ) and grade level in school, and interfere significantly with academic performances or daily life activities that require reading, writing or calculation skills [1]. Epilepsy is the most common serious neurological disorder affecting 0.5% of population. Up to fourth of patients with epilepsy are said to have LD and conversely, up to half of all patients with LD are said to have seizure disorder [2]. The prevalence rate of epilepsy amongst people with learning disabilities has

been reported as at least twenty times higher than for the general population, with seizures commonly multiple and resistant to drug treatment [3]. Symptomatic epilepsy secondary to organic brain lesions usually causes permanent impairment of learning while some epilepsy can cause temporary or state related cognitive impairment. The impaired learning in epileptic patients could be secondary to subclinical seizures, frequent electrical epileptiform discharges, behavioral and psychological issues related to the seizures. Cognitive and behavioral side effects of various antiepileptic drugs also may cause additional learning problems. There are certain genetic syndromes, metabolic disorders and neurocutaneous syndromes that may have learning disorder and epilepsy co-existent [2]. This study aimed to study prevalence of epilepsy as co

Manuscript received: 2<sup>nd</sup> April 2016  
Reviewed: 11<sup>th</sup> April 2016  
Author Corrected: 24<sup>th</sup> April 2016  
Accepted for Publication: 9<sup>th</sup> May 2016

morbidity to LD. It also studies the seizure factors that might place children at a higher risk for LD and implications of seizure therapy on the severity of LD.

## Methodology

This hospital based observational cross-sectional study was carried out in a tertiary care centre attached to a medical college, in Mumbai over a period of 18 months, after obtaining permission from the Institutional Ethics Committee. Children between the ages of 8 and 15 years, certified as having Learning Disability were included after obtaining the consent & informed assent where applicable. The study excluded children with Visual handicap (>60%); Hearing handicap (>60%); Physical handicap (e.g. Cerebral palsy), Febrile seizures, chronic physical illnesses (e.g., diabetes, asthma, cystic fibrosis); Borderline intellectual functioning and mental retardation (a measured IQ in the mental deficiency range on a full IQ test).

The sample size was calculated with Medcalc software V.11.3.3.0 with type I error (alpha) of 0.05 and type II error of 0.20. The minimum sample size came out to be 39. Hence we took a sample size of 50 for our study. The cases were selected with the help of computer generated Random Number Table.

The children participated in the study were diagnosed as learning disabled on the basis of a comprehensive developmental, psycho-educational evaluation at the medical centre by a team of experts including pediatricians, psychiatrists, psychologists and occupational therapists. A standard psycho-educational battery which includes tests of academic excellence (e.g. Woodcock Johnson test or WRAT) and tests of intelligence (e.g. WISC) were performed to aid the diagnosis [4]. The diagnosis of co morbidities was

## Results

In this observational study, among 50 children diagnosed with learning disabilities 9 (18%) had epilepsy, 41 (82%) had no epilepsy. Thus, the prevalence of epilepsy in children with LD in the study was found to be 18%. The mean age of children presenting for evaluation and diagnosed to have learning disability along with epilepsy was 12.22 years (SD of 1.72 years).

Among the 9 children diagnosed to have LD and epilepsy, 5 (55.6%) were males, 4 (44.4%) were females. The male to female ratio was 1.25:1.

In epilepsy group, 2 (4%) had complex partial type of seizures (CPS) and 7 (14%) had generalized tonic clonic type of seizures (GTC). The mean age at onset of seizures is 30.44 months (SD of 16.8 months). The earliest age at diagnosis was 4 months. The age of seizure onset was found to be much earlier (27.2 months) in those who had all three subtypes of learning disability as compared to those who had only two subtypes of LD.

confirmed by the consultant pediatricians and psychiatrists. All children were evaluated for vision and hearing defects. The assessment of children comprising of a detailed history and detailed clinical and neurological examination was carried out. Investigations as electroencephalograms (EEG), neuroimaging (magnetic resonance imaging-MRI or computerized tomography-CT) were carried out wherever required.

Seizure variables consisted of seizure control, seizure semiology and type, seizure etiology, medication status, age of onset, and current age. Cause of the seizures was determined and grouped as Structural, Metabolic, Cerebral dysfunction, post-infectious, post-traumatic and as undetermined. Medication status was dichotomized into presence or absence of polytherapy.

Complete data from all the case record forms was entered in a Master-chart in MS-EXCEL format for analysis. Qualitative Data (or Descriptive data) was represented in form of frequency and percentage. Association between qualitative variables was assessed by Chi-Square test with continuity correction for all 2x2 tables and with or without continuity correction in rest and Fisher's Exact test for all 2x2 tables where P-value of Chi-Square test was not valid due to small counts.

Quantitative Data was represented using Mean  $\pm$  Standard deviation and Median & inter quartile range. Relationship between quantitative data was assessed using Pearson's correlation if data passed 'Normality test' and by Spearman's correlation if data failed 'Normality test'. For analysis of predictiveness of different independent factors responsible for a particular outcome, correlation regression analysis was used for finding out possible statistical significance.

Comparison of Academic Difficulties faced by learning disabled children with epilepsy v/s without epilepsy was done. There was no significant difference found in the occurrence of difficulty in writing or math in learning disabled children with epilepsy. However, difficulty in reading was found to be significantly lower in these children (77.8%) compared to those without epilepsy (100%). This could probably be accounted for by the fact that epilepsy per se and the anti-epileptic drugs cause difficulty in motor issues, suggesting that epileptics may not have overt reading problems and this can be picked up only on psycho educational testing.

The study found a significant association of pregnancy related complications ( $p=0.009, df=2$ ), birth asphyxia ( $p=0.031, df=1$ ), neonatal seizures ( $p=0.031, df=1$ ) and meningitis ( $p=0.031, df=1$ ) in children diagnosed to have LD with epilepsy. This reaffirms the role of perinatal insult in developmental learning disabilities and epilepsy.

Higher occurrence of gross ( $p=0.002, df=1$ ) and fine motor ( $p=0.031, df=1$ ) developmental delay was found in epileptic children with learning disability. No significant difference in speech and language delay was found in the two groups. The presence of epilepsy and its treatment is known to cause greater delay in motor milestones than higher functions.

Out of the 9 children with Epilepsy and LD, 5 (55.6%) had no co-morbidities, 2 (22.2%) had Attention deficit disorder (ADD), 2 (22.2%) had attention deficit and hyperactivity disorder (ADHD). Out of the 41 children without Epilepsy with LD, 33 (80.5%) had no co-morbidities, 2 (4.9%) had ADD, 6 (14.6%) had ADHD. Co-morbidities- ADHD and ADD were found to be equally occurring in both the groups.

Of the 9 children, 1 had active seizure and rest were controlled, 3 were on polytherapy, 6 were on monotherapy. In the study, 6 of 9 children received monotherapy and all of them had generalized epilepsy. Two children with partial epilepsy and one with generalized epilepsy were on polytherapy.

All 3 children with polytherapy had all 3 subtypes of LD- dyslexia, dysgraphia, dyscalculia. IQ scores were found to be significantly lower in children with epilepsy associated with LD compared to children with only LD. (Table 1). All 3 children on polytherapy had their IQ scores (80-90), whereas of 6 children on monotherapy, 2 (80-90), 2 (91-110), 1 (111-120) and 1 (above 120).

There was no difference in the IQ scores of children on polytherapy or on monotherapy. There was significant difference in the mean of the SD of the achievement scores in the areas of Broad Reading, Broad Mathematics and Broad Writing between those learning disabled children with epilepsy on polytherapy compared to those on monotherapy.(Table 2)

**Table-1 Comparison of IQ scores between Epileptic and Non epileptic children with LD.**

IQ		Seizure		Total
		Present	Absent	
80 to 90	Count	5	2	7
	Percent	55.6%	4.9%	14.0%
91 to 110	Count	2	0	2
	Percent	22.2%	0.0%	4.0%
111 to 120	Count	1	24	25
	Percent	11.1%	58.5%	50.0%
Above 120	Count	1	15	16
	Percent	11.1%	36.6%	32.0%
Total	Count	9	41	50
	Percent	100.0%	100.0%	100.0%

Chi-Square test	Value	df	P Value	Association is
Pearson Chi-Square	27.470	3	0.000	Significant

**Table 2: Comparison of SD of achievement scores in LD with epilepsy on polytherapy vs monotherapy:**

SD between Potential and Achievement scores	Broad Reading	Broad Mathematics	Broad Writing
Polytherapy	4	3.62	4.56
Polytherapy	4.43	3.86	4.48
Polytherapy	4.5	3.8	4.36
Monotherapy	2.62	2.86	3.12
Monotherapy	2.48	2.94	3.24
Monotherapy	2.12	2.8	3.36
Monotherapy	2.06	2.82	3.42
Monotherapy	2.12	2.96	3.28
Monotherapy	2.34	2.36	3.12

Group Name	Number	Mean	Std Dev	Unpaired T test	P Value
Poly	3	4.31	0.271	11.87	0.00001
Mono	6	2.29	0.227	Diff is Significant	

There is significant difference in the mean of the SD of the achievement scores in the areas of Broad Reading, Broad Mathematics and Broad Writing between those learning disabled children with epilepsy on polytherapy compared to those on monotherapy.

## Discussion

Existence of epilepsy and learning disability as co-morbidities is not surprising, as both can be accounted for by aberrations in the central nervous system, which affect cognitive functions. The prevalence of epilepsy among children with learning disabilities in our study was found to be 18%, which is quite similar to that found in a study by Ramaa S (2002), wherein the prevalence of epilepsy was estimated to lie between 15 and 30% among people with learning disabilities [5]. The male to female ratio found in this study was 1.17:1. The mean age at diagnosis of LD was 11.82 years. In a study conducted by Karande et al in 2004, the mean age at diagnosis was found to be 11.4 years and male to female ratio was 2.3:1 [6]. In another study conducted by Huang et al in Taiwan in 2007, the mean age at diagnosis was 9.6 years with a male to female ratio of 5.8:1 [7]. A higher mean age at diagnosis in our study points toward a delay in referral. Our study showed that presence or absence of epilepsy in children with learning disability did not affect the age of presentation to LD OPD for evaluation and diagnosis of LD. Pregnancy related complications likely to affect the developing foetal brain putting the child at higher risk not only to develop epilepsy in future, but also probably learning disability as a co-morbidity. Studies by Karande et al have shown that prematurity, instrumentation and procedures during course of delivery increase the risk of occurrence of specific learning disabilities [8]. A longitudinal cohort study

conducted by Chaudhari et al, showed significantly higher percentage of mathematical and writing learning disabilities in low birth weight children [9]. A strong association between birth asphyxia, neonatal seizures and epilepsy in later life is well established. Our study further established the co-existence of LD in 11.1 % of such children. NICU stay and neonatal jaundice has definitively proven role in the causation of learning disabilities in children as observed in studies by Resnick et al, their role in causing co-existent epilepsy as well needs further evaluation[10].

Seizure type and epileptic syndrome have not been significantly related to achievement in most studies of children without mental retardation [11]. Children with early age of onset of epilepsy, would have longer duration of disorder and therapy with anti-epileptic drugs, leading to greater cognitive difficulties [11]. The same study showed higher incidence of learning problems in children with lesional / symptomatic syndromes vs idiopathic/cryptogenic. This study found higher incidence of LD in children with idiopathic epilepsy, compared to lesional or meningitis. IQ scores were found to be significantly lower in children with epilepsy associated with LD compared to children with only LD. Presence of epilepsy definitely affects the performance and verbal IQs and worsens the LD as was also observed in the psychoeducational tests for achievement in these children. Cognitive impairment is

a frequently occurring secondary consequence of epilepsy probably secondary to ictal and interictal cortical dysfunction [12]. Though the exact cause of lower IQ scores have not been explored fully, but three factors that may be involved are- etiology, the seizures type and the central side effects of the drug treatment. Memory impairments, mental slowing, and attention deficits are the most frequently reported cognitive problems [13]. For some children frequent seizures and medical investigations may result in many days of missed school that in itself will compromise learning. Some common side effects of antiepileptics that can have an impact on learning are drowsiness and unsteadiness, difficulties in alertness and attention, slowing of mental processing, slowing of fine motor and visual motor speed,- difficulties in mood and behavior . Although there was no statistical difference in the IQ scores within these two groups of LD children, we found that children on monotherapy did have higher IQ scores and to definitively establish this fact, cross-sectional studies with larger sample size are required. Most of the children on polytherapy in our study were receiving Phenobarbitone or Carbamazepine as part of the combination therapy. We found greater deviation in the achievement from their expected potential, in those children who were on carbamazepine and/ or phenobarbitone being used as one of the drugs in combination with others. Better achievement scores were obtained in children who were on valparin or phenytoin as monotherapy. Studies involving children with epilepsy by Farwell et al, Camfield et al have linked use of Phenobarbitone to lower IQ(mainly affecting non-verbal) scores and its discontinuation can improve total IQ [14]. Some studies suggest carbamazepine leads to deterioration of IQ and deterioration in measures of information processing speed and attention [15]. A number of studies have indicated that valproate exerts little detrimental impact on cognitive function [16].

There was significant difference in the mean of the SD of the achievement scores in the areas of Broad Reading, Broad Mathematics and Broad Writing between those learning disabled children with epilepsy on polytherapy compared to those on monotherapy. Polypharmacy shows a relatively severe impact on cognitive function when compared with monotherapy, irrespective of the type of AEDs included. Two drugs that individually have mild cognitive effects may induce serious cognitive impairment when used together, possibly because of potentiation of tolerability problems[16].

ADHD is a known co-morbid condition that goes hand in hand with both learning disability and epilepsy individually. Many children with LD or epilepsy develop secondary inattention and behavioural difficulties.

The two disorders occur simultaneously in 12% to 24% of individuals with dyslexia [17]. When we studied their incidence in two study groups, no significant difference was found in the occurrence of these co-morbidities in children diagnosed to have LD with or without epilepsy.

There are a few limitations of this study. In settings of a clinic, there could have been a referral bias. Also, some of the data like birth history and developmental history depended on memory of the parents which could have led to memory bias. A relatively smaller sample size limited the use of statistical analysis to validate the observations. Nevertheless, we believe the findings are important since few children in India get evaluated for specific learning disabilities. Moreover, data from India is lacking but the awareness is increasing. Limited research is available on the association of epilepsy and learning disabilities. The implications of this study need to be determined by future studies.

## Conclusion

There is definitely higher association of learning disability in children with epilepsy. Severity of cognitive side effects in antiepileptics may seem mild but may be amplified in specific conditions and become substantial in patients when crucial functions are involved such as learning, or when functions are already impaired in vulnerable patients such as in those with polytherapy, ADD or other major risk factors that impair the normal brain function and contribute to an impact on daily life functioning. Such consequences are more debilitating for the child than the seizures themselves. Hence it is worthwhile to evaluate and diagnose them for learning disabilities as early as possible and institute early remedial education.

**Acknowledgements:** Authors thank Dr. Sandeep Bavdekar, Professor and Head, Department of Pediatrics, T.N. Medical College and B.Y.L. Nair Hospital, Mumbai and to the Dean, TN Medical College and BYL Nair Hospital, Mumbai for permission to publish the manuscript.

**Funding:** Nil, **Conflict of interest:** Nil

**Permission from IRB:** Yes

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## How to cite this article?

Rathi S, Dr Kondekar A, Mandadi M, Shah H, Kondekar S. Study of prevalence of epilepsy and its co morbidities in children with learning disabilities (LD). *Int J Pediatr Res* 2016;3(5):323-328.doi:10.17511/ijpr.2016.i05.09